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MATHEMATICAL MODELLING OF LISTERIOSIS EPIDEMICS IN ANIMAL AND HUMAN POPULATION WITH OPTIMAL CONTROL

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Abstract. Listeriosis is a serious disease caused by the germ Listeria monocytogenes. People usually become ill with listeriosis after eating contaminated food including meat. The disease primarily affects pregnant women, newborns, older adults, and people with weakened immune systems. In this paper, we propose and scrutinize a model problem describing the transmission dynamics of Listeriosis epidemic in animal and human population using the stability theory of differential equations. The model is qualitatively analysed for the basic reproduction number as well as possibility of forward and backward bifurcation with respect to the stability of disease free and endemic equilibria. The impact of the model parameters on the disease was evaluated via sensitivity analysis. An extension of the model to include time dependent control variables such as treatment, vaccination and education of susceptible (human) is carried out. Using Pontryagin's Maximum Principle, we obtain the optimal control strategies needed for combating Listeriosis disease. Numerical simulation of the model is performed and pertinent results are displayed graphically and discussed quantitatively.

1. Introduction

Listeria monocytogenes is the causative agent of Listeriosis. The organism was initially described as a cause of epizootics in veld rodents from South Africa (Tiger River disease) by Pier and in 1926, [17]. Most clinical descriptions of both human and animal infection caused by listeria monocytogenes were published in the 1920s; But, the organism remained a laboratory problem until the World War II period, when it was known to be the major cause of neonatal sepsis and meningitis (25). Listeria monocytogenes can be found mostly 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, immunosuppression and as the individual ages [26].

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However, few studies have been undertaken to model Listeriosis mathematically. Most bacteria are usually useful in the food processing industries [30]. They are useful in the production of cheese, chemicals, yogurt and medicines. Bacteria play important roles to manufacture and synthesize food particles in the digestive system to produce energy. However, most zoonotic diseases that are bacteria related can be treated by antibiotics. Some of the diseases usually caused by bacteria are meningitis, gonorrhea, pneumonia, gastritis and anthrax. Also, bacteria organisms are responsible for many zoonotic diseases [32].

Listeriosis is the major cause of encephalitis in ruminants. This encephalitis is usually refereed to as "circling disease" because it occurs in the hind brain and can lead to ataxia in infected animals before death [25]. 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 to speculate that food borne infection could be responsible for human Listeriosis [25]. 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 [23]. Complex transmission dynamics of some diseases such as periodic orbits, Hoff bifurcations and multiple equilibrium have been described [7, 14].

A study conducted by [21] showed that Listeria monocytogenes is a food borne 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 [10], 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 cases of human Listeriosis.

Investigations conducted by [15]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 [22] showed that Listeria monocytogenes is among the food borne 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. [19, 29].

In an article published by [16], Listeriosis in human are rare but it is among the top serious food borne diseases in susceptible and vulnerable individuals in a population such as the immune compromised and pregnant women. The resurgence of food borne Listeriosis

was investigated by [1]. The significance of separating the pathogens as a necessary requirement for a correct epidemiological research and eradicating transmission can not be overemphasised. Moreover, [4], stated Listeriosis as one of leading causes of death from food borne pathogens. The disease continues to spread and cause sporadic outbreaks of illness.

Investigation of many huge epidemics of Listeriosis revealed that transmission of listeria monocytogenes in food are responsible for human diseases in the early 1980s [27]. An investigation conducted by [9] showed that listeria monocytogenes are the causative agent of gastrointestinal. The intestinal tract can be the main point of entry for Listeria monocytogenes. [3] conducted a research on the identification and reservours of pathogens for effective control of sporadic disease and epidemics. The dairy farm has been observed as a potential point and reservour for listeria monocytogenes.

Frequent diagnostic test, the availability of clinical data and electronic surveillance has facilitated the applications of mathematical models to critical examining of scientific hypotheses and the design of real-life strategies of controlling diseases [6, 8]. The increasing interest in mathematical modeling is as a result of emerging and reemerging of infectious diseases. Model can predict the relationship between diseases and also determine whether the associated diseases will spread through the population or die out [12, 19, 28]. Moreover, mathematical models can also estimate the effects, impact of a control measure and outline useful strategies to public health and government agencies for the eradication of diseases [2, 8].

2. Listeriosis model description and formulation

In this section, we divide the model into two parts, the total human and vector populations. These populations at any time, (t) are also divided into seven sub-populations (compartments) with respect to their disease status in the system as shown in Figure 1. The total human population also represented by N_h, is divided into sub-populations of Susceptible humans, S_h, Infected humans, I_h, and Recovered humans, R_h. The total human population is given by: $N_h(t) = S_h(t) + I_h(t) + R_h(t)$. The total vector population, represented by N_v, is divided into sub-populations of Susceptible vector, S_v, Infectious vector, I_v, Vaccinated vector, V_v, and Recovered vector, R_v. The total vector population becomes: $N_v(t) = S_v(t) + V_v(t) + I_v(t) + R_v(t)$.

The susceptible human compartment, S_h , include individuals who are at risk of developing an infection from the Listeriosis disease. Infectious human compartment I_h includes individuals that are showing the symptoms of the disease. The recovered human class, R_h , are those individuals who have recovered from the disease and got temporal immunity. The susceptible vector, S_v; these include animals(livestock) that are at risk of developing an infection from the Listeriosis. Vaccinated vector compartment, V_v are made up of animals(livestock)

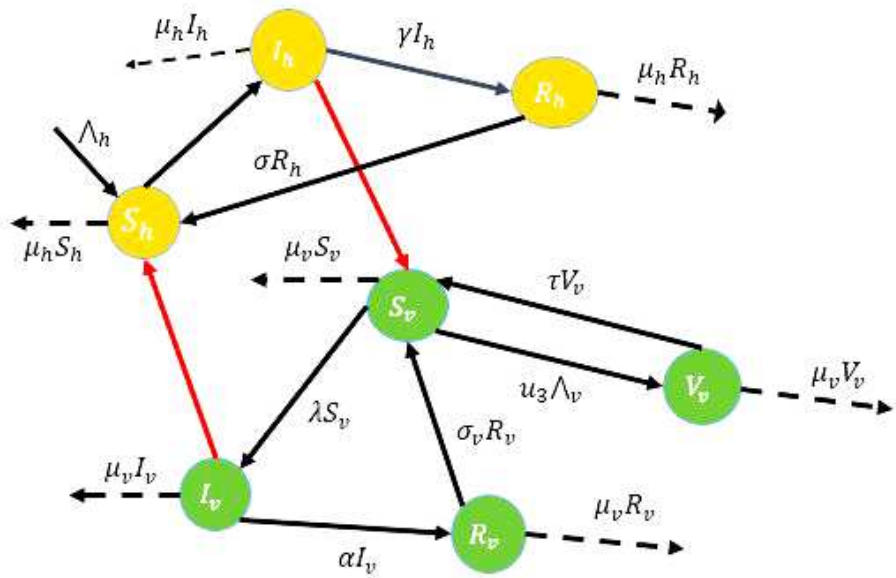

Figure 1: Flow diagram for the Listeriosis disease transmission. The gold balls indicates the human compartments and the green colour indicates the animal compartments.

that are vaccinated before Listeriosis out break. The infectious vector, I_v ; this compartment consists all animals(livestock) that are showing the symptoms of Listeriosis. The recovered vector, R_v ; these compartment is made up of animals(livestock) that have recovered from Listeriosis and got temporal immunity.

The Susceptible humans are recruited into the population at a rate, Λ_h. They are infected by the Listeriosis through ingestion of contaminated foods from infected animals, inhalation of spores and contact with infectious animals and humans at a rate $(I_v + I_h\beta)$. Infected individuals recover from the disease at a rate γ. Moreover, humans infected with the disease are treated under control at a rate $u_2(t)$ and the rate of efforts on prevention is given by $u_1(t)$. Individuals who are infected with Listeriosis die at a rate δ_h and they may loose immunity after recovery and return to the susceptible compartment at a rate σ_h. Natural death rate of all the human compartments is μ_h.

Susceptible vector population S_v are usually recruited into the population at a rate Λ_v, but a fraction of the animals are successfully vaccinated at a rate u_3, where $u_3 \in [0,1]$. Listeriosis can be acquired through contacts with infectious animals and humans at a rate $(I_v + I_h\lambda)$ and animals with Listeriosis are treated under control at a rate $u_4(t)$. The natural death rate of the animals is μ_v and the death rate as a result of the disease is δ_v. The animals recover at a rate α and a fraction of the vaccinated animals may move to the infected animal compartment at a rate $b\beta_m^*\lambda$ due to waning effect. Where $(1-b) \in [0,1]$ is the efficacy of the vaccine.

This is because the animals may loose immunity and move back to the susceptible compartment at a rate τ. Where, $\beta_m^* = I_h + I_v$. Incorporating the control efforts in the our model in Figure 1, we obtained the following system of ordinary differential equations:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \sigma_h R_h - (1-u_1)\,\beta_m^* \beta S_h - \mu_h S_h \\
\frac{dI_h}{dt} &= (1-u_1)\,\beta_m^* \beta S_h - \left(u_2+\gamma\right) I_h - \left(\mu_h+\delta_h\right) I_h \\
\frac{dR_h}{dt} &= \left(u_2+\gamma\right) I_h - \left(\sigma_h+\mu_h\right) R_h \\
\frac{dS_v}{dt} &= (1-u_3)\,\Lambda_v - (1-u_1)\,\beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v \\
\frac{dI_v}{dt} &= (1-u_1)\,\beta_m^* \lambda S_v + (1-u_1)\,b\beta_m^* \lambda V_v - (u_4+\alpha)\,I_v - \left(\mu_v+\delta_v\right) I_v \\
\frac{dR_v}{dt} &= (u_4+\alpha)\,I_v - \left(\sigma_v+\mu_v\right) R_v \\
\frac{dV_v}{dt} &= u_3 \Lambda_v - \left(\tau+\mu_v\right) V_v - (1-u_1)\,b\lambda\beta_m^* V_v
\end{aligned}\right\} \tag{2.1}$$

3. Analysis of the Listeriosis model

3.1. Positivity and boundedness of solutions

In this section, our objective or goal is to show that the solutions are non-negative because we are dealing with human population model. The conditions under which a system of differential equations under study has non-negative solutions is of paramount importance when dealing with human population models. Our Listeriosis model is epidemically meaningful on condition that all the solutions with non-negative initial data remain non-negative at every point in time. We apply the concept of a derivative of a function. The derivative of a function at a point determines the behaviour of that particular function. If the derivative of a function at a point is positive, we can conclude that the function is said to be increasing at that point. If the derivative of the function at a point is negative, we can conclude that the function is decreasing and if the derivative at any point is equal to zero, we say that the function is constant.

Theorem 1. *Let* $\Theta = \{(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t)) \in \mathbb{R}_+^7 :$

$$(S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), V_v(0), R_v(0)) > 0\},$$

then the solution of $\{(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t))\}$ *are non-negative for all time* $t \geq 0$.

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

The total human population at any time $(t)$is given by:

$$N_h(t) + NS_h(t) + I_h(t) + R_h(t). \tag{3.1}$$

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt}$$

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

When there are no mortality due to Listeriosis infections, the above equation becomes;

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

Solving the above differential equation;

$$\Lambda_h - \mu_h N_h \geq Ae^{-\mu_h t}, \text{ where } A \text{ is constant.}$$

$$N_h(0) = N_{h(0)},$$

$$\Lambda_h - \mu_h N_{h(0)} = A$$

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

As $t \to \infty$, the population size, $N_h \to \dfrac{\Lambda_h}{\mu_h}$.

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

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

$$\Theta_h = \{(S_h, I_h, R_h) \in \mathbb{R}_3^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h}. \tag{3.2}$$

The total vector(livestock) population at any time $(t)$is given by:

$$N_v(t) = S_v(t) + V_v(t) + I_v(t) + R_v(t). \tag{3.3}$$

$$\frac{dN_v}{dt} = \frac{dS_v}{dt} + \frac{dV_v}{dt} + \frac{dI_v}{dt} + \frac{dR_v}{dt}.$$

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

If there are no mortality due to Listeriosis infections; $\dfrac{dN_v}{dt} \leq \Lambda_v - \mu_v N_v$.

Solving the above;

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

As $t \to \infty$, the population size, $N_v \to \dfrac{\Lambda_v}{\mu_v}$.

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

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

$$\Theta_v = \left\{ (S_v, I_v, R_v, V_v) \in \mathbb{R}_+^4 : S_v + I_v + R_v + V_v \le \frac{\Lambda_v}{\mu_v} \right\}. \tag{3.4}$$

The feasible region for the system of ordinary differential equations in (0.3.1) is given by:

$$\Theta = \Theta_h \times \Theta_v \subset \mathbb{R}_+^3 \times \mathbb{R}_4^4. \tag{3.5}$$

Where , $\Theta_h = \{(S_h, I_h, R_h) \in \mathbb{R}_3^3 : S_h + I_h + R_h \le \dfrac{\Lambda_h}{\mu_h}$ and

$$\Theta_v = \left\{ (S_v, I_v, R_v, V_v) \in \mathbb{R}_+^4 : S_v + I_v + R_v + V_v \le \frac{\Lambda_v}{\mu_v} \right\}.$$

Where Θ is positively invariant.

3.2. Disease-free equilibrium for the Listeriosis model

The disease-free equilibrium of the system of ordinary differential equations in (2.1) only exists when $u_1 = 0$ and all other controls are held constant. By setting the system of differential equations in (2.1) to zero:

$$\frac{dS_h}{dt} = \Lambda_h + \sigma_h R_h - (1-u_1)\beta_m^* \beta S_h - \mu_h S_h = 0. \tag{3.6}$$

$S_h^* = \dfrac{\Lambda_h}{\mu_h}$.

At disease free equilibrium (DFE), there are no infections and recovery.

$$\frac{dV_v}{dt} = u_3 \Lambda_v - (\tau + \mu_v) V_v - (1-u_1) b\lambda \beta_m^* V_v = 0 \tag{3.7}$$

$V_v^* = \dfrac{u_3 \Lambda_v}{\tau + \mu_v}$.

$$\frac{dS_v}{dt} = (1-u_3)\Lambda_v - (1-u_1)\beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v = 0 \tag{3.8}$$

$S_v^* = \dfrac{(1-u_3)\Lambda_v + \tau V_v}{\mu_v}$. But $V_v^* = \dfrac{u_3 \Lambda_v}{\tau + \mu_v}$.

$$\xi_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v(\tau + \mu_v(1-u_3))}{\mu_v(\tau + \mu_v)}, 0, 0, \frac{u_3 \Lambda_v}{\tau + \mu_v} \right). \tag{3.9}$$

3.3. The basic reproductive number

In this section, we use the Next Generation Matrix approach to determine the linear stability of the disease-free equilibrium (ξ_0). The basic reproductive number or rate is the number of secondary cases produced on average by one infected animal or person when all are susceptible. It combines the biology of infections with the social and behaviour of the factors influencing contact rate. The basic reproduction rate gives the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individuals [18, 31]. The basic reproductive number is the threshold parameter that governs the spread of a disease. The next-generation matrix is defined as; $K = FV^{-1}$ and $R_0 = \rho\left(FV^{-1}\right)$. Where $\rho\left(FV^{-1}\right)$ denotes the spectral radius of FV^{-1}. The basic reproductive number R_0, is defined as the spectral radius of the next-generation matrix.

Considering only the infective classes in the system of differential equations in (2.1):

$$\left.\begin{aligned}\frac{dI_h}{dt} &= (1-u_1)(I_h+I_v)\beta S_h - \left(u_2+\gamma\right)I_h - \left(\mu_h+\delta_h\right)I_h \\ \frac{dI_v}{dt} &= (1-u_1)(I_h+I_v)\lambda S_v + (1-u_1)(I_h+I_v)b\lambda V_v - (u_4+\alpha)I_v - \left(\mu_v+\delta_v\right)I_v\end{aligned}\right\} \tag{3.10}$$

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

$$f = \begin{bmatrix} (1-u_1)(I_h+I_v)\beta S_h \\ \\ (1-u_1)(I_h+I_v)\lambda S_v + (1-u_1)(I_h+I_v)b\lambda V_v \end{bmatrix},$$

$$v = \begin{bmatrix} \left(u_2+\gamma\right)I_h + \left(\mu_h+\delta_h\right)I_h \\ \\ (u_4+\alpha)I_v + \left(\mu_v+\delta_v\right)I_v \end{bmatrix}.$$

The Jacobian matrix of f and v are obtained by F and V as follows:

$$F = \begin{bmatrix} (1-u_1)\beta S_h & (1-u_1)\beta S_h \\ \\ (1-u_1)\lambda S_v + (1-u_1)b\lambda V_v & (1-u_1)\lambda S_v + (1-u_1)b\lambda V_v \end{bmatrix} \tag{3.11}$$

$$V = \begin{bmatrix} \left(u_2+\gamma\right) + \left(\mu_h+\delta_h\right) & 0 \\ \\ 0 & (u_4+\alpha) + \left(\mu_v+\delta_v\right) \end{bmatrix}. \tag{3.12}$$

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

$$F = \begin{bmatrix} (1-u_1)\beta S_h^* & (1-u_1)\beta S_h^* \\ \\ (1-u_1)\lambda S_v^* + (1-u_1)b\lambda V_v^* & (1-u_1)\lambda S_v^* + (1-u_1)b\lambda V_v^* \end{bmatrix}, \tag{3.13}$$

$$V = \begin{bmatrix} (u_2+\gamma)+(\mu_h+\delta_h) & 0 \\ 0 & (u_4+\alpha)+(\mu_v+\delta_v) \end{bmatrix}. \tag{3.14}$$

$$FV^{-1} = \begin{bmatrix} \dfrac{(1-u_1)\beta S_h^*}{(u_2+\gamma)+(\mu_h+\delta_h)} & \dfrac{(1-u_1)\beta S_h^*}{(u_4+\alpha)+(\mu_v+\delta_v)} \\ \dfrac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{(u_2+\gamma)+(\mu_h+\delta_h)} & \dfrac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{(u_4+\alpha)+(\mu_v+\delta_v)} \end{bmatrix} \tag{3.15}$$

$$FV^{-1} = \begin{bmatrix} \dfrac{(1-u_1)\beta S_h^*}{(u_2+\gamma)+(\mu_h+\delta_h)} & \dfrac{(1-u_1)\beta S_h^*}{(u_4+\alpha)+(\mu_v+\delta_v)} \\ \dfrac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{(u_2+\gamma)+(\mu_h+\delta_h)} & \dfrac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{(u_4+\alpha)+(\mu_v+\delta_v)} \end{bmatrix}. \tag{3.16}$$

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

$$A^2 - \left[\left(\frac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{(u_4+\alpha)+(\mu_v+\delta_v)}\right)+\left(\frac{(1-u_1)\beta S_h^*}{(u_2+\gamma)+(\mu_h+\delta_h)}\right)\right]A = 0 \tag{3.17}$$

$$A_1 = 0 \text{ and } A_2 = \left[\left(\frac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{(u_4+\alpha)+(\mu_v+\delta_v)}\right)+\left(\frac{(1-u_1)\beta S_h^*}{(u_2+\gamma)+(\mu_h+\delta_h)}\right)\right].$$

Dominant eigenvalue is A_2. This implies that;

$$R_{hv} = \left[\left(\frac{(1-u_1)\beta S_h^*}{(u_2+\gamma)+(\mu_h+\delta_h)}\right)+\left(\frac{(1-u_1)\lambda S_v^*+(1-u_1)b\lambda V_v^*}{[(u_4+\alpha)+(\mu_v+\delta_v)]}\right)\right]. \tag{3.18}$$

$S_h^* = \dfrac{\Lambda_h}{\mu_h}$, $S_v^* = \dfrac{\Lambda_v(\tau+\mu_v(1-u_3))}{\mu_v(\tau+\mu_v)}$, and $V_v^* = \dfrac{u_3\Lambda_v}{\tau+\mu_v}$.

$$R_{hv} = \left(\frac{(1-u_1)\beta\Lambda_h}{\mu_h(u_2+\gamma)+(\mu_h+\delta_h)}\right) + \frac{(1-u_1)b\lambda\Lambda_v(\tau+\mu_v(1-2u_3))}{\mu_v(\tau+\mu_v)[(u_4+\alpha)+(\mu_v+\delta_v)]}. \tag{3.19}$$

Where, $R_{hq} = \left(\dfrac{(1-u_1)\beta\Lambda_h}{\mu_h(u_2+\gamma)+(\mu_h+\delta_h)}\right)$, $R_{vq} = \dfrac{(1-u_1)b\lambda\Lambda_v(\tau+\mu_v(1-2u_3))}{\mu_v(\tau+\mu_v)[(u_4+\alpha)+(\mu_v+\delta_v)]}$.

Proposition 2. *The disease-free equilibrium (DFE) of model (2.1) is locally asymptotically stable if* $(R_{hv}<1)$, *and unstable if* $(R_{hv}>1)$.

3.4. Global stability of the disease-free equilibrium

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

Proof. For a Lyapunov function;

$$P(t) = \left(\alpha + \mu_v + \delta_v\right) I_h + \left(\gamma + \mu_h + \delta_h\right) I_v \tag{3.20}$$

By computing the time derivative of P along the solutions of the system of ordinary differential equations in(2.1), the following is obtained,

$$\left.\begin{aligned}
\frac{dP(t)}{dt} &= \left(\alpha + \mu_v + \delta_v\right)\frac{dI_h}{dt} + \left(\gamma + \mu_h + \delta_h\right)\frac{dI_v}{dt} \\
&= \left(\alpha + \mu_v + \delta_v\right)\left(\beta S_h\left(I_h + I_v\right) - \left(u_2\gamma + \mu_h + \delta_h\right) I_v\right) \\
&\quad + \left(\gamma + \mu_h + \delta_h\right)\left[\lambda S_v\left(I_h + I_v\right)\right. \\
&\quad \left. + b\left(I_h + I_v\right)\lambda V_v - \left(u_4\alpha + \mu_v + \delta_v\right) I_v\right] \\
&\leq \left(\alpha + \mu_v + \delta_v\right)\frac{\beta\Lambda_h I_h}{\mu_h} + \left(\alpha + \mu_v + \delta_v\right)\frac{\beta\Lambda_h I_v}{\mu_h} \\
&\quad - \left(\alpha + \mu_v + \delta_v\right)\left(\gamma + \mu_h + \delta_h\right) I_h \\
&\quad + I_h\left(\gamma + \mu_h + \delta_h\right)\left(\frac{\lambda\Lambda_v\left(\tau + \mu_v\left(I - u_3\right)\right)}{\mu_v\left(\tau + \mu_v\right)}\right) \\
&\quad + I_v\left(\gamma + \mu_h + \delta\right)\left(\frac{\lambda\Lambda_v\left(\tau + \mu_v\left(I - u_3\right)\right)}{\mu_v\left(\tau + \mu_v\right)}\right) \\
&\quad + I_h\left(\gamma + \mu_h + \delta_h\right)\left(\frac{bu_3\lambda\Lambda_v}{\tau + \mu_v}\right) + I_v\left(\gamma + \mu_h + \delta\right)\left(\frac{bu_3\lambda\Lambda_v}{\tau + \mu_v}\right) \\
&\quad - I_v\left(\gamma + \mu_h + \delta\right)\left(\alpha + \mu_v + \delta_v\right) \\
&\leq -I_h\left(\gamma + \mu_h + \delta_h\right)\left(\alpha + \mu_v + \delta_v\right)\left(1 - R_{hv}\right) \\
&\quad - I_v\left(\gamma + \mu_h + \delta_h\right)\left(\alpha + \mu_v + \delta_v\right)\left(1 - R_{hv}\right) \\
&= -\left(I_h + I_v\right)\left(\gamma + \mu_h + \delta_h\right)\left(\alpha + \mu_v + \delta_v\right)\left(1 - R_{hv}\right)
\end{aligned}\right\} \tag{3.21}$$

The time derivative of P along the solutions of the system of differential equations in (2.1) gives the following:

$\left(\frac{dP(t)}{dt}\right) \leq 0$, if and only if $(R_{hv} < 0)$

$\left(\frac{dP(t)}{dt}\right) = 1$, if and only if $I_h + I_v = 0$ or $R_{hv} = 1$.

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

This implies that is ξ_0 globally asymptotically stable in Φ. By LaSalle's invariant principle [11, 13].

3.5. Endemic equilibrium

Considering the system of differential equations in (2.1), at equilibrium, $\beta_m^* = I_h + I_v = 0$.

This corresponds to the disease free equilibrium or the relation:

$$\Phi_0\beta_m^{*3} + \Phi_1\beta_m^{*2} + \Phi_2\beta_m^{*} + \Phi_3 = 0. \tag{3.22}$$

$\Phi_0 = 1, \Phi_1 = \dfrac{Q_*}{C}(1-R_w), \Phi_2 = \dfrac{T_1}{C}\left(1-R_f\right), \Phi_3 = \chi\left(1-R_{hv}\right).$

Where;

$$\begin{aligned}
R_{hv}^2 =& R_{hq} + R_{vq} = \frac{\beta\Lambda_h}{\mu_h\left(\gamma+\delta_h+\mu_h\right)} + \frac{\lambda\Lambda_v\left[\left(\tau+\left(1-\left(1-b\right)\right)u_3\right)\right]}{\left(\tau+\mu_v\right)\left(\alpha+\delta_v+\mu_v\right)},\\
C =& b\beta\lambda^2\left[\mu_v\left(\alpha+\delta_v+\mu_v\right)+\left(\mu_v+\delta_v\right)\sigma_v\right]\left[\mu_h\left(\gamma+\delta_h+\mu_h\right)+\left(\mu_h+\delta_h\right)\sigma_h\right],\\
G_1 =& b\lambda^2\left(\gamma+\delta_h+\mu_h\right)\left(\mu_h+\sigma_h\right)\left[\mu_v\left(\alpha+\delta_v+\mu_v\right)+\left(\mu_v+\delta_v\right)\sigma_v\right],\\
G_2 =& \frac{\beta\lambda\left[\mu_h\left(\gamma+\delta_h+\mu_h\right)+\left(\mu_h+\delta_h\right)\sigma_h\right]F_3 b\left(\mu_v+\delta_v\right)\left(\tau+\mu_v\right)\left(\alpha+\delta_v+\mu_v\right)}{\left(\tau+\left(1-\left(1-b\right)\right)u_3\right)},\\
Q_* =& G_1+G_2,\\
R_w^2 =& \frac{G_1R_{hq}+G_2R_{vq}}{Q_*},\\
F_1 =& \lambda\mu_h\left(\mu_h+\sigma_h\right)\left(\gamma+\delta_h+\mu_h\right)\left(\tau+\left(1+b\right)\mu_v\right)\left[\mu_v\left(\alpha+\delta_v+\mu_v\right)+\left(\mu_v+\delta_v\right)\sigma_v\right],\\
F_2 =& \beta\mu_h\left(\alpha+\delta_v+\mu_v\right)\left(\tau+\mu_v\right)\left(\mu_v+\sigma_v\right)\left[\mu_h\left(\gamma+\delta_h+\mu_h\right)+\left(\mu_h+\delta_h\right)\sigma_h\right],\\
F_3 =& \left[\left(\tau+\left(1+b\right)\mu_v\right)\left[\mu_v\left(\alpha+\delta_v+\mu_v\right)+\left(\mu_v+\delta_v\right)\sigma_v\right]+b\alpha\mu_v\right],\\
T_1 =& \lambda\left[\mu_h\left(\mu_h+\sigma_h\right)\left(\gamma+\delta_h+\mu_h\right)\left(\tau+\mu_v\right)\left[\mu_v\left(\alpha+\delta_v+\mu_v\right)+\left(\mu_v+\delta_v\right)\sigma_v\right]\right]\\
&-b\left[\Lambda_v\left(\mu_v+\sigma_v\right)+\beta\Lambda_h\alpha\mu_v\sigma_v\left(\mu_h+\sigma_h\right)+\left(\alpha+\delta_v+\mu_v\right)\left(\mu_v+\sigma_v\right)\right],\\
\chi =& \frac{\mu_h\mu_v\left(\mu_v+\sigma_v\right)\left(\mu_h+\sigma_h\right)\left(\tau+\mu_v\right)\left(\alpha+\delta_v+\mu_v\right)\left(\gamma+\delta_h+\mu_h\right)}{b\beta\lambda^2\left[\mu_v\left(\alpha+\delta_v+\mu_v\right)+\left(\mu_v+\delta_v\right)\sigma_v\right]\left[\mu_h\left(\gamma+\delta_h+\mu_h\right)+\left(\mu_h+\delta_h\right)\sigma_h\right]},\\
R_f^2 =& \frac{F_1^2R_{hq}+F_1^2R_{vq}}{T_1},
\end{aligned} \tag{3.23}$$

Remark. The system of differential equations in equation (2.1) is said to have an endemic equilibrium E^*, if $(R_{hv} > 1)$.This is satisfied by cases (2,4,6) in Table **??**. The system of differential equations can have more than one endemic equilibrium points if $(R_{hv} > 1)$. This is satisfied by case (8) in Table **??**. The system of differential equations in equation (2.1), have more than one equilibrium points if $(R_{hv} < 1)$, as satisfied by case (3,5,7).

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

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

3.6. Global stability of endemic equilibrium

The Global behaviour of the system of differential equations in equation (2.1) is analysed.

Theorem 4. *The system of differential equations in equation* (2.1)*, is said to have a unique endemic equilibrium if* $(R_{hv}>1)$*, and it is globally asymptotically stable.*

The endemic equilibrium can only exists if and only if $(R_{hv}>1)$. So by letting $(R_{hv}>1)$,it implies that the endemic equilibrium exists.

Considering the non-linear Lyapunov function bellow;

$$\left.\begin{aligned} L = \quad & S_h^{**}\left(\frac{S_h}{S_h^{**}} - ln\frac{S_h}{S_h^{**}}\right) + I_h^{**}\left(\frac{I_h}{I_h**} - ln\frac{I_h}{I_h^{**}}\right) \\ & + \frac{g_1 R_h^{**}}{\gamma}\left(\frac{R_h}{R_h^{**}} - ln\frac{R_h}{R_h**}\right) + S_v^{**}\left(\frac{S_v}{S_v^{**}} - ln\frac{S_v}{S_v^{**}}\right) \\ & + I_v^{**}\left(\frac{I_v}{I**} - ln\frac{I_v}{I_v^{**}}\right) + R_v^{**}\left(\frac{R_v}{R_h^{**}} - ln\frac{R_v}{R**}\right) \\ & + V_v^{**}\left(\frac{Vv}{V_v^{**}} - ln\frac{V_v}{V_v^{**}}\right). \end{aligned}\right\} \tag{3.24}$$

Where;

$g_1 = \left(u_2+\gamma\right)+\left(\mu_h+\delta_h\right)$, $g_2 = \left(\sigma_2+\mu_h\right)$,

$g_3 = (u_4+\alpha)+\left(\mu_v+\delta_v\right)$, $g_4 = \left(\sigma_v+\mu_v\right)$,

When the above Lyapunov function is differentiated with respect to time, we obtain the equation;

$$\begin{cases} \dfrac{dL}{dt} = \left(1-\dfrac{S_h^{**}}{S_h}\right)\dfrac{dS_h}{dt} + \left(1-\dfrac{I_h^{**}}{I_h}\right)\dfrac{dI_h}{dt} + \dfrac{g_1}{\gamma}\left(1-\dfrac{R**}{R_h}\right)\dfrac{dR_h}{dt} \\ \quad + \left(1-\dfrac{S_v^{**}}{S_v}\right)\dfrac{dS_v}{dt} + \left(1-\dfrac{I_v^{**}}{I_v}\right)\dfrac{dI_v}{dt} + \left(1-\dfrac{R_v^{**}}{R_v}\right)\dfrac{dR_v}{dt} \\ \quad + \left(1-\dfrac{V_v^{**}}{V_v}\right)\dfrac{dV_v}{dt}. \end{cases} \tag{3.25}$$

$$\begin{cases} \dfrac{dL}{dt} = \left(1-\dfrac{S_h^{**}}{S_h}\right)\left[\Lambda_h + \sigma_h R_h^{**} + (1-u_1)\beta\beta_m^{**}S_h^{**} + \mu_h S_h^{**} - \Lambda_h\right. \\ \quad \left. -\sigma R_h - (1-u_1)\beta\beta_m S_h - \mu_h S_h\right] + \left(1-\dfrac{I_h^{**}}{I_h}\right)\left[(1-u_1)\beta\beta_m S_h - g_1 I_h\right. \\ \quad \left. + \dfrac{g_1}{\gamma}\left(1-\dfrac{R_h^{**}}{R_h}\right)\left[\left(u_2+\gamma\right)I_h - g_2 R_h\right] + \left(1-\dfrac{S_v^{**}}{S_v}\right)\left[(1-u_3)\Lambda_v\right.\right. \\ \quad \left.\left. + (1-u_1)\lambda\beta\beta_m^{**}S_v^{**} + \mu_v S_v^{**} + \sigma_v R_v^{**} + \tau V_v^{**} - (1-u_3)\Lambda_v\right.\right. \\ \quad \left.\left. - (1-u_1)\lambda\beta_m S_v - \mu_v S_v - \sigma_v R_v - \tau V_v\right] + \left(1-\dfrac{I_v^{**}}{I_v}\right)\right. \\ \quad \left.\left[(1-u_1)\lambda\beta_m S_v + (1-u_1)b\lambda\beta_m V_v - g_3 I_v\right] + \dfrac{g_3}{\alpha}\left(1-\dfrac{R_v^{**}}{R_v}\right)\right. \\ \quad \left.\left[(u_4+\alpha)I_v - g_4 R_v\right] + \left(1-\dfrac{V_v^{**}}{V_v}\right)\left[u_3\Lambda_v + (1-u_1)b\lambda\beta_m^{**}V_v^{**}\right.\right. \\ \quad \left.\left. + \left(\tau+\mu_v\right)V_v^{**} - u_3\Lambda_v - (1-u_1)b\lambda\beta_m V_v - \left(\tau+\mu_v\right)V_v\right]. \end{cases} \tag{3.26}$$

Moreover, by further simplification, the following is obtained;

Basically, however, the arithmetic mean value exceeds the geometric mean value [24, 18]. This follows that;

$$
\begin{aligned}
2-\frac{S_h^{**}}{S_h}-\frac{S_h}{S_h^{**}} &\leq 0\\
1-\frac{R_h}{R_h^{**}} &\leq 0\\
1-\frac{R_h^{**}}{R_h}-\frac{g_1g_2S_h}{(u_2+\gamma)S_h^{**}}\left(1-\frac{R_h^{**}}{R_h}\right) &\leq 0\\
1-\frac{\beta_m}{\beta_h^{**}}-\frac{S_h^{**}}{S_h}-\frac{S_h\beta_m I_h^{**}}{S_h^{**}\beta_m^{**}} &\leq 0\\
1-\frac{I_h}{I_h^{**}}-\frac{(u_2+\gamma)I_h}{I_h^{**}}\left(1-\frac{R_h^{**}}{R_h}\right) &\leq 0\\
2-\frac{S_v^{**}}{S_v}-\frac{S_v}{S_v^{**}} &\leq 0\\
1-\frac{S_v^{**}}{S_v}-\frac{R_v}{R_v^{**}}+\frac{R_vS_v^{**}}{R_v^{**}S_v} &\leq 0\\
1-\frac{S_v^{**}}{S_v}-\frac{V_v}{V_v^{**}}-\frac{V_vS_v^{**}}{V_v^{**}S_v} &\leq 0\\
1-\frac{S_v^{**}}{S_v}+\frac{\beta_m}{\beta_h^{**}}-\frac{S_v\beta_m I_v^{**}}{S_v^{**}\beta_m^{**}I_v} &\leq 0\\
1-\frac{I_v}{I_v^{**}}-g_3(u_4+\alpha)\frac{I_v}{I_v^{**}}-g_3(u_4+\alpha)\frac{I_vR_v^{**}}{I_v^{**}R_v} &\leq 0\\
1-\frac{R_v}{R_v^{**}} &\leq 0\\
2-\frac{V_v^{**}}{V_v}-\frac{V_v}{V_v^{**}} &\leq 0\\
1-\frac{V_v^{**}}{V_v}+\frac{\beta_m}{\beta_h^{**}}-\frac{V_v\beta_m I_v^{**}}{V_v^{**}\beta_m^{**}I_v}.
\end{aligned}
\tag{3.27}
$$

From the assumption that all the model parameters are non-negative, it implies that the derivative of the Lyapunov function is less than zero $\left(\frac{dL}{dt}\leq 0\right)$, if the basic reproduction number of the system of differential equation in equation(2.1) is greater than one ($R_{hv}>1$). Therefore by LaSalle's Invariant Principle [11, 13], as t approaches infinity, all the solution of the equations of the system of differential equations in the model approaches the endemic equilibrium point if ($R_{hv}>1$).

4. Sensitivity analysis of the Listeriosis model

In this section, we employ sensitivity analysis approach to determine how robust a model is to parameter values. This approach helps identify the parameters with high impact on the basic reproduction number (R_{hv}). The essence of the basic reproduction number is to determine whether or not treatment of the infectives, mortality and vaccination could help in the control of the disease in the population [18].

Definition 5. The normalised forward sensitivity index of a variable, q, which depends differentially on a parameter, r, defined as:

$$\Upsilon_r^q = \frac{\partial q}{\partial r} \times \frac{r}{q}. \tag{4.1}$$

4.1. Sensitivity indices of the basic reproduction number R_{hv}.

In epidemiological models, the value of the basic reproductive number determines the ability of the disease or infection to spread within the population. We will determine the reduction in infection due to the diseases by computing the sensitivity indices of the basic reproduction Number R_{hv}, with respect to the parameter values in the model. The sensitivity indices serve as determinants of the significance of each parameter in the dynamics and prevalence of the diseases. They measure the change in model variables when a parameter changes. In this study, we will compute the sensitivity indices of R_{hv} to parameter values for

Table 2: Sensitivity indices of parameters to R_{hv}.

Parameter	Description	Sensitivity index(+ve/-ve)
Λ_h	human recruitment rate	+ve
Λ_v	livestock's recruitment rate	+ve
μ_h	death rate in humans	-ve
μ_v	death rate in livestock's	-ve
δ_h	human disease induced death rate	-ve
δ_v	livestock's disease induced death rate	-ve
u_3	proportion vaccinated	-ve
α	livestock's recovery rate	-ve
β	human transmission rate	+ve
γ	human rate of recovery	-ve
τ	waning rate	+ve
λ	livestock transmission rate	+ve
b	vaccine efficacy	+ve

the model which will be estimated from data available or already published papers in the literature. Considering the thirteen different parameters of the system of differential equations in model (2.1), as shown in Table (2), we therefore derive the sensitivity of R_{hv} to each of the parameters in the model. The sensitivity indices of the basic reproduction number of R_{hv} with respect to each of the parameters of the system of differential equations in model (2.1), are given in Table 2:

5. Optimal control of the Listeriosis model

In this section, the analysis of an optimal control is carried out to determine the impact of the four intervention control schemes. The optimal control problem is derived by incorporating the following controls into the Listeriosis disease model(2.1)and the introduction of an objective functional that seeks to minimise: (u_2, u_2, u_2, u_1) where u_1 is the preventive measures of the susceptible human population (S_h). These are efforts to reduce the acquisition of Anthrax through education. u_2 is the treatment efforts given to the infected humans (I_h) as a result of complications of infections. These are efforts to minimise infections by treating the infective human population. u_3 is the vaccination effort of the susceptible animals (S_v). This is the use of antimicrobial drugs and u_4 is the treatment efforts given to the infected animals (I_v) as a result of complications of infections. These are efforts to minimise infections by treating the infective animal population.

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:

$$J = \underset{u_1, u_2, u_3, u_4}{min} \int_0^{t_f} \left(B_1 I_v + B_2 I_h + B_3 u_1^2 + B_4 u_2^2 + B_5 m u_3^2 + B_6 u_4^2\right) dt. \tag{5.1}$$

subject to the system of differential equations in (2.1).

Where; $B_1, B_2, B_3, B_4, B_5, B_6$: These are referred to as the weight constants to aid balance the terms in the integral to avoid the dominance of one another. They are termed as the balancing cost factors.

$B_1 I_h, B_2 I_v$ are the costs associated with infected humans (I_h) and the infected animals (I_v). $B_3 u_1^2$, is the cost associated with preventive measures of the susceptible human population (S_h). $B_5 m u_3^2$, this is the cost associated with vaccination of the susceptible animals (S_v). The costs is as a result of antimicrobial drugs, where $(m)$is the number of infected animals. $B_4 u_2^2$, this is the costs involved in the treatment of the infected humans (I_h) as a result of complications of infections. This is the cost associated with treatment of infected humans. $B_6 u_4^2$, this is the cost associated with the treatment of infected animals (I_v). the costs involved in the treatment of the infected (I) animals as a result of complications of infections. t_f, is the period

of the intervention. This implies that $(B_1 I_h, B_2 I_v)$, represents a linear function for the cost associated with infections and $\left(B_3 u_1^2, B_4 u_2^2, B_5 m u_3^2, B_6 u_4^2\right)$, represents a quadratic function for the cost associated with controls [11, 18].

The model control efforts is by linear combination of $u_i^2(t)$, $(i = 1,2)$. It is a quadratic in nature because of the assumption that costs are generally non-linear in nature. Moreover, the nature of the functional is chosen in line with existing literature on epidemic models. Thus, our aim is to minimise the number of infectives and reduce cost of treatment.

The objective is finding the optimal functions $\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)\right)$ such that;

$$J\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)\right) = \min_{u_1,u_2,u_3,u_4 \epsilon \cup} J(u_1, u_2, u_3, u_4). \tag{5.2}$$

Where

$\cup = \left\{ u : u, 0 \le u_i(t) \le 1,\ t\ \epsilon\ [0, t_f],\ i = 1,2,3,4 \right\}$ is referred to as the control set.

5.1. Pontryagin's maximum principle

The Pontryagin's Maximum Principle provides the necessary conditions that an optimal must satisfy. The principle changes the system of differential equations in (2.1)and equation (5.2)into minimisation problem point-wise Hamiltonian (H), with respect to (u_1, u_2, u_3, u_4).

$$\begin{aligned}
H = {} & B_1 I_v + B_2 I_h + B_3 u_1^2 + B_4 u_2^2 + B_5 m u_3^2 + B_6 u_6^2 \\
& + M_{S_h}\left\{\Lambda_h + \sigma_h - (1-u_1)\beta(I_v + I_h) S_h - \mu_h S_h\right\} \\
& + M_{I_h}\left\{(1-u_1)\beta(I_v + I_h) S_h - \left(u_2 + \gamma\right) I_h - \left(\delta_h + \mu_h\right) I_h\right\} \\
& + M_{R_h}\left\{\left(u_2 + \gamma\right) I_h - \left(\sigma_h + \mu_h\right) R_h\right\} \\
& + M_{S_v}\left\{(1-u_3)\Lambda_v - (1-u_1)\lambda(I_v + I_h) S_v - \left(\mu_v S_v + \sigma_v R_v + \tau V_v\right)\right\} \\
& + M_{I_v}\left\{(1-u_1)\lambda(I_v + I_h) S_v + (1-u_1) b\lambda(I_v + I_h) V_v - (u_4 + \alpha) I_v - \left(\delta_v + \mu_v\right) I_v\right\} \\
& + M_{R_v}\left\{(u_4 + \alpha) I_v - \left(\sigma_v + \mu_v\right) R_v\right\} \\
& + M_{V_v}\left\{u_3 \Lambda_v - \left(\tau + \mu_v\right) V_v - (1-u_1) b\lambda(I_v + I_h) V_v\right\}
\end{aligned} \tag{5.3}$$

Where; M_{S_h} , M_{I_h} , M_{R_h} , M_{R_v} , M_{S_v} , M_{I_v} *and* M_{V_v} are referred to as the adjoint variables.

The adjoint or co-state variables are solutions of adjoint systems below;

$$\left.\begin{aligned}
\frac{dM_{S_h}}{dt} &= \left((1-u_1)(I_v+I_h)\beta\left(M_{S_h}-M_{I_h}\right)+\mu_h M_{S_h}\right)\\
\frac{dM_{I_h}}{dt} &= -B_2+(1-u_1)\beta S_h\left(M_{S_h}-M_{I_h}\right)+\left(u_2+\gamma\right)\left(M_{I_h}-M_{R_h}\right)\\
&\quad +\left(\mu_h+\delta_h\right)M_{I_h}+(1-u_1)\lambda S_v\left(M_{S_v}-M_{I_v}\right)+b\lambda V_v\left(M_{V_v}-M_{I_v}\right)\\
\frac{dM_{R_h}}{dt} &= -\sigma_h M_{S_h}+\left(\sigma_h+\mu_h\right)M_{R_h}\\
\frac{dM_{S_v}}{dt} &= (1-u_1)\lambda(I_v+I_h)\left(M_{S_v}-M_{I_v}\right)+\mu_v M_{S_v}\\
\frac{dM_{I_v}}{dt} &= -B_1+(1-u_1)\beta S_h\left(M_{S_h}-M_{I_h}\right)+(1-u_1)\lambda S_v\left(M_{S_v}-M_{I_v}\right)\\
&\quad +b\lambda(1-(u_1))\left(M_{V_v}-M_{I_v}\right)V_v+\left(\mu_v+\delta_v\right)M_{I_v}+(u_4+\alpha)\left(M_{I_v}-M_{R_v}\right)\\
\frac{dM_{R_v}}{dt} &= -\sigma_h M_{S_v}+\left(\sigma_v+\mu_v\right)M_{R_v}\\
\frac{dM_{V_v}}{dt} &= -\tau M_{S_v}+(1-u_1)b\lambda(I_v+I_h)\left(M_{V_v}-M_{I_v}\right)+\left(\tau+\mu_v\right)M_{V_v}.
\end{aligned}\right\} \tag{5.4}$$

The above satisfies the transversality condition;

$$M_{S_h}(tf)=M_{I_h}(tf)=M_{R_h}(tf)=M_{S_v}(tf)=M_{I_v}(tf)=M_{R_v}(tf)=M_{V_v}(tf)=0. \tag{5.5}$$

Now, combining the Pontryagin's Maximum Principle and the existence result of the optimal control [5, 20].

Theorem 6. *The optimal control vector* $\left(u_1^*(t),u_2^*(t),u_3^*(t),u_4^*(t)\right)$ *that maximises the objective function* (J) *over* $\cup$, *given by;*

$$\begin{aligned}
u_1^*(t) &= \max\left\{0,\min\left(1,\frac{\beta\left(M_{I_h}-M_{S_h}\right)(I_v+I_h)S_h^*}{2B_3}\right.\right.\\
&\qquad \left.\left.+\frac{\lambda\left(M_{I_v}-M_{S_v}\right)(I_v+I_h)S_v^*+b\lambda\left(M_{I_v}-M_{V_v}\right)(I_v+I_h)V_v^*}{2B_3}\right)\right\}\\
u_2^*(t) &= \max\left\{0,\min\left(1,\frac{\left(M_{I_h}-M_{R_h}\right)I_h^*}{2B_4}\right)\right\}\\
u_3^*(t) &= \max\left\{0,\min\left(1,\frac{\Lambda_v\left(M_{S_v}-M_{V_v}\right)}{2mB_5}\right)\right\}\\
u_4^*(t) &= \max\left\{0,\min\left(1,\frac{\left(M_{I_v}-M_{R_v}\right)I_v^*}{2B_6}\right)\right\}.
\end{aligned} \tag{5.6}$$

Where;

M_{S_h} , M_{I_h} , M_{R_h} , M_{R_v} , M_{S_v} , M_{I_v} *and* M_{V_v} *are the solutions of equation* (5.4) *and* (5.5).

Proof. The existence of an optimal control is as a result the convexity of the integrand of J with respect to u_1,u_2,u_3 and u_4, the Lipschitz property of the state system with respect to the state variables and a priori Boundedness of the state solutions [5]. The system in equation (5.4)was derived by differentiating the Hamiltonian function evaluated at optimal control. However, equating the derivatives of the Hamiltonian with respect to the controls to zero, the following are obtained;

$$u_1 = \tilde{u_1} := \left\{ \left(\frac{\beta \left(M_{I_h} - M_{S_h} \right) \left(I_v + I_h \right) S_h^*}{2B_3} + \frac{\lambda \left(M_{I_v} - M_{S_v} \right) \left(I_v + I_h \right) S_v^* + b\lambda \left(M_{I_v} - M_{V_v} \right) \left(I_v + I_h \right) V_v^*}{2B_3} \right) \right\}$$

$$u_2 = \tilde{u_2} := \left\{ \left(\frac{\left(M_{I_h} - M_{R_h} \right) I_h^*}{2B_4} \right) \right\}$$

$$u_3 = \tilde{u_3} := \left\{ \left(\frac{\Lambda_v \left(M_{S_v} - M_{V_v} \right)}{2mB_5} \right) \right\}$$

and

$$u_4 = \tilde{u_4} := \left\{ \left(\frac{\left(M_{I_v} - M_{R_v} \right) I_v^*}{2B_6} \right) \right\}.$$

Therefore, it can be concluded by standard control arguments involving the bounds on the controls that;

$$\left. \begin{array}{l} u_1^* = \begin{cases} 0, & \text{if } \tilde{u_1} \le 0 \\ \tilde{u_1}, & \text{if } 0 < \tilde{u_1} < 1 \\ 1 & \text{if } \tilde{u_1} \ge 1 \end{cases}, \; u_2^* = \begin{cases} 0, & \text{if } \tilde{u_2} \le 0 \\ \tilde{u_2}, & \text{if } 0 < \tilde{u_2} < 1 \\ 1 & \text{if } \tilde{u_2} \ge 1 \end{cases} \\ u_3^* = \begin{cases} 0, & \text{if } \tilde{u_3} \le 0 \\ \tilde{u_3}, & \text{if } 0 < \tilde{u_3} < 1 \\ 1 & \text{if } \tilde{u_3} \ge 1 \end{cases}, \; u_4^* = \begin{cases} 0, & \text{if } \tilde{u_4} \le 0 \\ \tilde{u_4}, & \text{if } 0 < \tilde{u_4} < 1 \\ 1 & \text{if } \tilde{u_4} \ge 1 \end{cases} \end{array} \right\} \tag{5.7}$$

The system in equation (5.7) above leads to the system in equation (5.6) in Theorem (7). Optimal control uniqueness for small tf was obtained as a result of the Lipschitz structure of the Ordinary Differential Equations and the priori boundedness of the state solutions and adjoint functions. The existence optimal control uniqueness quadruple is in line with the uniqueness of the optimal system, that comprises of equations (2.1), (5.4), (5.5) and (5.6).

The uniqueness of the optimal of the system is guaranteed, by imposing a condition on the time interval. This is always the case as a result of the opposite time orientations of the

optimal system. This is always the case because, the adjoint problem has the final values whereas the the state problem has the initial values. In optimal control problems, imposing a condition or applying a restriction is always common [11]. □

6. Numerical results

In this section, we solve the optimal system by using Runge-Kutta fourth order scheme. This optimal strategy was achieved as a results solving the state systems, adjoints equations and the transversality conditions. The problem is a two-point boundary-value problem which has two separate boundary conditions at times $t = 0$ and $t = t_f$. Our ultimate objective is to solve this optimal problem for the value $t_f = 120$ days. This chosen value represents value the time at which treatment and vaccination is expected to be stopped. We conducted the numerical simulation by solving the state equations (2.1) using Runge-Kutta fourth order scheme by guessing the controls over a simulated time. Secondly, we then use the current iteration of the state equations (2.1), the adjoint equations and the transversality conditions by a backward method. The controls are then updated by the use of a convex combination of the controls in the previous iterations as well as values from the characterizations of the system. We repeat the process and the iteration is stopped if the values of unknowns at the previous iteration are very close to those at the present iteration [18].

We considered the following combinations of optimal control strategies and selected the best three most effective strategies by using the parameter values in Table (3):

Table 3: Variable and parameter values of Listeriosis model.

Parameter	Estimated value	Reference
μ_h	0.004	assumed
δ_h	0.20	Adak et al., 2002.
Λ_v	0.0273	assumed
Λ_h	0.1	assumed
μ_v	0.002	assumed
δ_v	0.30	Adak et al., 2002.
α	0.002	assumed
β	0.200	assumed
τ	0.013	assumed
λ	0.27	http://www.about-listeria.com
b	0.005	assumed

Treatment of humans and vaccination of susceptible vectors. Prevention of susceptible vectors and prevention of susceptible vectors. Treatment of infective vectors and the vaccination of susceptible vectors. Prevention of and treatment control of humans. Prevention

of humans and the treatment of infective vectors. Treatment of humans, vaccination of susceptible vectors and treatment of infective vectors. Treatment of infective vectors and the treatment of infective humans. Prevention of susceptible humans, treatment of infective humans and the vaccination of susceptible humans. Treatment of infective vectors, treatment of humans and prevention of humans. Treatment of infective vectors, prevention of susceptible vectors and prevention of humans. Table (3), shows the variable and parameter values used in the model.

6.1. Bifurcation analysis

The Figure (2) shows the simulation of model (2.1) indicating the existence of backward bifurcation. The model shows that both disease free equilibrium and the endemic equilibrium exists simultaneously. The biological implication is that, the phenomenon of eradicating a disease with basic reproduction number less than one is no longer sufficient. Figure (2), is evidence of the existence of backward bifurcation.

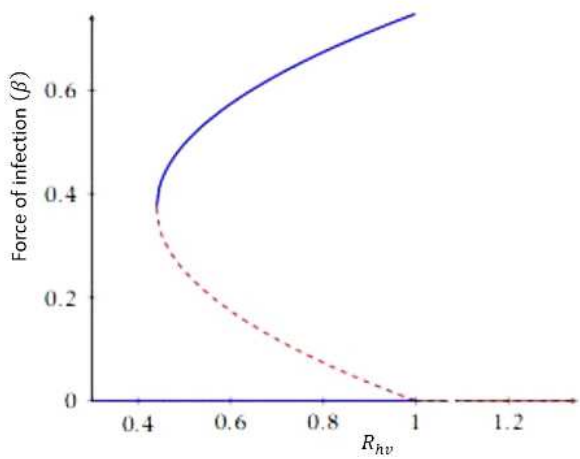

Figure 2: Simulation of model (2.1)showing the concept of backward bifurcation of the endemic equilibrium when $R_{hv} > 1$ and two equilibria for $R^*_{hv} < R_{hv} < 1$.The blue line represents stable equilibrium and the red line represents unstable equilibrium.

6.2. Strategy A: Optimal treatment of infective vectors and vaccination of susceptible vectors

We optimise the objective functional by using the treatment of infective vectors control, (u_4) and the vaccination of vectors control strategy, (u_3). This was done by setting all other controls to zero. It can be observed from the figure that there has been a complete reduction in the number of infective vectors, (I_v) and infective humans, (I_h). The epidemiological

implication is that the spread of Listeriosis can be effectively tackled through the treatment of infective animals and the vaccination of susceptible vectors. Achieving this strategy, there should be proper vaccination of susceptible animals as well as treatment of infective animals in the community as shown in Figure (3). Cases without control are indicated with red lines and cases with control are indicated with green lines as indicated in Figure (3) and Figure (4).

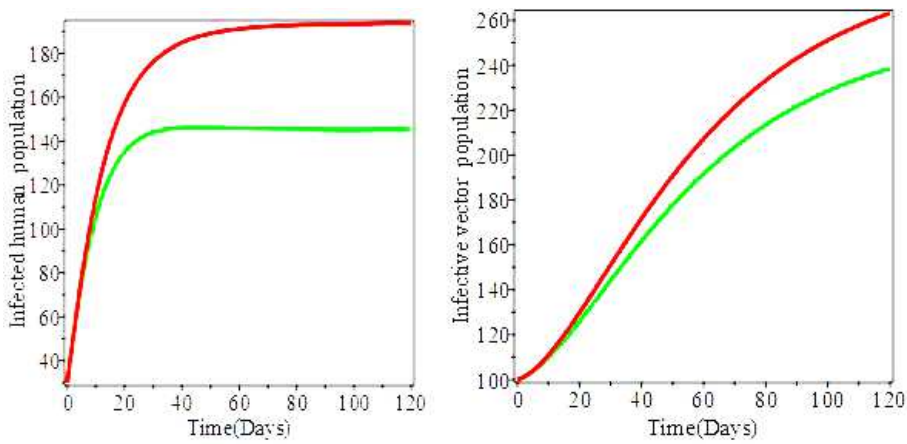

Figure 3: Simulation of Listeriosis model: Optimal treatment of infective vectors and vaccination of susceptible vectors.

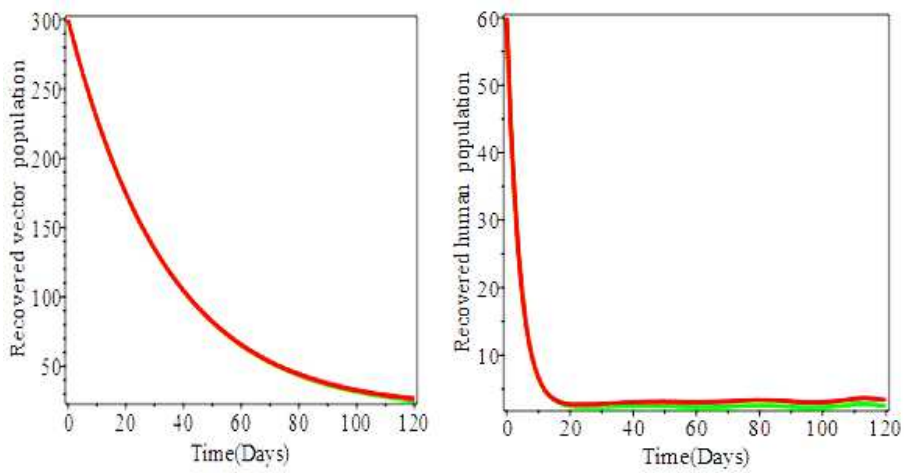

Figure 4: Simulation of Listeriosis model: Optimal treatment of infective vectors and vaccination of susceptible vectors.

6.3. Strategy B: Optimal treatment of infective humans, vaccination of vectors and treatment of infective vectors

The treatment control (u_2) of infective humans, vaccination control (u_3) of susceptible

vectors and the treatment control of infective vectors (u_4)were used to optimise the objective functional while the prevention control (u_1) of susceptible humans is set to zero. We observe that this strategy has caused a reduction in the number of infective vectors (I_v) and infective humans (I_h) as indicated in Figure (5). This optimal strategy can best be achieved by increasing the rate of vaccination of susceptible vectors, increasing the rate of treatment of infective humans and increasing the rate of treatment of infective vectors. Cases without control are indicated with red lines and cases with control are indicated with green lines as shown in Figure (5) and Figure (5).

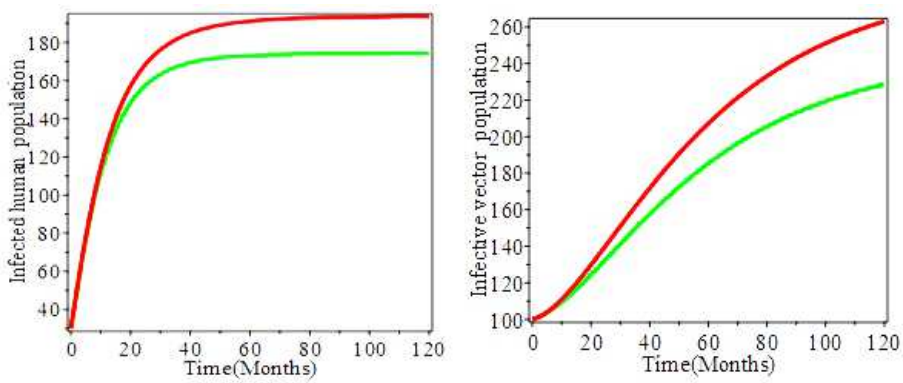

Figure 5: Simulation of Listeriosis model: Optimal treatment of infective humans, vaccination of susceptible vectors and treatment of infective vectors.

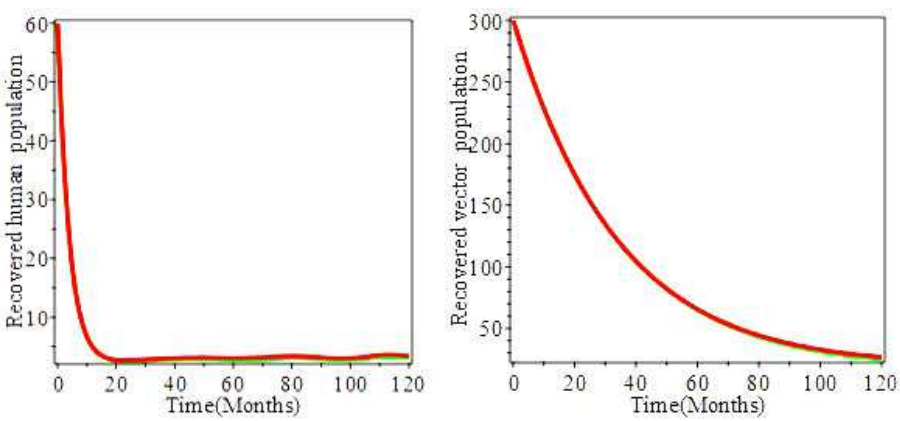

Figure 6: Simulation of Listeriosis model: Optimal treatment of infective humans, vaccination of susceptible vectors and treatment of infective vectors.

6.4. Strategy C: Optimal treatment of infective vectors and treatment of infective humans

We optimise the objective function by using treatment control of infectives vectors (u_4) and treatment control of infective humans (u_2). The optimisation was done by setting the pre-

vention control on humans (u_1) and vaccination control of susceptible vectors (u_3) to zero. As a result of this strategy, it can be observed in Figure (7), that there has been a reduction in the number of infective vectors (I_v) and infective humans (I_h). The epidemiological implication is that the spread of Listeriosis can be controlled through regular treatment of infective vectors and the treatment of infective humans. This optimal strategy can best be achieved by treating all infective animals and humans that are having the infections. Cases without control are indicated with red lines and cases with control are indicated with green lines as shown in Figure (7) and Figure (8).

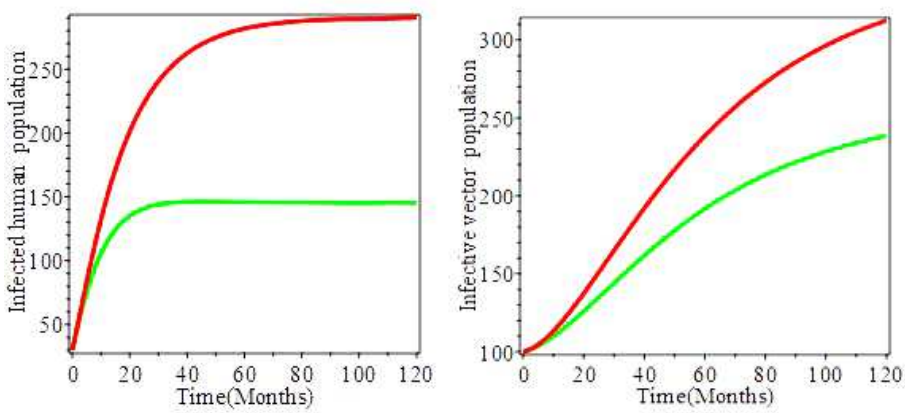

Figure 7: Simulation of Listeriosis model: Optimal treatment of infective vectors and treatment of infective humans.

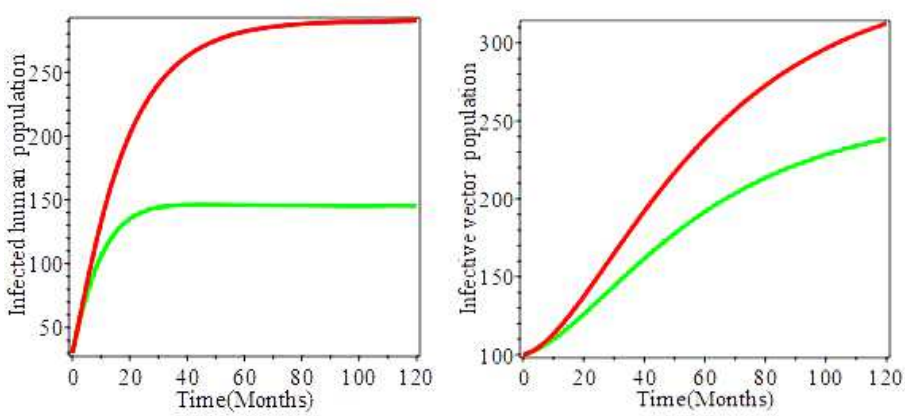

Figure 8: Simulation of Listeriosis model: Optimal treatment of infective vectors and treatment of infective humans.

7. Conclusion

In this paper, we formulated and analysed a deterministic model for the transmission mechanism of Listeriosis disease by the inclusion of vaccination with waning immunity, treatment of infectious humans and treatment of infectious vectors. We determined the basic reproductive number, and carried stability analysis and existence of the equilibrium points. We established from the qualitative analysis of the model that there exist multiple endemic equilibrium. In epidemiology, implication of this is that, effective control of the disease can be reached if the basic reproductive number, is less than unity (the critical value).

We then carried out the sensitivity analysis of the basic reproduction number. This analysis showed that, increasing human natural death rate, livestock natural death rate and livestock recovery rate, there would be a decrease in the basic reproduction number. Moreover, decreasing human natural death rate, livestock natural death rate and livestock recovery rate, would increase the basic reproductive number. Also, by increasing the human recruitment, livestock or vector recruitment rate, human transmission rate and livestock transmission rate, would cause an increase in the basic reproduction number and by decreasing human recruitment rate, vector or livestock recruitment rate, human transmission rate and livestock transmission rate, there would be a corresponding decrease in the basic reproduction number.

The qualitative analysis of optimal control was performed and the necessary conditions for the optimality of Listeriosis disease was analysed. The three most effective strategies according to our model are as follows: The combination of treatment of infectious vectors and treatment of infectious humans, combination of vaccination of susceptible vectors and the prevention of susceptible humans and combination of vaccination of susceptible vectors and the treatment of infectious vectors.

Data Availability Statement

The data supporting this compartmental model analysis are from previously published articles and reported studies which have been cited in this paper. 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

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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