

Analysis of Listeriosis Transmission Dynamics with Optimal Control

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Abstract

Listeriosis is an illness caused by the germ *Listeria monocytogenes*. Generally, humans are infected with listeriosis after eating contaminated food. Listeriosis mostly affects people with weakened immune systems, pregnant women and newborns. In this paper, a model describing the dynamics of Listeriosis is developed and analysed using ordinary differential equations. The model was analysed both quantitatively and qualitatively for its local and global stability, basic reproductive number and parameter contributions to the basic reproductive number to understand the impact of each parameter on the disease spread. The Listeriosis model has been extended to include time dependent control variables such as treatment of both humans and animals, vaccination and education of humans. Pontryagin's Maximum Principle was introduced to obtain the best optimal control strategies required for curbing Listeriosis infections. Numerical simulation was performed and the results displayed graphically and discussed. Cost effectiveness analysis was conducted using the intervention averted ratio (IAR) concepts and it was revealed that the most effective intervention strategy is the treatment of infected humans and animals.

Keywords

Listeriosis Model, Basic Reproductive Number, Optimal Control, Pontryagin's Maximum Principle, Cost Effectiveness

1. Introduction

Listeriosis is an illness caused by the germ *Listeria monocytogenes*. Generally, humans are infected with listeriosis after eating contaminated food. Listeriosis

mostly affects people with weakened immune systems, pregnant women and newborns. The organism was initially described as a cause of epizootics in veld rodents from South Africa (Tiger River disease) by Pier and in 1926 [1]. The organism remained a laboratory problem until the World War II, when it was officially known to be the cause of neonatal sepsis and meningitis [2]. *Listeria monocytogenes* is mostly found in the environment and it is responsible for meningoencephalitis and stillbirths in a number of animals. The disease usually occurs in human in the setting of pregnancy, immunosuppressive and as the individual ages [3].

Listeriosis is the major cause of encephalitis in ruminants. This encephalitis is usually referred to as “circling disease” because it occurs in the hindbrain and can lead to ataxia in infected animals before death [2]. Listeriosis can or may be a potential risk for veterinarians who are normally working with infected animals. This revelation from veterinary medicine has made epidemiologists speculate that foodborne infection could be responsible for human Listeriosis [2] [4].

The work done by [5] showed that *Listeria monocytogenes* is a foodborne pathogen that is responsible for the cause of serious invasive illness, mostly in certain class of individuals including elderly and immune compromised patients, new born children and pregnant women. In a study conducted by [6], *Listeria monocytogenes* has been rated among the most increasing and major food-associated pathogen and many countries of the European Union have always recorded an annual case of human Listeriosis.

The study conducted by [7] on the incidence and transmission of *Listeria monocytogenes* in ready-to-eat products in retail and food services environments proved that contamination of food products with *Listeria monocytogenes* can exist or show up at multiple stages before consumption. A research conducted by [8] showed that *Listeria monocytogenes* is among the foodborne pathogens responsible for invasive illness in certain class of people. The findings revealed an association between preventive measures and reduction on human Listeriosis. Listeriosis is an invasive illness that mainly attacks immune compromised individuals, neonates and pregnant women. The commonest sources of getting infected with the disease are raw milk and meats [9] [10].

A study conducted by [11], revealed that Listeriosis in human are rare but it is among the top serious foodborne diseases in susceptible and vulnerable individuals in a population such as the immune compromised and pregnant women. The resurgence of foodborne Listeriosis was investigated by [12]. The significance of separating the pathogens as a necessary requirement for a correct epidemiological research and eradicating transmission cannot be overemphasised. Moreover, [13], stated Listeriosis as one of leading causes of death from foodborne pathogens. The disease continues to spread and cause sporadic outbreaks of illness.

Research on the epidemics of Listeriosis revealed that transmission of *Listeria monocytogenes* in food is responsible for human diseases in the early 1980s [3].

An investigation conducted by [14] showed that *Listeria monocytogenes* are the causative agent of gastrointestinal. The intestinal tract can be the main point of entry for *Listeria monocytogenes*. [15] conducted a research on the identification and reservoir of pathogens for effective control of sporadic disease and epidemics. The dairy farm has been observed as a potential point and reservoir for *Listeria monocytogenes*.

In recent times, mathematical models describing the phenomenon and dynamics of infectious diseases have played a key role in the control of diseases in epidemiology. Some of the models are able to explain the dynamics and mode of disease transmission [16] [17]. Complex transmission dynamics of some diseases such as periodic orbits, Hopf bifurcations and multiple equilibria have been described [10] [18].

This is a situational report on Listeriosis outbreaks in South Africa. The data in **Table 1** gives the outcome of persons with laboratory-confirmed Listeriosis by province in South Africa. The names of these provinces have been abbreviated for convenience purposes. The data is from the National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Services (NHLS). This data is between January, 2017 and March, 2018.

Table 1. Outcome of 967 persons with laboratory-confirmed Listeriosis by province in South Africa between January, 2017 and March, 2018.

Province	Died	Discharged	Pending	Total
EC	10	18	22	50
FS	8	19	7	34
GA	98	261	213	572
KZ	11	30	27	68
LP	7	25	15	47
MP	10	34	2	46
NC	3	2	1	6
NW	7	17	5	29
WC	29	80	6	115
Total	183	486	298	967

Figure 1 shows the situational report of dead and discharged individuals affected with Listeriosis in South Africa between January, 2017 and March, 2018.

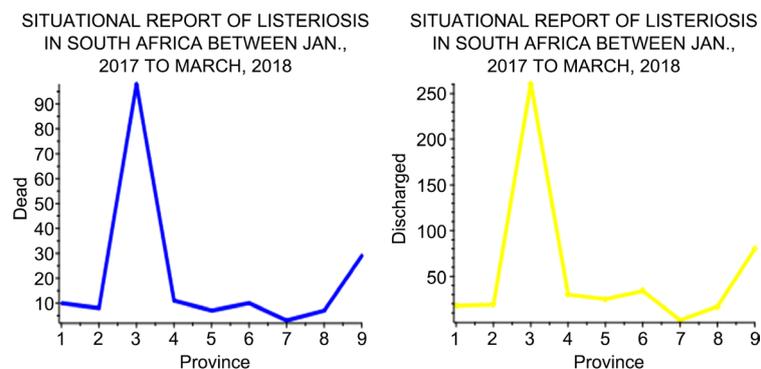


Figure 1. Listeriosis in 9 provinces of South Africa between Jan., 2017 and March, 2018.

2. Listeriosis Model Description and Formulation

The Listeriosis model is divided into two parts, human and vector populations as shown in **Figure 2**. The populations at any time t are also divided into six subcompartments with respect to their disease status in the system. Human population represented by (N_h) , is divided into subpopulations of Susceptible humans (S_h) , Infected humans (I_h) , and Recovered humans (R_h) .

The total human population is given by:

$$N_h(t) = S_h(t) + I_h(t) + R_h(t). \tag{1}$$

The animal population represented by N_v , is divided into subpopulations of Susceptible animals (S_v) , Infectious animals (I_v) , and Recovered animals (R_v) .

The total vector population becomes:

$$N_v(t) = S_v(t) + I_v(t) + R_v(t). \tag{2}$$

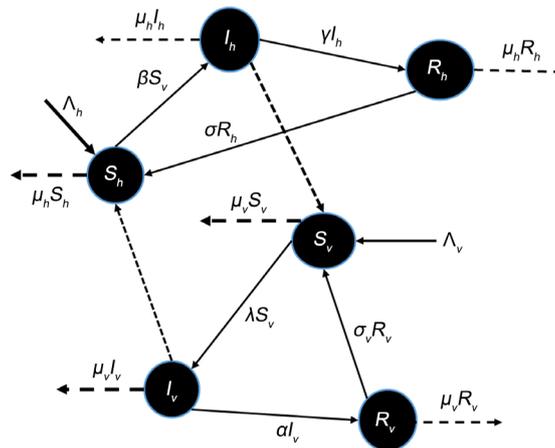


Figure 2. Flow diagram of Listeriosis model.

Table 2 shows the Listeriosis model variables and their interpretations as used in the model formulation.

Table 2. Listeriosis model variables and their interpretations.

Variable	Interpretations
$S_h(t)$	Individuals who are at risk of contracting Listeriosis infections.
$I_h(t)$	Individuals who are showing symptoms of Listeriosis infections.
$R_h(t)$	Individuals who have recovered from Listeriosis infections.
$S_v(t)$	Animals that are at risk of contracting Listeriosis infections.
$I_v(t)$	Animals that are showing symptoms of Listeriosis infections.
$R_v(t)$	Animals that have recovered from Listeriosis infections.

Table 3 shows Listeriosis model parameters with their interpretations as used in model formulation.

Table 3. Listeriosis model parameters and their interpretations.

Parameter	Interpretations
Λ_h	Human recruitment rate.
β	Human contact rate.
γ	Human recovery rate.
δ_h	Human Listeriosis induced death rate.
σ_h	Human waning immunity.
μ_h	Human natural death rate.
Λ_v	Animal recruitment rate.
λ	Animal contact rate.
α	Animal recovery rate.
δ_v	Animal Listeriosis induced death rate.
σ_v	Animal waning immunity.
μ_v	Animal natural death rate.

Humans can be infected with Listeriosis through ingestion of contaminated foods from infected animals, inhalation of spores and contact with infected animals and humans at a rate $(I_v + I_h)\beta$. Listeriosis can be acquired through contacts with infected animals and humans at a rate $(I_v + I_h)\lambda$, where, $\beta_m^* = (I_h + I_v)$.

The following system of ordinary differential equations is obtained from the model:

$$\left. \begin{aligned} \frac{dS_h}{dt} &= \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h \\ \frac{dI_h}{dt} &= \beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h \\ \frac{dR_h}{dt} &= \gamma I_h - (\sigma_h + \mu_h) R_h \\ \frac{dS_v}{dt} &= \Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v \\ \frac{dI_v}{dt} &= \beta_m^* \lambda S_v - \alpha I_v - (\mu_v + \delta_v) I_v \\ \frac{dR_v}{dt} &= \alpha I_v - (\sigma_v + \mu_v) R_v \end{aligned} \right\} \quad (3)$$

3. Listeriosis Model Analysis

3.1. Positivity and Boundedness of Solutions

The Listeriosis model is epidemically meaningful if all the solutions with non-negative initial data remain non-negative at every point in time.

Theorem 1 Let

$$\Theta = \left\{ (S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), R_v(t)) \in \mathbb{R}_+^6 : \right. \\ \left. (S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), R_v(0)) > 0 \right\},$$

then the solution of $\left\{ (S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), R_v(t)) \right\}$ is non-negative at all time $t \geq 0$.

This implies that, if $S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), R_v(0)$ are non-negative, then $S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), R_v(t)$ are also non-negative for all time $t > 0$.

Human population at any time, t is given by:

$$N_h(t) = S_h(t) + I_h(t) + R_h(t). \quad (4)$$

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt} \quad (5)$$

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h S_h - (\mu_h + \delta_h) I_h - (\sigma_h + \mu_h) R_h. \quad (6)$$

In the absence of mortality due to Listeriosis infections:

$$\frac{dN_h}{dt} \leq \Lambda_h - \mu_h N_h.$$

$$N_h \leq \frac{\Lambda_h}{\mu_h} - \left(\frac{\Lambda_h - \mu_h N_h(0)}{\mu_h} \right) e^{-\mu_h t}. \quad (7)$$

As $t \rightarrow \infty$, the population size, $N_h \rightarrow \frac{\Lambda_h}{\mu_h}$.

$$0 \leq N_h \leq \frac{\Lambda_h}{\mu_h} \quad \text{and} \quad N_h(t) \leq \frac{\Lambda_h}{\mu_h}.$$

Also, if $N_h(0) \leq \frac{\Lambda_h}{\mu_h}$, then $N_h(t) \leq \frac{\Lambda_h}{\mu_h}$.

$$\Theta_h = \left\{ (S_h, I_h, R_h) \in \mathbb{R}_+^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\} \quad (8)$$

Vector (livestock) population at any time (t) is given by:

$$N_v(t) = S_v(t) + I_v(t) + R_v(t). \quad (9)$$

$$\frac{dN_v}{dt} = \frac{dS_v}{dt} + \frac{dI_v}{dt} + \frac{dR_v}{dt}. \quad (10)$$

$$\frac{dN_v}{dt} = \Lambda_v - \mu_v S_v - (\mu_v + \delta_v) I_v. \quad (11)$$

In the absence of mortality due to Listeriosis infections:

$$\frac{dN_v}{dt} \leq \Lambda_v - \mu_v N_v.$$

$$N_v \leq \frac{\Lambda_v}{\mu_v} - \left(\frac{\Lambda_v - \mu_v N_v(0)}{\mu_v} \right) e^{-\mu_v t}. \quad (12)$$

As $t \rightarrow \infty$, the population size, $N_v \rightarrow \frac{\Lambda_v}{\mu_v}$.

$$0 \leq N_v \leq \frac{\Lambda_v}{\mu_v} \quad \text{and} \quad N_v(t) \leq \frac{\Lambda_v}{\mu_v}.$$

Also, if $N_v(0) \leq \frac{\Lambda_v}{\mu_v}$, then $N_v(t) \leq \frac{\Lambda_v}{\mu_v}$.

Therefore,

$$\Theta_v = \left\{ (S_v, I_v, R_v) \in \mathbb{R}_+^3 : S_v + I_v + R_v \leq \frac{\Lambda_v}{\mu_v} \right\}. \quad (13)$$

Feasible region is given by:

$$\Theta = \Theta_h \times \Theta_v \subset \mathbb{R}_+^3 \times \mathbb{R}_+^3 \quad (14)$$

where,

$$\Theta_h = \left\{ (S_h, I_h, R_h) \in \mathbb{R}_+^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\} \quad (15)$$

and

$$\Theta_v = \left\{ (S_v, I_v, R_v) \in \mathbb{R}_+^3 : S_v + I_v + R_v \leq \frac{\Lambda_v}{\mu_v} \right\} \quad (16)$$

where Θ is positively invariant.

3.2. Disease-Free Equilibrium

By setting the system of equations in (3) to zero, we obtain the DFE of the model. However, DFE, there are no infections. Hence;

$$\left. \begin{array}{l} I_h^* = 0 \\ R_h^* = 0 \end{array} \right\} \quad \text{and} \quad \left. \begin{array}{l} I_v^* = 0 \\ R_v^* = 0 \end{array} \right\}$$

The DFE of the Listeriosis model is given by;

$$\xi_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0 \right) \quad (17)$$

3.3. Listeriosis Reproductive Number

Using the ‘‘Next Generation Matrix’’ approach, we determine R_{hv} and its linear stability. Listeriosis reproductive number refers to the number of secondary cases produced on average by one infected animal or person in a completely susceptible population. This combines the biology of infections with the social and behavioural factors influencing contact rate [19] [20] [21]. It is the threshold parameter that determines or governs the spread of a disease.

Considering only the infection classes in the system in (3):

$$\left. \begin{array}{l} \frac{dI_h}{dt} = (I_h + I_v)\beta S_h - \gamma I_h - (\mu_h + \delta_h)I_h \\ \frac{dI_v}{dt} = (I_h + I_v)\lambda S_v - \alpha I_v - (\mu_v + \delta_v)I_v \end{array} \right\} \quad (18)$$

Let f be the number of new infection coming into the system and v be the number of infections that are leaving the system either by death or birth.

$$f = \begin{bmatrix} (I_h + I_v) \beta S_h \\ (I_h + I_v) \lambda S_v \end{bmatrix}, \quad v = \begin{bmatrix} \gamma I_h + (\mu_h + \delta_h) I_h \\ \alpha I_v + (\mu_v + \delta_v) I_v \end{bmatrix}.$$

The Jacobian matrix of f and v at disease free equilibrium is obtained by F and V as follows:

$$F = \begin{bmatrix} \beta S_h^* & \beta S_h^* \\ \lambda S_v^* & \lambda S_v^* \end{bmatrix}, \tag{19}$$

$$V = \begin{bmatrix} \gamma + (\mu_h + \delta_h) & 0 \\ 0 & \alpha + (\mu_v + \delta_v) \end{bmatrix}. \tag{20}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta S_h^*}{(\mu_h + \gamma) + (\mu_h + \delta_h)} & \frac{\beta S_h^*}{(\mu_v + \alpha) + (\mu_v + \delta_v)} \\ \frac{\lambda S_v^*}{\gamma + (\mu_h + \delta_h)} & \frac{\lambda S_v^*}{\alpha + (\mu_v + \delta_v)} \end{bmatrix} \tag{21}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} & \frac{\beta S_h^*}{\alpha + (\mu_v + \delta_v)} \\ \frac{\lambda S_v^*}{\gamma + (\mu_h + \delta_h)} & \frac{\lambda S_v^*}{\alpha + (\mu_v + \delta_v)} \end{bmatrix} \tag{22}$$

Now, computing the eigenvalues of FV^{-1} and selecting the dominant eigenvalue. Let A represent the eigenvalue of the matrix.

$$\begin{vmatrix} \frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} - A & \frac{\beta S_h^*}{\alpha + (\mu_v + \delta_v)} \\ \frac{\lambda S_v^*}{\gamma + (\mu_h + \delta_h)} & \frac{\lambda S_v^*}{\alpha + (\mu_v + \delta_v)} - A \end{vmatrix} = 0 \tag{23}$$

$$A^2 - \left[\left(\frac{\lambda S_v^*}{\alpha + (\mu_v + \delta_v)} \right) + \left(\frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} \right) \right] A = 0 \tag{24}$$

$$A_1 = 0 \quad \text{and} \quad A_2 = \left[\left(\frac{\lambda S_v^*}{\alpha + (\mu_v + \delta_v)} \right) + \left(\frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} \right) \right].$$

Dominant eigenvalue is A_2 . This implies that;

$$R_{hv} = \left[\left(\frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} \right) + \left(\frac{\lambda S_v^*}{\alpha + (\mu_v + \delta_v)} \right) \right]. \tag{25}$$

Hence, R_{hv} is given by;

$$R_{hv} = \left(\frac{\beta \Lambda_h}{\mu_h (\gamma) + (\mu_h + \delta_h)} \right) + \left(\frac{\lambda \Lambda_v}{\mu_v [(\alpha) + (\mu_v + \delta_v)]} \right). \tag{26}$$

where:

$$R_{hq} = \left(\frac{\beta \Lambda_h}{\mu_h (\gamma) + (\mu_h + \delta_h)} \right), \text{ for human population.}$$

$$R_{vq} = \frac{\lambda \Lambda_v}{\mu_v [\alpha + (\mu_v + \delta_v)]}, \text{ for animal population.}$$

3.4. Local Stability of the Disease Free Equilibrium

Theorem 2. *The disease free equilibrium is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

$$\text{The DFE was obtained as; } \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0 \right).$$

The Jacobian matrix of the system is given by:

$$\begin{pmatrix} -(\beta_m^* \beta + \mu_h) & -\beta S_h^* I_v^* & \sigma_h & 0 & \beta S_h I_h & 0 \\ \beta_m^* \beta & r_1 & 0 & 0 & \beta S_h I_h & 0 \\ 0 & \gamma & -(\sigma_h + \mu_h) & 0 & 0 & 0 \\ 0 & -\lambda S_v^* I_h^* & 0 & -(\beta_m^* \lambda + \mu_v) & -\lambda S_v^* I_h^* & \sigma_v \\ 0 & \lambda S_v^* I_h^* & 0 & \beta_m^* \lambda & r_2 & 0 \\ 0 & 0 & 0 & 0 & \alpha & -(\sigma_v + \mu_v) \end{pmatrix} \quad (27)$$

where:

$$r_1 = (\beta S_h^* I_v^* - \mu_h - \delta_h - \gamma)$$

$$r_2 = \lambda S_v^* I_h^* - (\alpha + \mu_v + \delta_v)$$

$$\text{Jacobian matrix at disease free equilibrium: } DFE = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0 \right)$$

$$\begin{pmatrix} -\mu_h & 0 & \sigma_h & 0 & 0 & 0 \\ 0 & -(\mu_h + \delta_h + \gamma) & 0 & 0 & 0 & 0 \\ 0 & \gamma & -(\sigma_h + \mu_h) & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu_v & 0 & \sigma_v \\ 0 & 0 & 0 & 0 & -(\alpha + \mu_v + \delta_v) & 0 \\ 0 & 0 & 0 & 0 & \alpha & -(\sigma_v + \mu_v) \end{pmatrix} \quad (28)$$

Determining the eigenvalues:

$$\begin{vmatrix} -\mu_h & 0 & \sigma_h & 0 & 0 & 0 \\ 0 & -(\mu_h + \delta_h + \gamma) & 0 & 0 & 0 & 0 \\ 0 & \gamma & -(\sigma_h + \mu_h) & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu_v & 0 & \sigma_v \\ 0 & 0 & 0 & 0 & -(\alpha + \mu_v + \delta_v) & 0 \\ 0 & 0 & 0 & 0 & \alpha & -(\sigma_v + \mu_v) \end{vmatrix} = 0 \quad (29)$$

The eigenvalues are as follows:

$$\left. \begin{matrix} -\mu_v \\ -\mu_h \\ -(\mu_v + \delta_v) \end{matrix} \right\}, \left. \begin{matrix} -(\mu_h + \delta_h) \\ -(\alpha + \mu_v + \delta_v) \\ -(\gamma + \mu_h + \delta_h) \end{matrix} \right\}$$

All eigenvalues are negative. This implies that disease free equilibrium is locally asymptotically stable [22] [23] [24].

3.5. Global Stability of the Disease-Free Equilibrium

Theorem 3. *If $R_{hv} \leq 1$, the disease-free equilibrium is globally asymptotically stable in the interior of Φ .*

Proof: By considering the Lyapunov function:

$$P(t) = (\alpha + \mu_v + \delta_v)I_h + (\gamma + \mu_h + \delta_h)I_v \quad (30)$$

Computing the time derivative of P along the solutions of the system in (3);

$$\begin{aligned} \frac{dP(t)}{dt} &= (\alpha + \mu_v + \delta_v) \frac{dI_h}{dt} + (\gamma + \mu_h + \delta_h) \frac{dI_v}{dt} \\ &= (\alpha + \mu_v + \delta_v) (\beta S_h (I_h + I_v) - (\gamma + \mu_h + \delta_h) I_v) \\ &\quad + (\gamma + \mu_h + \delta_h) [\lambda S_v (I_h + I_v) - (\alpha + \mu_v + \delta_v) I_v] \\ &\leq (\alpha + \mu_v + \delta_v) \frac{\beta \Lambda_h I_h}{\mu_h} + (\alpha + \mu_v + \delta_v) \frac{\beta \Lambda_h I_v}{\mu_h} \\ &\quad - (\alpha + \mu_v + \delta_v) (\gamma + \mu_h + \delta_h) I_h \\ &\quad + I_h (\gamma + \mu_h + \delta_h) \left(\frac{\lambda \Lambda_v}{\mu_v (\tau + \mu_v)} \right) \\ &\quad + I_v (\gamma + \mu_h + \delta_h) \left(\frac{\lambda \Lambda_v}{\mu_v (\tau + \mu_v)} \right) + I_h (\gamma + \mu_h + \delta_h) \\ &\quad + I_v (\gamma + \mu_h + \delta_h) - I_v (\gamma + \mu_h + \delta_h) (\alpha + \mu_v + \delta_v) \\ &\leq -I_h (\gamma + \mu_h + \delta_h) (\alpha + \mu_v + \delta_v) (1 - R_{hv}) \\ &\quad - I_v (\gamma + \mu_h + \delta_h) (\alpha + \mu_v + \delta_v) (1 - R_{hv}) \\ &= -(I_h + I_v) (\gamma + \mu_h + \delta_h) (\alpha + \mu_v + \delta_v) (1 - R_{hv}) \end{aligned} \quad (31)$$

The time derivative of P along the solutions of the system of differential equations in (3):

$$\begin{aligned} \left(\frac{dP(t)}{dt} \right) &\leq 0, \text{ if and only if } R_{hv} < 0 \\ \left(\frac{dP(t)}{dt} \right) &= 1, \text{ if and only if } I_h + I_v = 0 \text{ or } R_{hv} = 1. \end{aligned}$$

Highest compact invariant set in $\left\{ S_h, I_h, I_v, \in \Phi, \frac{dP(t)}{dt} = 0 \right\}$, if $R_{hv} \leq 1$ is the singleton ξ_0 .

Hence, ξ_0 globally asymptotically stable in Φ , by LaSalle's invariant principle [10] [25].

3.6. Endemic Equilibrium

Consider the system in (3), at equilibrium,

$$\beta_m^* = I_h + I_v = 0.$$

This corresponds to the DFE or the relation:

$$\Phi_0 \beta_m^{*3} + \Phi_1 \beta_m^{*2} + \Phi_2 \beta_m^* + \Phi_3 = 0. \quad (32)$$

Let

$$\Phi_0 = 1, \Phi_1 = \frac{Q^*}{C}(1 - R_w), \Phi_2 = \frac{T_1}{C}(1 - R_f), \Phi_3 = \chi(1 - R_{hv}).$$

where:

$$\left. \begin{aligned} R_{nv}^2 &= R_{nq} + R_{vq} = \frac{\beta\Lambda_h}{\mu_h(\gamma + \delta_h + \mu_h)} + \frac{\lambda\Lambda_v}{(\alpha + \delta_v + \mu_v)}, \\ C &= \beta\lambda^2 [\mu_v(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\sigma_v] [\mu_h(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\sigma_h], \\ G_1 &= \lambda^2(\gamma + \delta_h + \mu_h)(\mu_h + \sigma_h) [\mu_v(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\sigma_v], \\ G_2 &= \beta\lambda [\mu_h(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\sigma_h] F_3(\mu_v + \delta_v)(\tau + \mu_v)(\alpha + \delta_v + \mu_v), \\ Q^* &= G_1 + G_2, \\ R_w^2 &= \frac{G_1 R_{nq} + G_2 R_{vq}}{Q^*}, \\ F_1 &= \lambda\mu_h(\mu_h + \sigma_h)(\gamma + \delta_h + \mu_h) [\mu_v(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\sigma_v], \\ F_2 &= \beta\mu_h(\alpha + \delta_v + \mu_v)(\mu_v + \sigma_v) [\mu_h(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\sigma_h], \\ F_3 &= [\mu_v(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\sigma_v] + \alpha\mu_v, \\ T_1 &= \lambda [\mu_h(\mu_h + \sigma_h)(\gamma + \delta_h + \mu_h) [\mu_v(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\sigma_v]] \\ &\quad - [\Lambda_v(\mu_v + \sigma_v) + \beta\Lambda_h\alpha\mu_v\sigma_v(\mu_h + \sigma_h) + (\alpha + \delta_v + \mu_v)(\mu_v + \sigma_v)], \\ \chi &= \frac{\mu_h\mu_v(\mu_v + \sigma_v)(\mu_h + \sigma_h)(\alpha + \delta_v + \mu_v)(\gamma + \delta_h + \mu_h)}{\beta\lambda^2 [\mu_v(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\sigma_v] [\mu_h(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\sigma_h]}, \\ R_f^2 &= \frac{F_1^2 R_{nq} + F_2^2 R_{vq}}{T_1}, \end{aligned} \right\} (33)$$

Table 4. Possible positive real roots of $P(\beta_m^*)$ for $R_{hv} > 1$ and $R_{nv} < 1$.

Cases	Φ_0	Φ_1	Φ_2	Φ_3	R_{nv}	No. of sign change	No. of positive real roots
1	+	+	+	+	$R_{nv} < 1$	0	0
2	+	+	+	-	$R_{nv} > 1$	1	1
3	+	+	-	+	$R_{nv} < 1$	2	0.2
4	+	+	-	-	$R_{nv} > 1$	1	1
5	+	-	-	+	$R_{nv} < 1$	2	0.2
6	+	-	-	-	$R_{nv} > 1$	1	1
7	+	-	+	+	$R_{nv} < 1$	2	0.2
8	+	-	+	-	$R_{nv} > 1$	3	1.3

Remark. The system in Equation (3) is said to have an EE, (E^*), if $R_{nv} > 1$. This is satisfied by cases (2, 4, 6) as shown in **Table 4**. The system in (3) can have more than one EE point if $R_{nv} > 1$. This is satisfied by case (8) as shown in **Table**

4. The system in (3), has more than one equilibrium point if $R_{hv} > 1$, as satisfied by case (3, 5, 7).

3.7. Global Stability of Endemic Equilibrium

In this section, the global behaviour of the system in (3) is analysed.

Theorem 4. *The system of differential equations in Equation (3), is said to have a unique endemic equilibrium if $R_{hv} > 1$, and it is globally asymptotically stable.*

The EE can only exist if and only if $R_{hv} > 1$. So by letting $R_{hv} > 1$, it implies that the EE exists.

Considering the Lyapunov function defined by:

$$\begin{aligned} L(S_h^*, I_h^*, R_h^*, S_v^*, I_v^*, R_v^*) &= \left(S_h - S_h^* - S_h^* \ln \frac{S_h}{S_h^*} \right) + \left(I_h - I_h^* - I_h^* \ln \frac{I_h}{I_h^*} \right) \\ &+ \left(R_h - R_h^* - R_h^* \ln \frac{R_h}{R_h^*} \right) + \left(S_v - S_v^* - S_v^* \ln \frac{S_v}{S_v^*} \right) \\ &+ \left(I_v - I_v^* - I_v^* \ln \frac{I_v}{I_v^*} \right) + \left(R_v - R_v^* - R_v^* \ln \frac{R_v}{R_v^*} \right) \end{aligned} \quad (34)$$

Computing the derivative of L along the solution of the system in (3) directly;

$$\begin{aligned} \frac{dL}{dt} &= \left(\frac{S_h - S_h^*}{S_h} \right) \frac{dS_h}{dt} + \left(\frac{I_h - I_h^*}{I_h} \right) \frac{dI_h}{dt} + \left(\frac{R_h - R_h^*}{R_h} \right) \frac{dR_h}{dt} \\ &+ \left(\frac{S_v - S_v^*}{S_v} \right) \frac{dS_v}{dt} + \left(\frac{I_v - I_v^*}{I_v} \right) \frac{dI_v}{dt} + \left(\frac{R_v - R_v^*}{R_v} \right) \frac{dR_v}{dt} \end{aligned} \quad (35)$$

Hence:

$$\begin{aligned} \frac{dL}{dt} &= \left(\frac{S_h - S_h^*}{S_h} \right) \left[\Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h \right] \\ &+ \left(\frac{I_h - I_h^*}{I_h} \right) \left[\beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h \right] \\ &+ \left(\frac{R_h - R_h^*}{R_h} \right) \left[\gamma I_h - (\sigma_h + \mu_h) R_h \right] \\ &+ \left(\frac{S_v - S_v^*}{S_v} \right) \left[\Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v \right] \\ &+ \left(\frac{I_v - I_v^*}{I_v} \right) \left[\beta_m^* \lambda S_v - \alpha I_v - (\mu_v + \delta_v) I_v \right] \\ &+ \left(\frac{R_v - R_v^*}{R_v} \right) \left[\alpha I_v - (\sigma_v + \mu_v) R_v \right] \end{aligned} \quad (36)$$

This can also be written as:

$$\begin{aligned}
 \frac{dL}{dt} = & \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h - \frac{\Lambda_h S_h^*}{S_h} + \beta_m^* \beta S_h^* - \frac{\sigma_h R_h S_h^*}{S_h} + \mu_h S_h^* \\
 & + \beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h - \frac{\beta_m^* S_h I_h^*}{I_h} + \gamma I_h^* + \mu I_h^* + \delta I_h^* + \gamma I_h \\
 & - (\sigma_h + \mu_h) R_h - \frac{\gamma_h I_h R_h^*}{R_h} + \sigma_h R_h^* + \mu_h R_h^* + \Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v \\
 & + \sigma_v R_v - \frac{\Lambda_v S_v^*}{S_v} + \beta_m^* \lambda S_v^* - \frac{\sigma_v R_v S_v^*}{S_v} + \mu_v S_v^* + \beta_m^* \lambda S_v - \alpha I_v - \mu_v I_v \\
 & - \delta_v I_v - \frac{\beta_m^* S_v I_v^*}{I_v} + \alpha I_v^* + \mu_v I_v^* + \delta_v I_v^* + \alpha I_v - \sigma_v R_v - \mu_v R_v \\
 & - \frac{\alpha I_v R_v^*}{R_v} + \sigma_v R_v^* + \mu_v R_v^*
 \end{aligned} \tag{37}$$

Given:

$$\frac{dL}{dt} = M - N \tag{38}$$

where M and N are positive and negative respectively.

Therefore:

$$\begin{aligned}
 M = & \Lambda_h + \sigma_h R_h + \mu_h S_h^* + \beta_m^* \beta S_h + \gamma I_h^* + \mu I_h^* + \delta I_h^* + \gamma I_h \\
 & + \sigma_h R_h^* + \mu_h R_h^* + \Lambda_v + \sigma_v R_v + \beta_m^* \lambda S_v^* + \mu_v S_v^* + \beta_m^* \lambda S_v \\
 & + \alpha I_v^* + \mu_v I_v^* + \delta_v I_v^* + \alpha I_v + \sigma_v R_v^* + \mu_v R_v^*
 \end{aligned} \tag{39}$$

and

$$\begin{aligned}
 N = & \mu_h S_h + \frac{\Lambda_h S_h^*}{S_h} + \frac{\sigma_h R_h S_h^*}{S_h} + \gamma I_h + (\mu_h + \delta_h) I_h + \frac{\beta_m^* S_h I_h^*}{I_h} \\
 & + (\sigma_h + \mu_h) R_h + \frac{\gamma_h I_h R_h^*}{R_h} + \beta_m^* \lambda S_v + \mu_v S_v + \frac{\Lambda_v S_v^*}{S_v} \\
 & + \frac{\sigma_v R_v S_v^*}{S_v} + \alpha I_v + \mu_v I_v + \delta_v I_v + \frac{\beta_m^* S_v I_v^*}{I_v} \\
 & + \sigma_v R_v + \mu_v R_v + \frac{\alpha I_v R_v^*}{R_v}
 \end{aligned} \tag{40}$$

Imposing the condition that if $M < N$, then the derivative of the Lyapunov function with respect to time is less than or equal to zero.

If $M < N$, then $\frac{dL}{dt} \leq 0$.

But $\frac{dL}{dt} = 0$, if and only if:

$$S_h = S_h^*, I_h = I_h^*, R_h = R_h^*, S_v = S_v^*, I_v = I_v^*, R_v = R_v^*$$

The largest invariant set in:

$$\left\{ (S_h^*, I_h^*, R_h^*, S_v^*, I_v^*, R_v^*) \in \Phi : \frac{dL}{dt} = 0 \right\} \tag{41}$$

is singleton E^* , where E^* is the EE.

Since all the model parameters are assumed to be non-negative, then the derivative of the Lyapunov function is less than or equal to one, if R_{hv} of the system in (3) is greater than one, ($R_{hv} > 1$). Hence by LaSalle's Invariant Principle, as t approaches infinity, all the solution of the system in (3) approaches the EE point if $R_{hv} > 1$, [25] [26]. Hence, EE is globally asymptotically stable in the invariant set if $M < N$.

4. Sensitivity Analysis of R_{hv}

In this section, we determine the robustness of a model to parameter values. This concept identifies parameters with high impact on R_{hv} . Using the approach in [20] [27] [28], we determine the sensitivity indices of R_{hv} , with respect to parameter values in the model.

In biological models, the value of R_{hv} determines the tendency of the disease to spread within the population. Considering all the parameters of R_{hv} , we compute the sensitivity of R_{hv} to each parameter and are represented in **Table 5**. A positive sensitivity index implies that the parameter contributes to the rise in the basic reproduction number.

Table 5. Sensitivity indices of parameters to R_{hv} .

Parameter	Description	Sensitivity index (+ve/-ve)
Λ_h	Human recruitment rate.	+ve
Λ_v	Animal recruitment rate.	+ve
μ_h	Human death rate.	-ve
μ_v	Animal death rate.	-ve
δ_h	Human Listeriosis induced death rate.	-ve
δ_v	Animal Listeriosis induced death rate.	-ve
α	Animal recovery rate.	-ve
β	Human transmission rate.	+ve
γ	Human rate of recovery.	-ve
λ	Animal transmission rate.	+ve

5. Listeriosis Model Extension to Optimal Control

In this section, we carried out an analysis of optimal control to determine the impact of all intervention of the control schemes. This is derived by incorporating the following controls into the model in (3) and the introduction of an objective functional that seeks to minimise: (u_1, u_2, u_3) , where u_1 denotes prevention of S_h , u_2 denotes treatment of I_h and u_3 denotes treatment of I_v .

By introducing all the controls, the system in model (3) becomes:

$$\left. \begin{aligned} \frac{dS_h}{dt} &= \Lambda_h + \sigma_h - (1-u_1)\beta(I_v + I_h)S_h - \mu_h S_h \\ \frac{dI_h}{dt} &= (1-u_1)\beta(I_v + I_h)S_h - (u_2 + \gamma)I_h - (\delta_h + \mu_h)I_h \\ \frac{dR_h}{dt} &= (u_2 + \gamma)I_h - (\sigma_h + \mu_h)R_h \\ \frac{dS_v}{dt} &= \Lambda_v - (1-u_1)\lambda(I_v + I_h)S_v - (\mu_v S_v + \sigma_v R_v) \\ \frac{dI_v}{dt} &= (1-u_1)\lambda(I_v + I_h)S_v - \alpha I_v - (\delta_v + \mu_v)I_v \\ \frac{dR_v}{dt} &= \alpha I_v - (\sigma_v + \mu_v)R_v \end{aligned} \right\} \quad (42)$$

In epidemiological models, the essence of optimal control analysis is to minimise the spread or number of infections and the cost of treatment, preventive measures and vaccination controls. The objective functional that can be used to achieve this is given by:

$$J = \min_{(u_1, u_2, u_3)} \int_0^{t_f} (B_1 I_v + B_2 I_h + B_3 u_1^2 + B_4 u_2^2 + B_5 u_3^2) dt. \quad (43)$$

subject to the system of differential equations in (3).

Where; B_1, B_2, B_3, B_4, B_5 are weight constants to aid balance terms in integral so as to avoid the dominance of one another. $B_1 I_h, B_2 I_v$, are costs associated with I_h and I_v respectively. $B_3 u_1^2$, is cost associated with prevention of S_h . $B_4 u_2^2$, is costs of treatment of I_h and $B_5 u_3^2$, is cost associated with treatment of I_v . Where, t_f , is period of intervention. Hence, $(B_1 I_h, B_2 I_v)$ denotes a linear function for cost associated with infections and $(B_3 u_1^2, B_4 u_2^2, B_5 u_3^2)$, denotes a quadratic function for the cost associated with controls [29] [30] [31].

Control efforts of model in (3) are by linear combination of $u_i^2(t)$, ($i=1,2$). It is assumed to be a quadratic in nature by the assumption that cost is generally non-linear in nature. Thus, the aim is to minimise the number of infection and reduce cost of treatment. The objective is to find the optimal functions $(u_1^*(t), u_2^*(t), u_3^*(t))$ such that;

$$\begin{aligned} &J(u_1^*(t), u_2^*(t), u_3^*(t)) \\ &= \min_{(u_1, u_2, u_3)} \in \cup J(u_1, u_2, u_3) \end{aligned} \quad (44)$$

where: $\cup = \{u : u, 0 \leq u_i(t) \leq 1, t \in [0, t_f], i=1,2,3\}$ denotes the control set.

Pontryagin's Maximum Principle

This principle provides the necessary conditions that an optimal must satisfy. It changes the system in (3) and Equation (43) into minimisation problem point-wise Hamiltonian (H), with respect to (u_1, u_2, u_3) .

$$\begin{aligned}
 H = & B_1 I_v + B_2 I_h + B_3 u_1^2 + B_4 u_2^2 + B_5 u_3^2 \\
 & + M_{S_h} \{ \Lambda_h + \sigma_h - (1 - u_1) \beta (I_v + I_h) S_h - \mu_h S_h \} \\
 & + M_{I_h} \{ (1 - u_1) \beta (I_v + I_h) S_h - (u_2 + \gamma) I_h - (\delta_h + \mu_h) I_h \} \\
 & + M_{R_h} \{ (u_2 + \gamma) I_h - (\sigma_h + \mu_h) R_h \} \\
 & + M_{S_v} \{ \Lambda_v - (1 - u_1) \lambda (I_v + I_h) S_v - (\mu_v S_v + \sigma_v R_v) \} \\
 & + M_{I_v} \{ (1 - u_1) \lambda (I_v + I_h) S_v - (u_3 + \alpha) I_v - (\delta_v + \mu_v) I_v \} \\
 & + M_{R_v} \{ (u_3 + \alpha) I_v - (\sigma_v + \mu_v) R_v \}
 \end{aligned} \tag{45}$$

where: $M_{S_h}, M_{I_h}, M_{R_h}, M_{S_v}, M_{I_v}, M_{R_v}$ are referred to as the adjoint variables.

The adjoint (co-state) variables are solutions of adjoint systems below:

$$\left. \begin{aligned}
 \frac{dM_{S_h}}{dt} &= \left((1 - u_1) (I_v + I_h) \beta (M_{S_h} - M_{I_h}) + \mu_h M_{S_h} \right) \\
 \frac{dM_{I_h}}{dt} &= -B_2 + (1 - u_1) \beta S_h (M_{S_h} - M_{I_h}) + (u_2 + \gamma) (M_{I_h} - M_{R_h}) \\
 &\quad + (\mu_h + \delta_h) M_{I_h} + (1 - u_1) \lambda S_v (M_{S_v} - M_{I_v}) + b \lambda V_v (M_{V_v} - M_{I_v}) \\
 \frac{dM_{R_h}}{dt} &= -\sigma_h M_{S_h} + (\sigma_h + \mu_h) M_{R_h} \\
 \frac{dM_{S_v}}{dt} &= (1 - u_1) \lambda (I_v + I_h) (M_{S_v} - M_{I_v}) + \mu_v M_{S_v} \\
 \frac{dM_{I_v}}{dt} &= -B_1 + (1 - u_1) \beta S_h (M_{S_h} - M_{I_h}) + (1 - u_1) \lambda S_v (M_{S_v} - M_{I_v}) \\
 &\quad + (\mu_v + \delta_v) M_{I_v} + (u_4 + \alpha) (M_{I_v} - M_{R_v}) \\
 \frac{dM_{R_v}}{dt} &= -\sigma_h M_{S_v} + (\sigma_v + \mu_v) M_{R_v}
 \end{aligned} \right\} \tag{46}$$

This satisfies the transversality condition:

$$M_{S_h}(t_f) = M_{I_h}(t_f) = M_{R_h}(t_f) = M_{S_v}(t_f) = M_{I_v}(t_f) = M_{R_v}(t_f) = 0. \tag{47}$$

By combining the Pontryagin’s Maximum Principle and the existence of the optimal control [32] [33] [34].

Theorem 5. *The optimal control vector $(u_1^*(t), u_2^*(t), u_3^*(t))$ that maximises the objective function (J) over \cup , given by:*

$$\left. \begin{aligned}
 u_1^*(t) &= \max \left\{ 0, \min \left(1, \frac{\beta (M_{I_h} - M_{S_h}) (I_v + I_h) S_h^*}{2B_3} + \frac{\lambda (M_{I_v} - M_{S_v}) (I_v + I_h) S_v^*}{2B_3} \right) \right\} \\
 u_2^*(t) &= \max \left\{ 0, \min \left(1, \frac{(M_{I_h} - M_{R_h}) I_h^*}{2B_4} \right) \right\} \\
 u_3^*(t) &= \max \left\{ 0, \min \left(1, \frac{(M_{I_v} - M_{R_v}) I_v^*}{2B_5} \right) \right\}
 \end{aligned} \right\} \tag{48}$$

where: $M_{S_h}, M_{I_h}, M_{R_h}, M_{S_v}, M_{I_v}, M_{R_v}$ are the solutions of Equation (46) and (47).

Proof. The existence of an optimal control is as a result the convexity of the integral of J with respect to u_1, u_2 and u_3 , the Lipschitz property of the state system with respect to the state variables and a priori Boundedness of the state solutions [33]. The system in (46) was obtained by differentiating the Hamiltonian function and evaluated at optimal control. However, by equating the derivatives of the Hamiltonian with respect to the controls to zero, the following are obtained:

$$\left. \begin{aligned} u_1 = \tilde{u}_1 &:= \left\{ \left(\frac{\beta(M_{I_h} - M_{S_h})(I_v + I_h)S_h^*}{2B_3} + \frac{\lambda(M_{I_v} - M_{S_v})(I_v + I_h)S_v^*}{2B_3} \right) \right\} \\ u_2 = \tilde{u}_2 &:= \left\{ \left(\frac{(M_{I_h} - M_{R_h})I_h^*}{2B_4} \right) \right\} \\ u_3 = \tilde{u}_3 &:= \left\{ \left(\frac{(M_{I_v} - M_{R_v})I_v^*}{2B_5} \right) \right\} \end{aligned} \right\}$$

In conclusion, by standard control arguments involving bounds on controls:

$$\left. \begin{aligned} u_1^* &= \begin{cases} 0, & \text{if } \tilde{u}_1 \leq 0 \\ \tilde{u}_1 & \text{if } 0 < \tilde{u}_1 < 1 \\ 1 & \text{if } \tilde{u}_1 \geq 1 \end{cases} \\ u_2^* &= \begin{cases} 0, & \text{if } \tilde{u}_2 \leq 0 \\ \tilde{u}_2 & \text{if } 0 < \tilde{u}_2 < 1 \\ 1 & \text{if } \tilde{u}_2 \geq 1 \end{cases} \\ u_3^* &= \begin{cases} 0, & \text{if } \tilde{u}_3 \leq 0 \\ \tilde{u}_3 & \text{if } 0 < \tilde{u}_3 < 1 \\ 1 & \text{if } \tilde{u}_3 \geq 1 \end{cases} \end{aligned} \right\} \tag{49}$$

The system in (48) leads to system in (47) in Theorem (5). The optimal control uniqueness for small t_f was gotten as a result of the Lipschitz structure of system of equations and the priori boundedness of the state solutions and adjoint functions. Existence of optimal control uniqueness is in line with uniqueness of optimal system, that comprises of Equations (3), (46), (47) and (48) [20] [22].

6. Numerical Results

In this section, the optimal system was solved using Range-Kutta fourth order scheme. This was done by solving the state systems, adjoints equations and the transversality conditions.

This is a two point boundary value problem and it has two separate boundary conditions at times $t = 0$ and $t = t_f$. The objective is to solve for the value, $t_f = 120$ days. This was chosen on the basis of the assumption that a period of

four month is enough for the disease spread.

Numerical simulation was done by solving the state equations of the model in **Figure 2** using Range-Kutta fourth order scheme by making a guess on controls over a simulated time.

Secondly, the use of current iteration of state equations of **Figure 2**, the adjoint equations and the transversality conditions by a backward method. These controls are then updated by use of convex combination of controls in the previous iterations and values from characterizations of the system.

This process is repeated and iteration is stopped when values of unknowns at the previous iteration are close to those at present iteration [35].

The following combinations of optimal control were considered and the best three most effective selected: Treatment and prevention of humans, treatment of animals and prevention of humans, treatment of animals and humans, prevention of humans and treatment of animals, treatment and prevention of humans, Prevention of humans only, treatment animals only and treatment humans only.

Table 6 shows values of parameters and variables used in the simulation of the model in **Figure 2**. Some of these parameters were assumed and others taken from published data.

Table 6. Variable and parameter values of Anthrax model.

Parameter	Value	Reference
μ_h	0.004	assumed
δ_h	0.2	[31]
Λ_v	0.0273	assumed
Λ_h	0.1	assumed
μ_v	0.002	assumed
δ_v	0.30	[31]
α	0.002	assumed
β	0.200	assumed
λ	0.270	[31]
b	0.005	assumed

6.1. Strategy 1: Optimal Prevention of Humans and Treatment of Animals

Objective functional is optimised by using the prevention control on humans, (u_1) and the treatment control on animals (vector), (u_3) by setting treatment control on humans to zero. **Figure 3** shows significant reduction in the number of infected animals (vectors), (I_v) and infected humans, (I_h). **Figure 4** shows the dynamics of recovery. The epidemiological implication; the spread of Listeriosis can be tackled effectively through treatment of animals and prevention of humans. Hence, there should be effective prevention of humans as well as treatment of animals (vectors) in the system.

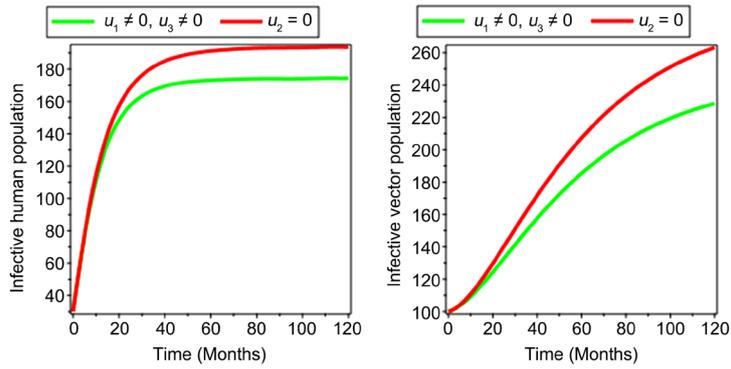


Figure 3. Simulation of Listeriosis model: optimal prevention of humans and treatment of animals.

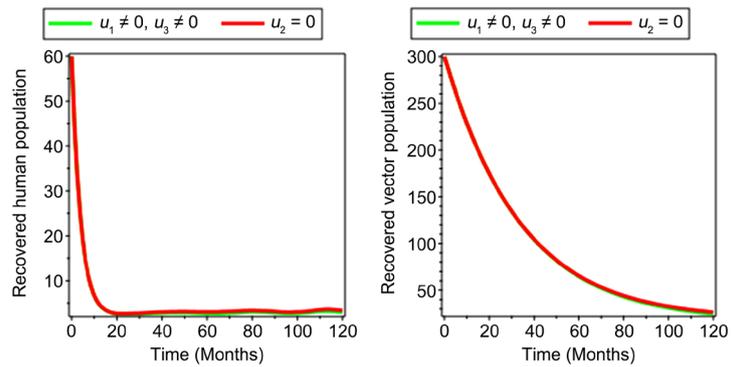


Figure 4. Simulation of Listeriosis model: optimal treatment of animals and prevention of humans.

6.2. Strategy 2: Optimal Prevention of Humans and Treatment of Humans

The treatment control, (u_2) of infected humans and prevention of humans, (u_1) were used in optimising the objective functional and setting (u_3) to zero. **Figure 5** shows that this strategy has caused a substantial reduction in the number of infected animals, (I_v) and infected humans, (I_h) drastically. **Figure 6** showed the dynamics of the recovered population. In order to achieve this optimal strategy, there should be more treatment of infected humans and prevention of susceptible humans.

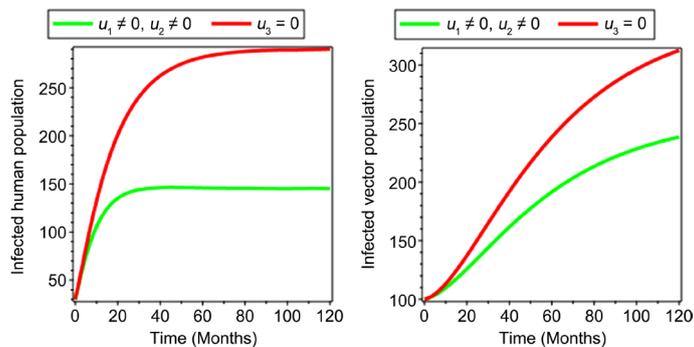


Figure 5. Optimal treatment of infected humans and prevention of susceptible humans.

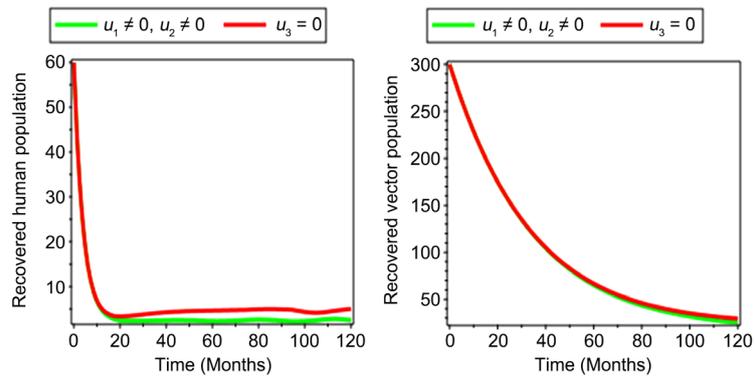


Figure 6. Optimal treatment of infected humans and prevention of susceptible humans.

6.3. Strategy 3: Optimal Treatment of Animals and Treatment of Humans

The objective functional was optimised by using (u_3) and (u_2) and setting the prevention control on humans, (u_1) to zero. This strategy resulted in reduction of both infected animals, (I_v) and humans, (I_h) as indicated in Figure 7. Biological implication; Listeriosis can be controlled by frequent treatment of animals and humans simultaneously. Moreover, Figure 8 shows the dynamics of the recovered populations.

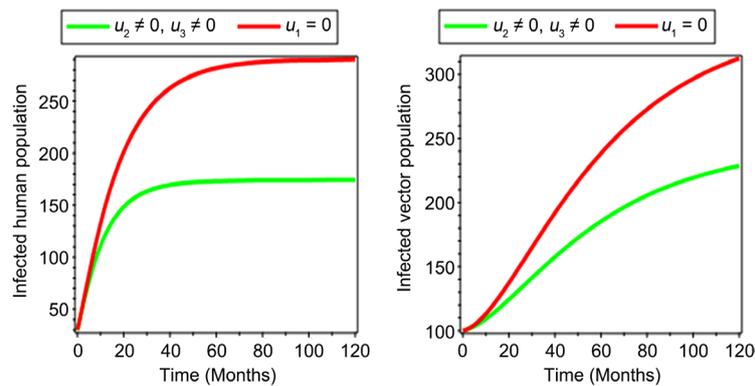


Figure 7. Simulation of model: optimal treatment of infected animals and treatment of humans.

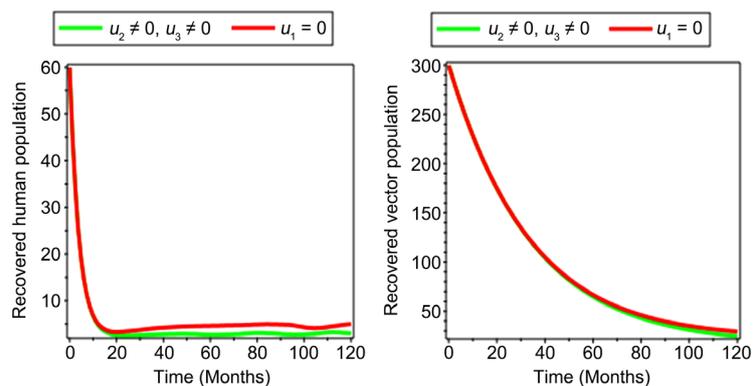


Figure 8. Simulation of model: optimal treatment of animals and treatment of humans.

7. Analysis of Cost Effectiveness

In this section, we conduct an analysis of cost effectiveness to justify the benefits associated with treatment of humans, prevention of humans and treatment of animals. We consider infection averted ratio (IAR) approach and incremental cost effectiveness ratio (ICER) approach.

7.1. Intervention Averted Ratio (IAR)

This is the ratio of number of infection averted to the number of recovered. Infection averted refers to the difference in infected population without control to infected population with control. The ratio for each strategy was computed by using the parameter values of the model. Strategy with highest ratio is considered the most effective intervention to be implemented.

$$\text{IAR} = \frac{\text{Number of infection averted}}{\text{Number of recovered}} \quad (50)$$

Table 7 reveals (IAR) for each intervention strategy. Strategy 3 has highest ratio as shown in **Table 7** and **Figure 9** and therefore considered the best intervention to be implemented in combating the infection in the system. Strategy 2 has the second highest ratio and should be a priority in a situation where two alternative strategies were to be considered. We can conclude that treatment of infected humans and animals should be a priority intervention in fighting the spread of Listeriosis infection. This can be achieved by educating farmers on the need to report any sign of Listeriosis infection for treatment. Health authorities should as well educate the public on the need to treat any suspected Listeriosis infection. Moreover, since prevention and treatment control on humans has the second highest ratio, there should be campaign on prevention and treatment of Listeriosis on humans.

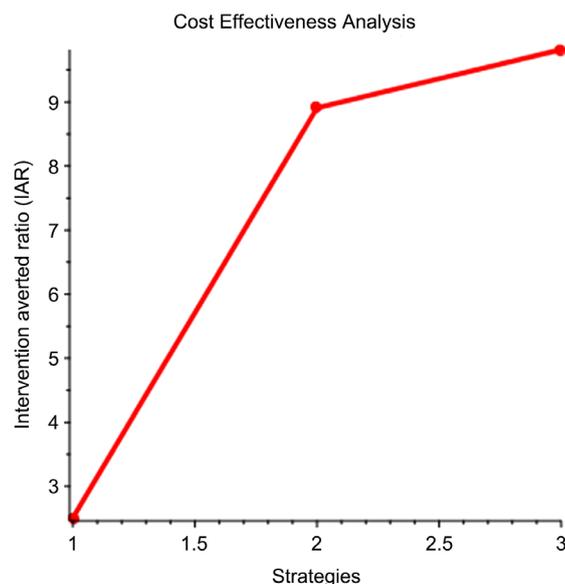


Figure 9. A plot of strategies against infection averted ratio.

Table 7. Infection averted ratio.

Strategy	Total infection averted	Infection Averted Ratio (IAR)
1	75.3510	2.5117
2	240.5533	8.9094
3	216.1587	9.8182

7.2. Incremental Cost Effectiveness Ratio (ICER)

It can be both labour and cost intensive to eradicate a disease in an environment. It is therefore important to consider the best intervention strategy to be implemented. This calls for cost effectiveness analysis to determine the most intervention approach to be used. We can obtain this by comparing the various costs and benefits of these interventions. The analysis of ICER assumes that the costs of the various interventions are proportional to the number of controls employed. Competing strategies are usually compared incrementally by comparing one strategy to the next less effective alternative. The total cost function for each strategy is computed from the various costs functions.

$$\text{ICER} = \frac{\text{Differences in averted cost between strategies}}{\text{Differences in total infection averted between strategies}}$$

Generally, ICER is applied by first arranging all strategies in increasing order of infection averted as shown in **Table 8**.

Table 8. Total infected averted and total cost.

Strategy	Total infection averted	Total cost
1	75.3510	2621.2517
3	216.1587	3115.0574
2	240.5533	3298.0511

ICER is implemented by simulating the model with all the interventions or strategies. The control strategies are then ranked in increasing order of effectiveness depending on infections averted.

Considering strategy A as the base line and comparing ICER (1) and ICER (3);

$$\text{ICER (1)} = \frac{2621.2517}{75.3510} = 34.7872$$

and

$$\text{ICER (3)} = \frac{3115.0574 - 2621.2517}{216.1587 - 75.3510} = 3.5070$$

Comparing the ICER for 1 and 3, we reject intervention strategy 1 since it is most expensive to implement as compared to strategy 3. It saves 3.5070 more than strategy 1.

Now comparing strategy 3 and 2 by computing the ICER (3) and ICER (2);

$$\text{ICER (3)} = \frac{3115.0574}{216.1587} = 14.4110$$

and

$$\text{ICER (2)} = \frac{3298.0511 - 3115.0574}{240.5533 - 216.1587} = 7.5014$$

Comparing ICER (2) and ICER (3), we reject intervention strategy 3 since it is most expensive to implement as compared to strategy 2. It saves 7.5014 more than strategy 3. In conclusion, the most expensive intervention strategy to implement is the prevention of humans and treatment of infected animals, strategy 1. However, the most effective and less cost strategy to be implemented is the prevention of susceptible humans and treatment of infected humans, strategy 2.

8. Conclusions

It was established that the model exhibited existence of multiple endemic equilibria. The epidemiological implications are that, effective control of Listeriosis can be achieved if R_{nv} , is less than unity.

We then carried out the sensitivity analysis of the basic reproduction number, (R_{nv}). This analysis showed that, increasing livestock recovery rate, would cause a decrease in the basic reproduction number, (R_{nv}). Moreover, decreasing livestock recovery rate, would increase the basic reproductive number, (R_{nv}). Also, increasing human transmission rate and livestock transmission rate, would cause an increase in the basic reproduction number, (R_{nv}) and decreasing human transmission rate and livestock transmission rate, would cause a corresponding decrease in the basic reproduction number, R_{nv} .

The rate of Listeriosis infection can be reduced by ensuring that the rate of interaction between susceptible humans and infected animals, (β) is minimised. Moreover, the spread of Listeriosis infection can be curbed by reducing the rate of interaction between susceptible animals and contact with infected animals.

The qualitative analysis of optimal control was performed and the necessary conditions for the optimality of Listeriosis disease were analysed. The three most effective strategies according to our model are as follows: the combination of treatment of infected vectors, (I_v) and treatment of infected humans, (I_h), the combination of prevention of susceptible humans, (S_h) and the treatment of infected animals, (I_v) and the combination of prevention of susceptible humans, (S_v) and the treatment of infected humans, (I_v).

The best and most effective intervention approach is strategy 3 as shown in **Table 7**. Strategy 2 has the second highest ratio and should be a priority in a situation where two alternative strategies were to be considered. We can conclude that the treatment of infected humans and animals should be a priority intervention in fighting the spread of Listeriosis infection. Alternatively, by implementing the incremental cost effectiveness ratio, the best intervention strategy to be considered is strategy 2.

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Data Availability Statement

The data supporting this compartmental model analysis are from National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Services (NHLS), South Africa. Some of the parameter values are assumed and others are taken from published articles and are cited in **Table 3** of this paper. These published articles are also cited at relevant places within the text as references.

Conflict of Interest

We declare that there is no conflict of interest regarding the publication of this paper.

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