

# SIRS Model For The Dynamics Of Non-Typhoidal Salmonella Epidemics

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## ABSTRACT:

A continuous mathematical model of salmonella diarrhea is introduced in this paper. According to the pathogenesis of salmonella, the model had been designed as an SIRS system comprising of a non-constant population. The disease-free state and the basic reproduction number ( $R_0$ ) have been computed for this system. In epidemics, there are always two cases:  $R_0 < 1$  (disease-free state) and  $R_0 > 1$  (epidemic existing state). Simulations of the system have been presented for both these cases which show the variations of the population in different situations. Data that has been used for examples and simulations is based on the demographics and disease outbreaks in Botswana.

**KEYWORDS:** Salmonella, Salmonellosis, Diarrhea, Mathematical Modeling, Epidemics, Epidemic Modeling, Basic Reproduction Number

## I. INTRODUCTION

In the context of global health, the repeated threats presented by infectious diseases cannot be disregarded. It has been recorded that in 2008, infectious diseases accounted for about 16% of deaths worldwide [23]. Infectious diseases are also known as transmissible diseases and as the name suggests, these diseases can be transmitted throughout a certain population. Considering a closed population, the introduction of an infective individual or an external vector can result in the spread of an infectious disease within the population [1]. Examples of external vectors include water, air, body fluids or biological vectors which carry infectious agents such as protozoa, bacteria or virus. Among many other communicable diseases, water related diseases occupy a significant position as water is essential to life and many diseases can easily be transmitted through water. Direct or indirect ingestion of contaminated water containing pathogenic micro-organisms can cause the spread of numerous infectious diseases.

### 1.1. Diarrhea – global and national burden

Diarrhea is one of the most common infectious diseases that is transmitted through contaminated water. The WHO (World Health Organization) estimates that there are about 1.7 billion diarrhea cases per year around world-wide [2]. Diarrhea is listed as the second leading cause of mortality in children causing around 700000 child deaths per year, with children under five at higher risks of getting severe diarrhea [2]. Although a land-locked country, Botswana has predominant water bodies which contribute to the transmission of infectious diseases to a noteworthy extent. Since their daily routine is very closely related to the natural water reservoirs, the inhabitants of the areas containing water bodies are very likely to catch the diseases and spread them as infected individuals. According to the health statistics of the country, there were about 15000 cases of diarrhea reported in 2012. Together with this, there were an approximate of about 200 deaths recorded due to diarrhea [3]. Other neighboring countries show similar statistics in relation to diarrhea. Zambia also faces about 15000 deaths annually due to diarrhea [24] and about 30% of child mortality in Namibia is ruled by diarrhea [25]. The situation was at extremes in Zimbabwe reporting approximately half a million diarrheal cases in 2012 [26]. This shows that necessary prevention and precaution methods need to be employed so as to avoid health hazards in Botswana.

### 1.2. Salmonellosis

Diarrhea is transmitted by several pathogens – virus, bacteria and protozoa.

There are many types of each pathogen that can cause diarrhea as a disease or can cause other diseases that result in diarrhea. Salmonella is a bacteria genus that is closely related to diarrhea. A specific serotype, Salmonella enteritis, causes salmonellosis which is a communicable intestinal infection. Common symptoms of salmonellosis include diarrhea, fever and abdominal cramps [4]. Extremes of age and immunosuppressive conditions act as high risk factors and thus small children and elderly people are more prone to diseases like salmonellosis [13]. Although the fecal–oral route plays a vital role in the transmission of the bacteria, there are certain foodstuffs that are considered to cause a large number of infections. On a global level, salmonella is the second most common pathogen causing diarrhea. Even in Botswana, salmonella occupies a noteworthy rank in the cause and spread of diarrhea. Based on research work at the National Health Laboratory in the country, it was concluded that Salmonella is one of the most common bacterial pathogens that causes diarrhea [5]. Thus, a system that incorporates the dynamics and transmission of salmonella diarrhea will prove to be of great advantage in combating diarrheal outbreaks in the country. It is envisaged that the system will act as a tool that will provide appropriate information as output results that can be used by the public health sectors to build up prevention strategies which will be employed in controlling bacterial transmission and hence disease outbreaks.

### **1.3. Overview of the model**

Epidemic modeling is a distinctive approach to understanding the disease dynamics. With the increasing threats of infectious diseases throughout the world, models depicting the respective transmission are becoming more important. These models are simply tools that are used to predict the infections mechanisms and future outbreaks of diseases. Although many treatment methods are employed across the globe to combat epidemics such as the diarrhea, many individuals fail to receive or respond to these methods. Thus, the epidemic models focus more on the prevention mechanisms. Various studies carried out in Botswana prove the importance of prevention. One of the most common and strong treatments of diarrhea is the oral rehydration salt (ORS) therapy. A research work in Botswana showed that a certain part of the population did not have the ORS. Out of the people who had ORS at their residence, only 74% of them had the knowledge about the preparation and usage. Therefore, while ORS was found out to be widely available, the expected result of successfully defeating the disease was not gained [27]. In such situations, prevention is highly recommended which can be obtained by exploiting the proposed model herewith. In the present study, a proposed model is portrayed which aims to reduce the transmission and occurrence of salmonellosis. The model describes the dynamics of the disease and is predictive in nature. Any probability of a future disease outbreak will be alerted using this model thus it will help in developing a prevention strategy. On completion, the structure will be incorporated into a system of active maps of the country such that the future prediction will be shown on the maps using graphics highlighting on the expected areas and time periods of infection. This feature will be greatly useful to the public health sector of Botswana as it will ensure that the necessary prevention methods are employed to prevent diarrheal outbreaks. A communication platform will also be included in the model which will present an automated alert service to the general public. Using this communication interface, all the information about the disease can be passed on to a major portion of the public. It is anticipated that once they receive alerts, the public will also take the necessary steps to protect themselves such that the disease is avoided in every way. The initial stage of building the dynamics of salmonella diarrhea has been elaborated in this paper. The model presented herewith signifies as the base on which the further enhancements will be done to achieve the whole system.

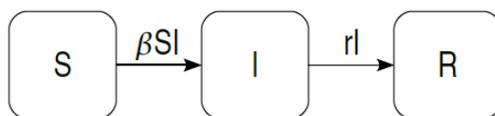
Prevention methods will be greatly enhanced by the above model which will prove to be very advantageous for the society. The population having a lower socio-economic level is most likely to catch a disease like diarrhea. Individuals in such populations are generally not aware of the treatment methods and if at all the treatment is given, they may not respond to it due to the unavailability of adequate facilities [27]. In such a situation, prevention will help in reducing the untimely death of millions across the globe. On the other hand, diseases such as salmonellosis cause heavy economic burdens under the veil of simple treatment. It has been estimated that approximately \$2.8 billion is spent annually in the United States for Salmonella infections [20]. The model described here is highly cost effective and does not require any profound knowledge for operation. If such an undemanding model is exploited for the prevention of these diseases, it is exceptionally clear that countries worldwide will benefit economically too.

## **II. BACKGROUND**

### **2.1. Other Models**

Epidemic models have been implemented in various forms with regard to infectious diseases. Among them, continuous epidemic models are most common. In 1927, Karmack and McKendrick introduced a

compartmental epidemic model consisting of three compartments - the Susceptible-Infected-Recovered (SIR) model [6]. In its simplest form, the SIR model can be shown as follows:



**Figure 1. The basic SIR model**

Ordinary Differential Equations and some defined parameters are used to define the SIR model as shown below in equations (1) to (3). In the model,  $\beta$  represents the infectivity parameter and  $r$  is the rate of recovery. This implies that no randomness is involved in the model [6].

$$\frac{dS}{dt} = -\beta SI \quad (1)$$

$$\frac{dI}{dt} = \beta SI - rI \quad (2)$$

$$\frac{dR}{dt} = rI \quad (3)$$

The SIR model has been largely used in Epidemic modeling and is generally found to act as the basis for other models. Using the above traditional model as a foundation, other continuous models have been built for epidemiology. The Biomedical Modeling Centre, LA uses this model for influenza [7]. By adding a few extensions and modifications, a model which calculates the daily incidence of influenza for different transmission rates has been prepared. The SIR model has also been used to develop other types of models for epidemics. For example, the University of New South Wales, Australia, has used the basic SIR model and created an agent based model for the Hepatitis C Virus which gives rise to liver diseases. This model uses inputs such as age, sex and immigrant status and delivers outputs such as infections, cure and death rates related to the disease [8]. Discrete modeling is also widely used in epidemics as data needed for modeling epidemics is usually collected at discrete times [9]. Modeling in the discrete mode involves the calculation of the population size for the next time interval. This characteristic of discrete models discloses the predictive ability of the model and thus proves to be very advantageous. SARS (Severe Acute Respiratory Syndrome) in China has been modeled using discrete modeling. Three more compartments are added to the basic SIR model namely the exposed, quarantined and diagnosed individuals. In this model, the basic reproduction number was used to formulate the asymptotic behavior of the disease and prove the importance of quarantine for such diseases [10]. Some diseases can be modeled successfully using only two compartments from the basic SIR model – the susceptible and infected classes. Gonorrhoea and malaria are such examples. The dynamical behavior of these diseases can be determined using discrete SI and SIS models [11]. An additional research on these diseases included the effects of seasonality in the model. This work uses the fact that seasonal factors directly affect the pathogens related to such diseases [12].

## 2.1. Disease epidemiology and pathogenesis

As the levels of infectious diseases are increasing at remarkable rates around the globe, several efforts are being executed for their eradication. Epidemic modeling is one such effort that can be used to plan the methods of prevention of infectious diseases. Prevention of diseases lessens the possibility of outbreaks and thus reduces economic requirements too. Infectious diseases can be classified into many subsets including water – borne, vector – borne and food – borne. Water – borne diseases are infectious diseases spread mainly through water and they have a significant impact on health, globally. One of the most widespread water related disease is diarrhoea and it continues to endanger the population at large. Diarrhoea is caused by bacteria, virus or other parasitic organisms and is predominantly transmitted through contaminated food and water. In order to reduce the speed of the transmission of this disease, it is necessary to recognize the disease characteristics and pathogenesis as this forms the basis of the methods that can be implemented to fight the diffusion of the pathogens. Diarrhoea is an infectious disease that is characterized by the passage of three or more liquid stools per day. Other symptoms of diarrhoea include abdominal pain, fever and dehydration [13]. Dehydration is the most severe of all the symptoms as it results in the loss of many necessary salts and chemicals along with water. The condition of dehydration can eventually turn out to be extremely harsh causing death, especially in small children. Diarrhoea can present in an individual as a disease on its own or a symptom of another disease. In both cases, there are many pathogens that can transmit diarrhoea. According to the national health records of Botswana, the four main pathogens that are attributed to diarrhoea in Botswana are the rotavirus, the protozoan

cryptosporidium and the bacteria shigella and salmonella. Out of many other bacteria, salmonella is one of the most common causes of diarrhea in Botswana [5]. Salmonella infections can cause typhoid or can be non-typhoidal. Diarrhea appears as a major symptom in non-typhoidal salmonella infections. Although sometimes overlooked, non-typhi serotypes of salmonella cause a higher proportion of infections in developed countries [13]. The global burden of non-typhoidal salmonellosis is estimated to be approximately 93 million cases annually. As the main transmission method of salmonella happens to be foodstuffs, 80 million of the above cases are food borne [14]. In humans, salmonella is widely acquired by the ingestion of contaminated food material. Out of all foods, eggs and poultry are found to be often highly infected with salmonella. Apart from contaminated food, indirect transmission by unhygienic hand washing habits and contaminated surfaces can also occur. The bacteria can also be caught through pet reptiles and rodents [15]. The infective dose of the bacteria is quite high ranging to about 100000 bacilli [13] but this does not reduce the danger of the pathogen due to its easy transmission.

Symptoms begin to appear after about 24 hours following ingestion of contaminated food or water [16] and may manifest in different forms like gastroenteritis, bacteremia and enteric fever [15]. Out of these, gastroenteritis is associated with diarrhea which may last for about a week [15]. In general, an oral rehydration therapy is carried out for treatment of gastroenteritis to replace the lost fluids and electrolytes. Antibiotics may be used in severe cases or for immunosuppressed individuals. Symptoms subside after a few days but the patient may remain contagious for even months [17, 18]. Almost any person is susceptible to salmonella and can become infected by the ingestion of contaminated food. Upon treatment, the infected individual may completely recover which means that the total bacterial population is flushed out of the body, or may become an asymptomatic carrier. An asymptomatic carrier does not show any symptoms but since the bacteria are still in the body, they are shed into the environment perpetuating the spread of the disease. Both types of infected people gradually become recovered with the exception cases of severity. As salmonellosis becomes more severe, it results in further complications in the body such as septic arthritis and pneumonia [16]. At this point, minor symptoms such as diarrhea normally fade away. Because this research is mainly based on the eradication of diarrhea, the extreme severe cases of salmonellosis have not been included. After a certain time period of recovery, a person becomes re-susceptible to the bacteria as the immune system gradually declines. The above mentioned practical stages of infection have been implemented into a model and manipulated to show the dynamics of the disease.

### III. THE MODEL

#### 3.1. Description

The model considered herewith is a redesigned version of the fundamental SIR model based on the properties of salmonella infections. There are four compartments included in the system, which can be described as follows:

1. Susceptible (S) – this represents the individuals of the whole human population that can catch the disease
2. Symptomatic Infected ( $I_S$ ) – these are the individuals who have been infected by the bacteria and show clinical manifestations of the disease. They are capable of transmitting the disease to other susceptible individuals.
3. Asymptomatic Infected ( $I_A$ ) – the people in this group have externally recovered from the disease but continue to carry the bacteria. They do not show any symptoms and are capable of infecting the susceptible class.
4. Recovered (R) – this class consists of the individuals who have completely recovered from the disease meaning they neither show symptoms nor do they carry the bacteria. These individuals gradually lose their immunity and become susceptible after a certain period of time.

A schematic illustration of the model is given below. All the associated parameters are described in Table 1.

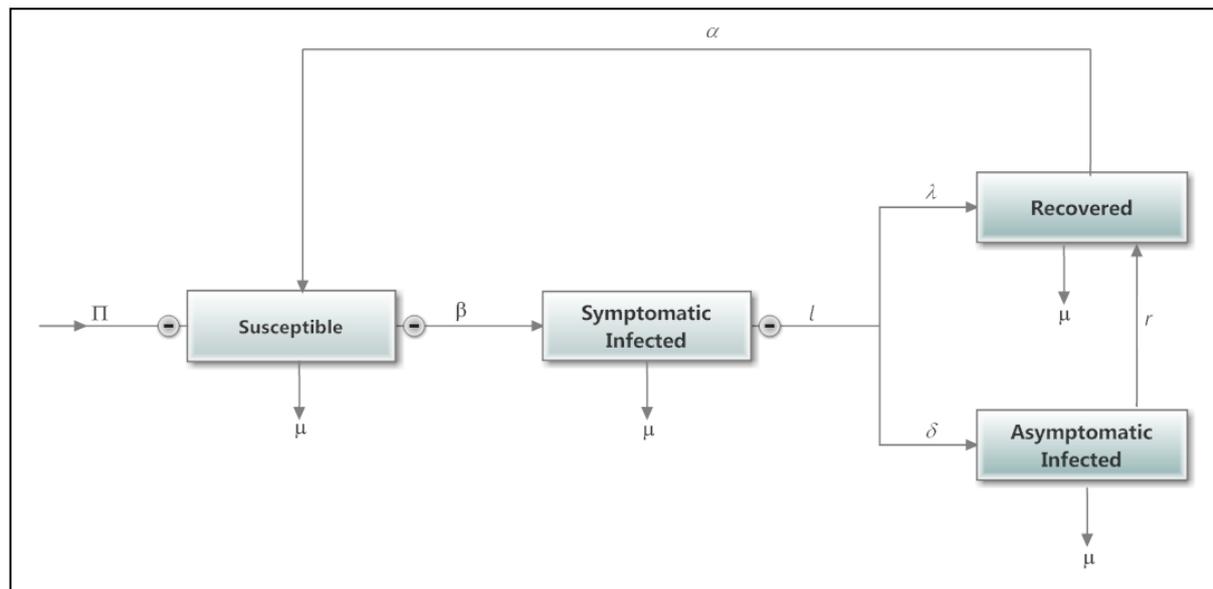


Figure 2. The SIRS model

Table 1. Parameter Description

Parameter	Description
$\Pi$	Population renewal rate
$\beta$	Infectivity rate
$\mu$	Natural death rate
$l$	Rate of losing symptoms
$\lambda$	Direct recovery rate
$\delta$	Rate of pathogen prevalence in body
$r$	Indirect recovery rate
$\alpha$	Immunity loss rate

The susceptible population, as the name suggests, is non-resistant to the disease and gets in contact with the pathogen through the infected population. Both the infected classes contribute to the pathogen population and hence transmit the disease. Resolution of the symptoms could mean that one has become a bacteria carrier or he has recovered. The asymptomatic carrier also recovers progressively as the pathogen clears from his body. For some time, the body maintains an immunity level and the individual remains in the recovered class but gradually, this immunity level can drop rendering the recovered population to become susceptible to the disease again.

In the above described system, the following assumptions are made:

1. The shedding rate of bacteria by the infected population consists of both direct and indirect shedding
2. All individuals are born as susceptible
3. Salmonella persists in the environment for several days [19], hence the pathogen death rate is assumed to be zero.

Using the above mentioned parameters and assumptions, the extended compartmental model can be defined using the following equations:

$$\begin{aligned} \frac{dS}{dt} &= \Pi - \mu S - \beta SI_S - \beta l \delta SI_S + \alpha R \\ \frac{dS}{dt} &= \Pi - \mu S - \beta SI_S (1 + l \delta) + \alpha R \end{aligned} \quad (4)$$

Equation 4 describes the rate of change of the susceptible population. A constant population renewal rate  $\Pi$  adds to the susceptible population while a constant death rate  $\mu$  reduces it. The susceptible class gains infections from the symptomatic class at a rate  $\beta$  and from the asymptomatic class at the rate  $l\delta$ . Susceptible individuals are related to the symptomatic class by the infectivity rate and they are related to the asymptomatic class through the symptomatic group by the symptom loss and pathogen prevalence rates. Further additions are supplied to the susceptible class by the recovered individuals who lose their immunity at the immunity loss rate.

$$\frac{dI_S}{dt} = \beta SI_S(1 + l\delta) - \mu I_S - lI_S \quad (5)$$

The above equation defines the change rates in the symptomatic infected group. The susceptible population that becomes infected automatically joins this class. A constant death rate and symptom loss rate decrease the symptomatic infected population.

$$\frac{dI_A}{dt} = l\delta I_S - \mu I_A - rI_A \quad (6)$$

The rate of change in the asymptomatic class can be described using equation 6 above. Symptomatic individuals lose their symptoms at the rate  $l$  and preserve bacteria within their bodies at rate  $\delta$ . These individuals add up into the asymptomatic class. Natural death and recovery reduce the population of this class also at the rate  $\mu$  and  $r$  respectively.

$$\frac{dR}{dt} = l\lambda I_S + rI_A - \mu R - \alpha R \quad (7)$$

Equation 7 represents the dynamics of the recovered class. The population of this class is increased as the symptomatic individuals lose their symptoms at rate  $l$  and recover at a direct recovery rate  $\lambda$  and also as the asymptomatic people recover at rate  $r$ . Constant death rate  $\mu$  and the immunity loss rate  $\alpha$  reduce the population of the recovered group.

### 3.2. Parameter calculations

For the analysis of the above model, the first step is to calculate the disease-free equilibrium. The disease-free equilibrium (DFE) is the state at which there are no infections at all in the population. If the population has to be free of the disease and pathogens, it directly implies that the infectious states need to be assumed to be zero, i.e.  $I_A = I_S = 0$ . Since the infectious population has been assumed to be zero, it entails that there will be no recovered population either. Therefore  $R = 0$ . At this state, the only non-zero class is the susceptible class. At the DFE, all the classes are denoted with an asterisk. In order to get the asymptotic state, the non-zero components on the right hand side of equation (4) will be equated to zero. Because the infectious states and the recovered state have been assumed to be zero, the population renewal parameter and death rate are the only non-zero components on the right hand side of equation (4).

$$\Pi - \mu S^* = 0 \quad (8)$$

$$S^* = \frac{\Pi}{\mu}$$

Thus, the DFE can be described using equation 9 as follows:

$$DFE = \left( \frac{\Pi}{\mu}, 0, 0, 0 \right) \quad (9)$$

After the calculation of the DFE, the evaluation of the basic reproduction number ( $R_0$ ) follows. The basic reproduction number is defined as the number of disease cases that are generated by a single infection [20]. In epidemic models, the basic reproduction number has a crucial role as it is used to establish the existence of the epidemic. It is stated that if  $R_0 > 1$ , an epidemic exists as there are increasing number of cases. Likewise, if  $R_0 < 1$ , then there is no epidemic as the number of cases of infections are decreasing [21].  $R_0$  can be calculated using the next generation matrix,  $G$  [20]. The next generation matrix is computed using the infected state(s) and is defined as follows:

$$G = FV^{-1} \quad (10)$$

Where  $F$  is the Jacobian matrix of the new infections matrix ( $f$ ) and  $V$  is the Jacobian matrix of the other changes matrix ( $v$ ) in the infected state(s). Calculations here are done at the DFE state.  $R_0$  is defined as the highest eigenvalue of the next generation matrix. For the system above, there are two infectious states, the symptomatic infected and the asymptomatic infected. Using these two states, the two matrices  $f$  and  $v$  can be expressed as follows:

$$f = \begin{bmatrix} \beta SI_S(1 + l\delta) \\ l\delta I_S \end{bmatrix} \quad v = \begin{bmatrix} (\mu + l)I_S \\ (\mu + r)I_A \end{bmatrix}$$

If calculated at the DFE,  $S^* = \frac{\Pi}{\mu}$ , therefore,

$$f = \begin{bmatrix} \frac{\beta \Pi I_S (1 + l\delta)}{\mu} \\ l\delta I_S \end{bmatrix} \quad v = \begin{bmatrix} (\mu + l)I_S \\ (\mu + r)I_A \end{bmatrix}$$

Calculating the Jacobian matrices:

$$F = \begin{bmatrix} \frac{\beta\Pi_s(1+l\delta)}{\mu} & 0 \\ l\delta & 0 \end{bmatrix} \quad V = \begin{bmatrix} (\mu+l) & 0 \\ 0 & (\mu+r) \end{bmatrix}$$

Using the above matrices the next generation matrix, G is evaluated to be:

$$G = \begin{bmatrix} \frac{\beta\Pi(1+l\delta)}{\mu(\mu+l)} & 0 \\ \frac{l\delta}{(\mu+l)} & 0 \end{bmatrix}$$

By calculating the largest eigenvalue of the next generation matrix, the basic reproduction number of this model is worked out as:

$$R_0 = \frac{\beta\Pi(1+l\delta)}{\mu(\mu+l)} \quad (11)$$

### 3.3. Numerical simulations and discussion

In order to show that the SIRS model depicts a steady system that complies with the stability theorem based on  $R_0$ , the model was simulated using MATLAB. Table 2 shows the values used for the variables during simulation:

**Table 2 – Values of parameters used for simulation**

Parameter	Value
$\Pi$	10
$\mu$	0.012 [22]
$l$	0.5
$\lambda$	0.14
$\delta$	0.9
$r$	0.05
$\alpha$	0.25

All other parameter values have been assumed other than the death rate,  $\mu$ . The infectivity rate,  $\beta$ , is used to govern the value of the basic reproduction number. Two circumstances have to be considered:  $R_0 < 1$  and  $R_0 > 1$ . For this, first the value of the infectivity rate will be worked out for  $R_0 = 1$ . Using this value as a base, the infectivity rate will be altered such that the above two situations are obtained.

For  $R_0 = 1$ ;

$$\begin{aligned} \Pi\beta(1+l\delta) &= \mu(\mu+l) \\ \beta &= \frac{\mu(\mu+l)}{\Pi(1+l\delta)} \quad (12) \end{aligned}$$

Using the above assumed values of the various parameters, the infectivity rate for  $R_0 = 1$  is calculated as 0.000423. Using equation (11), it can be seen that if  $\beta < 0.000423$  then  $R_0 < 1$  and if  $\beta > 0.000423$ ,  $R_0 > 1$ .

Simulations have been done for different values of  $\beta$  and are shown below. These values have been divided into the two different circumstances of epidemic existence and disease free state.

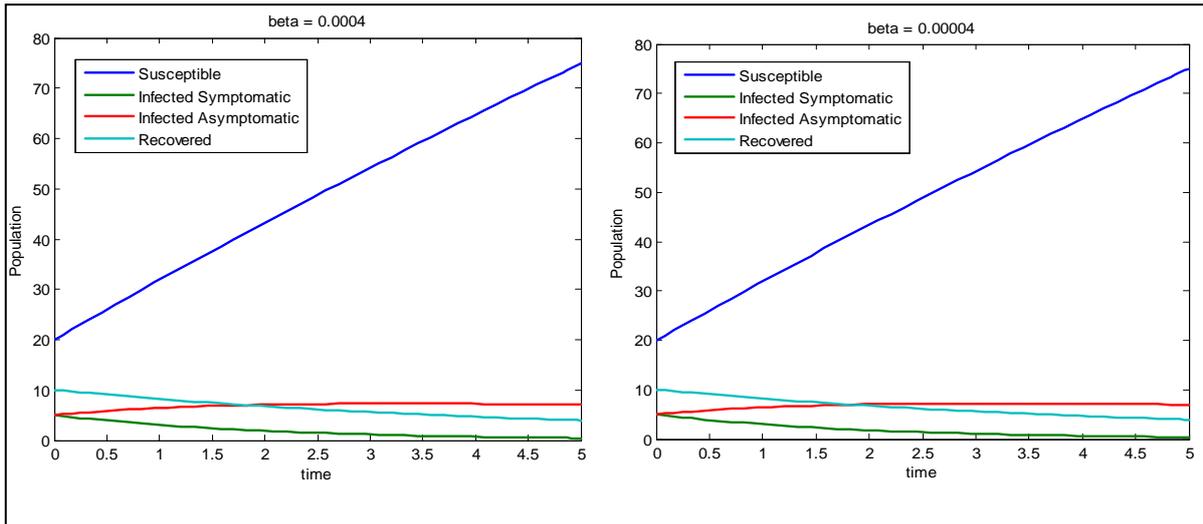


Figure 3. Simulations for disease free state

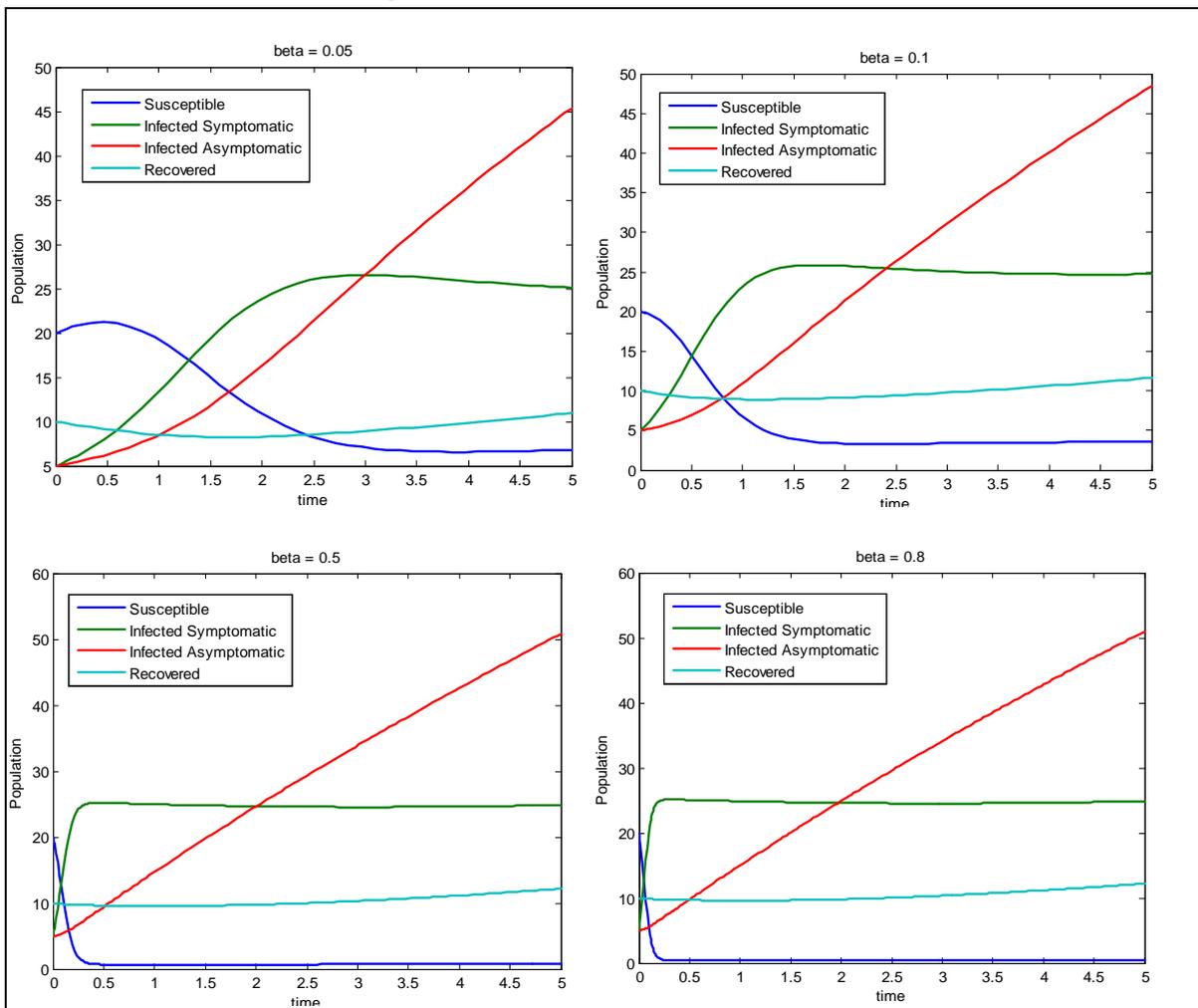


Figure 4. Simulations for the epidemic existence

Figure 3 shows the population variation for the values of  $\beta < 0.000546$ . In this case, the values of  $R_0$  is lesser than 1 and there is no epidemic. If there is no disease within a population, the susceptible group of people increases. The symptomatic infected population reduces and the asymptomatic infected class remains at the same level. Since there is an overall reduction in the infected class, it follows that the recovered population will also decrease. These statements are shown clearly in figure 3. It can also be seen from the graphs in figure 3 that lowering the value of  $\beta$  further does not cause any significant changes in the population. Hence, it can be deduced that as long as  $R_0 < 1$ , the population will remain disease – free.

Figure 4 illustrates the epidemic situation in the population. When  $\beta$  has higher values,  $R_0$  becomes more than 1 and an epidemic arises in the population. On the advent of the epidemic, it is obvious that the susceptible population will begin to decline. Both the infected populations will grow in size. The recovered population remains at about the same size as the infections increase highly thus individuals are not able to recover at a fast rate. Furthermore, in an epidemic situation, immunity is lost faster and therefore the recovered population does not show an increment in size. Figure 4 shows all the above described dynamics. Together with this, it should be noted that as the value of  $\beta$  increases, the changes in the population size become steeper. When  $\beta$  increases,  $R_0$  also increases and as a consequence, the disease is now transmitted at higher rates. Respective changes in the susceptible and infected states thus become higher and steeper. In this way, it can be deduced that all efforts should be made in order to keep the basic reproduction number very low.

#### IV. CONCLUSION

This paper presented a continuous model on diarrhea caused by salmonella enteritis thus provided an increased understanding of the dynamics of the disease in a country like Botswana. Analysis of the system was done by evaluating the basic reproduction number and the model was simulated using this evaluated parameter. It was proved that as long as the value of  $R_0$  is kept minimal, the disease can be eradicated from the population. The model shows that the higher the value of  $R_0$ , the more likely an epidemic will spread at higher rates.  $R_0$  can be kept low by employing various policies such as increasing knowledge of public in terms of prevention and treatment, increased hygiene conditions at work places and better water treatment facilities.

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