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Dynamic Optimal Control for Multi-chemotherapy Treatment of Dual Listeriosis Infection in Human and Animal Population

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Abstract

Following the rising cases of high hospitalization versa-vise incessant fatality rates and the close affinity of listeriosis with HIV/AIDS infection, which often emanates from food-borne pathogens associated with listeria monocytogenes infection, this present paper seek and formulated as penultimate model, an 8-Dimensional classical mathematical Equations which directly accounted for the biological interplay of dual listeriosis virions with dual set of population (human and animals). The model was studied under multiple chemotherapies (trimethoprim-sulphamethoxazole with a combination of penicillin or ampicillin and/or gentamicin). Using ODE's, the positivity and boundedness of system solutions was investigated with model presented as an optimal control problem. In the analysis that follows, the study explored classical Pontryagin's Maximum Principle with which the model optimality control system as well as existence and uniqueness of the control system were established. In correlating the derived model with clinical implications, numerical validity of the model was conducted. Results indicated that under cogent and adherent to specify multiple chemotherapies, maximal recovery of both human and animal infected population was tremendously achieved with consequent rapid decline to near zero infection growth. The study therefore suggests further articulation of more chemotherapies and early application at onset of infection for a visible elimination of listeriosis infection.

Keywords: Listeria-monocytogenes; Listeriosis; Trimethoprim-sulphamethoxazole; Maximal-recovery; Optimality-system; Gastrointestinal-infection; Multiple-chemotherapy

MSC 2010 No.: 93A30, 93C15, 65L07, 65K15, 49J15

1. Introduction

Listeria monocytogenes is said to be the causative agent of an infectious disease called listeriosis, which is adaptive to living organism and commonly known for meningoencephalitis and stillbirth in both human and animals. From the history of mankind in relation to infectious diseases, it has been established that apart from the dreaded human immunodeficiency virus (HIV) and the constant reoccurrence of Ebola virus (EBV), listeriosis virus infection have been adjudged the third most fastest and dangerous human pathogen of mankind and animals and the second after salmonellosis as the most frequent causes of foodborne infection-related death in Europe, Pichler et al. (2011). Yet the virus has not been given the much desired attention mostly in developing countries with sparsely exceptions of early observation in the developed countries.

One of the most interesting characteristics of this very virus is its close affinity with HIV infection as patients with symptoms/risk factors of HIV are more prone to listeriosis infection. Listeriosis as an infectious disease came of scientific knowledge in the early 60s with substantial outbreaks in early 1980s. Moreso, gastrointestinal infection as a consequential factor of listeriosis monocytogenes is a zoonotic foodborne pathogen often contacted following habitual consumption of raw food in the range of raw milk, raw fresh and frozen meat, hot-dogs, cheese, coleslaw, cabbages, cold cuts, poultry, seafood and dairy products (Murray et al. (1926), Osman et al. (2018), Jemmi et al. (2006)). A situation that speaks volume as indicated by microbiological food recalls in food processing environments. Other isolated ecological environments include soil, vegetation, sewage, water, animal feed, slaughterhouse waste and faces of healthy animals, (Osman et al. (2018)). A survey on *L. monocytogenes* infections from consumption of raw meat and raw milk from notable different countries is summarized by Jemmi et al. (2006). In animal (vectors), rhombencephalitis infection is directly associated with the ingestion of contaminated silage with *L. monocytogenes*, which forms the commonest food for animals. Therefore, animals as major carriers of *L monocytogenes*, which are consumed by human, are known to be the source of hospital food and processing food plants. A situation that has been vindicated by high hospitalization rate (91%) and subsequent cases of fatality rate believed to emanate from foodborne pathogen versa-vise *L. monocytogenes.* The indiscriminate feeding of ruminants with silage under high pH , which are often contaminated with large amount of listeria, causes meningoencephalitis, septicaemia and abortions in animals and other non-pregnancy-associated cases.

Therefore, the class of most vulnerable is the elderly $(\geq 65 year)$, immunocompromised patients, new born children and pregnant women. In pregnant women mostly at their trimester (including neonates within the first 4 weeks of birth), *L. monocytogenes* takes advantage of the natural localized immunosuppressed body mechanism at maternal-fetal interface to cause abortions. Thus, infected pregnant women typically develop non-specific flu-like symptoms of which many remain asymptomatic. The incubation period for this disease varies from 11 – 70 days (with median of 21 days) in humans, (Jemmi et al. (2006), Allerberger et al. (2009), AL-Tawfiq (2008)). Other underlying conditions that predispose patients to acquiring listeriosis infection include cancer related infection or patients undergoing treatment with steroids or cytotoxic drugs, neonates, renal transplant recipients, AIDS patients, diabetes or alcoholic patients, Donnelly (2001). The studies, (Pichler et al. (2011), Jemmi et al. (2006), Allerberger et al. (2009), Slutsker et al. (1999), Mossey et al. (1985)) also revealed that collagen vascular disease, sarcoidosis, ulcerative colitis, aplastic

anemia, transfusional iron overload and intravenous drug abuse, mother-to-child in utero or during passage through infected birth canal, nosocomial transmission, milking, slaughtering process of asymptomatic animal carriers as conditions that predispose patients to listeriosis. In a more explicit term, the spread of *L. monocytogenes* is the consequence of predator-prey consumption-flow.

Perturbingly, the continuous survival and sustainability of listeriosis virus reservoir is informed by its natural ubiquitous, which transform to its high resistive ability in forming biofilms within and around food processing environments. Moreso, these characteristics is enhanced by the acidic or salty conditions with its multiplicity favored by non-refrigeration or poor room temperature refrigeration, (Pichler et al. (2011), Jacobson (2008), Borucki et al. (2003)). From the biology of listeria reservoir, the virus is characterized by six species: *L. monocytogenes, L. innocua, L. ivanovil, L. welshieri, L. seeligeri and L. grayi* with only *L. monocytogenes* recognized to be associated to human pathogen. *L. monocytogenes* is known to survive freezing and drying conditions with relative resistant to heat and *pH* range of $4.3-9.6$. These outbreaks have not been left without measureable treatment/preventive measures. In vitro, activity has shown that *L. monocytogenes* is susceptible to a wide range of antibiotics. Detail of trial chemotherapies used for the treatment of listeriosis patients can be found in Pichler et al. (2011). In that study, a number of antibiotics in the range of penicillin or ampicillin and/or gentamicin as well as trimethoprim-sulphamethoxazole or erythromycin were suggested as single dose, while in animals, successful antibiotics include linezolid, meropenem and rifampicin (Morosi et al. (2006), Hugo, et al. (2019)), Mylonakis et al. (2002), Pichler et al. (2009), Lorber (2006)). However, same studies recommended that gentamicin supplement protocol is not been suitable for pregnant women due to teratogenic effects, while $\beta-lactam$ are not advisable for patients with $\beta-lactam$ allergy.

Resourcefully, from the above literature on listeriosis infection very little or no attention have been given to the evaluation of listeriosis infection and treatment measures via optimality control theory. An approach that involves the possible maximization of susceptible, recovered and vaccinated human and animal population under minimized systemic cost. Taking on the above as an integral motivational factor, this present study considering listeriosis infection as a dual infectivity (invasive and non-invasive, (WOAH – OIE (2004), Disson et al. (2008)) seek to clinically subject these class of illness to multiple choice of chemotherapies (trimethoprim-sulphamethoxazole and oral amoxicillin or oral ampicillin). Therefore, the novelty of this study is well-informed by the subjection of dual listeriosis infection to multiple chemotherapies leading to the formulation via ODEs a penultimate classical mathematical listeriosis dynamic model. The study is posed to explore classical optimality control theory – the Pontryagin's maximum principle.

Thus, the structural content of this work is generated as a manuscript of seven fragmentations with section 1, covering the introductory aspect. Section 2 is devoted to material and methods, which embedded the model problem statement and mathematical Equations. This section involves verification of system positivity and boundedness of solution as well as stability analysis for an untreated listeriosis infection. Transformation of derived system to an optimal control problem and its characterization is discussed in section 3. Section 4 focuses on the optimality system and uniqueness of an optimal control pair. The functionality of the established system is numerically illustrated in section 5 with results clearly analyzed in section 6. Finally, section 7 accounts for a succinct conclusion and coincide remarks based on the conclusive investigation with appendices of results in tabular form after references. The study is anticipated to provide somewhat insight to the containment of *L. monocytogenes* infection.

2. Material and Methods

The material and methods of this present study is constitute of the problem statement and mathematical Equations of the model derived for an uncontrolled listeriosis infection in human and animal population; the model schematic representation; analysis of the positivity and boundedness of solution for the model state variables as well as model stability analysis.

2.1. Model problem statement and Equation derivation

From Pichler et al. (2011), an epidemiological scenario of the spread of listeriosis virus was studied following the inter-environmental relation of host victims (human population) with infectious vectors – listeria monocytogenes often from animals and food-borne pathogen infections. In that model, vaccinated susceptible vector compartment was incorporated among the dynamics of the model state variables under consideration. The governing Equations of the model read thus:

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

The model focuses on the varying stability analysis. For detail of model formulation and description, readers are referred to the aforementioned model.

In this present study, with the incorporation of novel state variable – vaccinated susceptible human population and subjection of both infectious human and vectors (livestock) to multiple chemotherapies (for suppressive and malignancy drugs), a set of 8-Dimensional continuous differential mathematical dynamic Equations is formulated as an extended version of the model, Pichler et al. (2011). Thus, this present study is primed by the investigation of the biological and physiological interaction of listeriosis virions considered as non-invasive and invasive listeriosis with dual living organism (human and animal population).

Therefore, if the model state variables represents the varying population subgroups, measured in units' volume of $cells / mm^3$ such that $S_{h,v}$ defines susceptible human and vector population; $I_{h,v}$ - infected human and vector population, $R_{h,v}$ - recovered human and vector population and $V_{h,v}$ - vaccinated human and vector population, then the governing epidemiological model Equation is derived as:

$$
\begin{aligned}
\dot{S}_h &= b_h + \sigma_h R_h - [(1+u_1) + B_h]S_h - \mu_h S_h + \tau_1 V_h,\\
\dot{I}_h &= B_h S_h + (1-\Lambda_h)\gamma_h V_h - (\lambda + \mu_h + \alpha_h)I_h,\\
\dot{R}_h &= \lambda I_h + u_1 R_h - (\sigma_h + \mu_h)R_h,\\
\dot{V}_h &= (1-u_1)S_h - (\tau_1 + \mu_h)V_h - (1+\Lambda_h)\gamma_h \beta_m^1 V_h,\\
\dot{S}_v &= b_v + \sigma_v R_v - [(1+u_2) + B_v]S_v - \mu_v S_v + \tau_2 V_v,\\
\dot{I}_v &= B_v S_v + (1-\Lambda_v)\gamma_v V_v - (\rho + \mu_v + \alpha_v)I_v,\\
\dot{R}_v &= \rho I_v + u_2 R_v - (\sigma_v + \mu_v)R_v,\\
\dot{V}_v &= (1-u_2)S_v - (\tau_2 + \mu_v)V_v - (1+\Lambda_v)\gamma_v \beta_m^2 V_v,
\end{aligned}
\tag{2}
$$

with initial values, $I_{h,v}(0) = I_{(0)h,v}$, $R_{h,v}(0) = R_{(0)h,v}$ and $V_{h,v}(0) = V_{(0)h,v}$ at $t = t_0 \geq 0$ and satisfying the biological state variables and parameter values as depicted by tables (3 & 4) below. From Equation (2), if N_h and N_v represent the total population of both human and vectors, then total population under investigation is given by $N_h(t)$ and $N_v(t)$ at time t. Moreso, if u_1, u_2 represent control functions, then for an untreated model, $(1-u_1)S_h, (1-u_2)S_v = 0$ and $u_1 R_h, u_2 R_v = 0$ respectively. Thus, the algebraic Equations for the differential population of human and vector understudy are obtained as:

$$\frac{N_h(t)}{N_h} = S_h(t) + I_h(t) + R_h(t) + V_h(t) = 1,$$

and

$$\frac{N_v(t)}{N_v} = S_v(t) + I_v(t) + R_v(t) + V_v(t) = 1.$$

The forces of infection (incidence rates) denoted by B_h and B_v are expressed in relation to $I_h/N_h, I_h/N_h, I_h/N_h$ and $I_v/N_v, I_v/N_v, I_v/N_v$ of listeriosis infected population, Schuchat et al. (1991). Therefore,

$$
\begin{cases}
B_h = (C_h^1 + C_h^2)\gamma_h[\beta_h I_h + \beta_v I_v,\\
B_v = (C_v^1 + C_v^2)\gamma_v[\beta_h I_h + \beta_v I_v.
\end{cases}
\tag{3}
$$

Equation (3) is an improved forces of infection when compared to Equation (2.1) of the model, Pichler et al. (2011), with $\beta_m^* \beta$ a force of infection, where $\beta_m^* = I_h + I_v$. The effective infection circulating system is obtained by transforming the basic Equations (2) and (3) into proportions. This is essential as it reduces the seeming complex Equations for easy handling, initiate biological meaning and distinctly define the prevalence rate of infection. To this effect, letting $N_h(0) = N_h$ and $N_v(0) = N_v$, then

$$
\begin{cases}
s_h = S_h/N_h, i_h = I_h/N_h, r_h = R_h/N_h, v_h = V_h/N_h,\\
s_v = S_v/N_v, \mathrm{i}_v = I_v/N_v, r_v = R_v/N_v, v_v = V_v/N_v.
\end{cases}
\tag{4}
$$

Therefore, the transformed version of Equations (2) and (3) are of the forms:

$$\begin{aligned}
\dot{s}_h &= b_h + \sigma_h r_h - [(1+u_1) + B_h]s_h - \mu_h s_h + \tau_1 v_h, \\
\dot{i}_h &= B_h s_h + (1-\Lambda_h)\gamma_h v_h - (\lambda + \mu_h + \alpha_h)i_h, \\
\dot{r}_h &= \lambda i_h + u_1 r_h - (\sigma_h + \mu_h)r_h, \\
\dot{v}_h &= (1-u_1)s_h - (\tau_1 + \mu_h)v_h - (1+\Lambda_h)\gamma_h \beta_m^1 v_h, \\
\dot{s}_v &= b_v + \sigma_v r_v - [(1+u_2) + B_v]s_v - \mu_v s_v + \tau_2 v_v, \\
\dot{i}_v &= B_v s_v + (1-\Lambda_v)\gamma_v v_v - (\rho + \mu_v + \alpha_v)i_v, \\
\dot{r}_v &= \rho i_v + u_2 r_v - (\sigma_v + \mu_v)r_v, \\
\dot{v}_v &= (1-u_2)s_v - (\tau_2 + \mu_v)v_v - (1+\Lambda_v)\gamma_v \beta_m^2 v_v,
\end{aligned} \tag{5}$$

where

$$\begin{cases} B_h = (C_h^1 + C_h^2)\gamma_h[\beta_h i_h + \beta_v i_v, \\ B_v = (C_v^1 + C_v^2)\gamma_v[\beta_h i_h + \beta_v i_v, \end{cases} \tag{6}$$

with initial conditions of Equation (2) sustained. Equation (5) represents the physiological and biological listeriosis transmission dynamics for an untreated human and animal vector system for all $u_{i=1,2} = 0$.

For cohesive assimilation of model (5), the epidemiological descriptions of the terms are as follows: from the first and fifth Equations, the first terms b_h, b_v defines birth rates/natural source of human and vector susceptible population, which are proliferated by recovered proportion of infected under treatment and vaccinated population who loose immunity denoted by $\tau_1 v_h, \sigma_h r_h$ and $\tau_2 v_v, \sigma_v r_v$, respectively. The second terms $(1-u_1)s_h, (1-u_2)s_v$ describe the proportions of susceptible that are subjected to immune vaccination. The third terms $B_h s_h, B_v s_v$ represent rate at which susceptible becomes infected, while the fourth terms $\mu_h s_h, \mu_v s_v$ denotes natural death rate of both susceptible groups and the last terms $\tau_1 v_h, \tau_2 v_v$ denotes the number of vaccinated population that loose immunity and join the susceptible population.

From the second and sixth Equations – the terms $B_h s_h, B_v s_v$ describes the rates at which susceptible becomes infectious. This is proliferated by vaccinated population that loses immunity - $(1-\Lambda_h)\gamma_h v_h, (1-\Lambda_v)\gamma_v v_v$ and become infectious. The infectious is being differentiated by the proportion that receives treatment, natural death and clearance rates due to infection as depicted by the third terms of the Equations - $(\lambda + \mu_h + \alpha_h)i_h$ and $(\rho + \mu_v + \alpha_v)i_v$. The third and seventh Equation presents the biological behaviors of the recovered human and vector populations. Here, with the introduction of chemotherapies (vaccinations) - $u_1 r_h, u_2 r_v$, significant recovery are expected as denoted by $\sigma_h r_h, \sigma_v r_v$ with natural clearance rates of $\mu_h r_h, \mu_v r_v$.

Finally, the proportions of vaccinated groups of both human and vector from susceptible populations are depicted by Equations four and eight of model (4). The first terms - $(1-u_1)s_h$ and

$(1-u_2)s_v$ describes the actual vaccinated groups, which is differentiated by loose of immunity - $\tau_1 s_h$ and $\tau_2 s_v$ as well as clearance rate due to natural death. Thus, the structural representation of the system model is as seen in Figure 1 below:

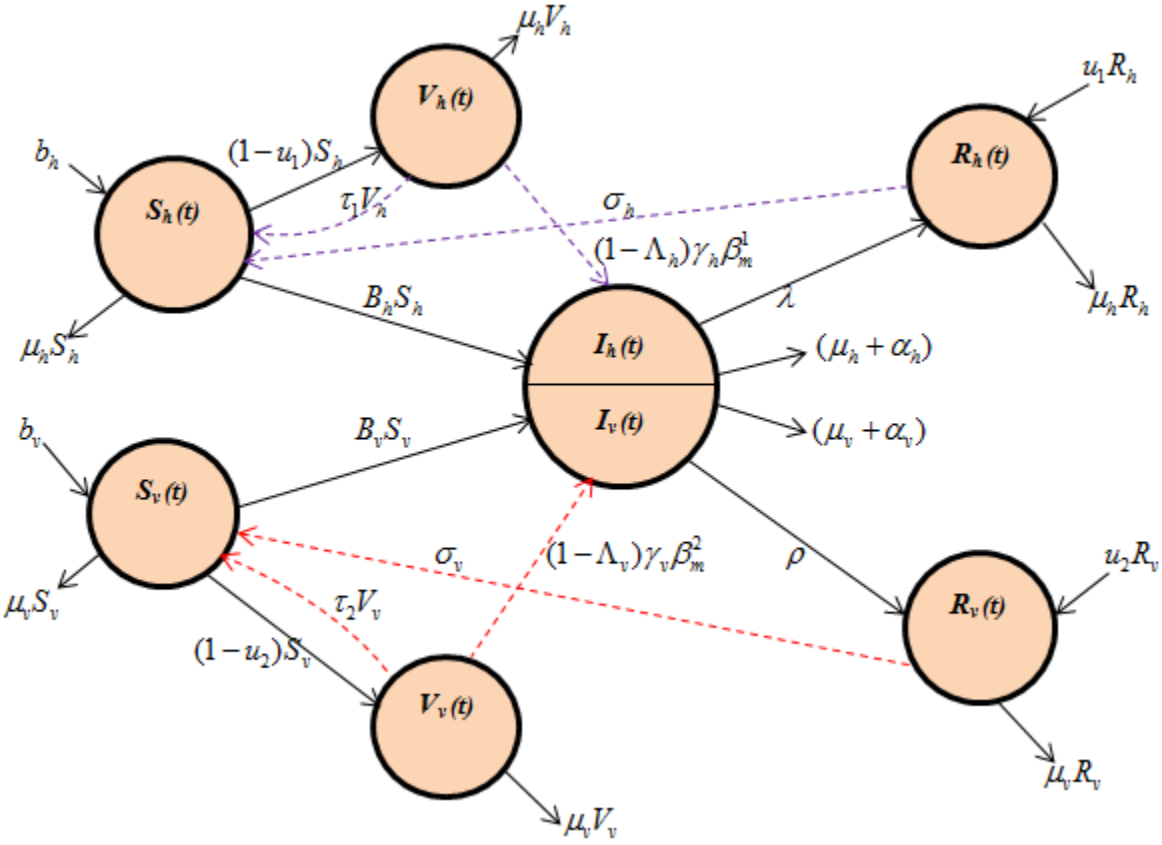


Figure 1. Schematic structure for the dynamic flow of dual listeria infection in human and animal population

The state and parameter values with which the system is clinically validated are as given by Tables (1 and 2) below:

Table 1. Description of state variables with values – model (5)

Variables	Dependent variables Description	Initial values	Units
s_h	Susceptible human population to listeriosis virus	0.5	*cells/mm*^{3}
i_h	Infected human population to listeriosis virus	0.2	
r_h	Recovered human population from listeriosis virus	0.15	
v_h	Vaccinated human population from listeriosis virus	0.15	
s_v	Susceptible vector population to listeriosis virus	0.5	

i_v	Infected vector population to listeriosis virus	0.2	
r_v	Recovered vector population from listeriosis virus	0.15	
v_v	Vaccinated vector population from listeriosis virus	0.15	

Table 2. Summary of constants and parameter values - model (5)

Parameter symbols	Parameters and constants: Description	Initial values	Units
b_h, b_v	Birth/source rate of susceptible human and vector population	0.01; 0.25	$cell / mm^3 d$
λ, ρ	Recovery rate of human and vectors from infection	0.005;0.0002	$cell / mm^3$
$(1-u_1),(1-u_2)$	Fraction of susceptible human and vectors popn. vaccinated	0.025;0.05	***$mm^3 d^{-1}$***
Λ_h, Λ_v	Rate at which vaccinated population loses immunity	0.025;0.05	
$\mu_{h,v}$	Natural death rate of human and vectors	0.004;0.02	
$\alpha_{h,v}$	Death rate of human and vectors due to infection	0.2;0.3	
$\sigma_{h,v}$	Rate at which recovered human and vectors loses immunity	0.03;0.005	
$\beta_{h,v}$	Probability of human and vectors becoming infected by listeriosis virus	0.02;0.27	***day^{-1}***
$\beta_m^{1,2}$	Probability of transmission by vaccinated v_h, v_v	0.005;0.05	
$C_{h.v}^1$	Average number of contacts by infected human and vectors with rest population	0.5;0.5	
$C_{h.v}^2$	Average number of contacts by recovered human and vectors with rest population	0.5;0.5	
$\gamma_{h,v}$	Transmission rate of vaccinated v_h, v_v due to loose of immunity	0.02;0.2	$mm^3 d^{-1}$
$B_{h,v}$	Rates at which susceptible human and vectors becomes infected (*incidence rate or force of infection*)	***see eqn. (5) and parameters values***	
$\tau_{1,2}$	Rate at which vaccinated loses immunity and becomes susceptible	0.012;0.013	$mm^3 d^{-1}$
$u_{1,2}$	Treatment control functions (vaccinations)	$u_{1,2} \in [0,1)$	
$\varphi_{1,2}$	Optimal control weight factors on $u_{1,2}$	200;25	

Note: Tables 3&4 are clinically generated from certified data of [1, 3]

From Equation (5) and Figure 1, the adaptability of this model follows from the following assumptions:

Assumption 1

In addition to assumptions from motivating factor model, the basic assumption of the present model includes:

i. Only the infected and infectious transmit virus.
ii. The recovered are recruited to the susceptible population.
iii. Vaccinated class may lose immunity and becomes susceptible and/or infectious.

iv. Immunity is time dependent (i.e., immunity is soluble).
v. Listeria monocytogenes are either via non-invasive or invasive (i.e., neonatal infection).

Thus, from the last assumption, it is necessary to verify that the model state variables are all non-negative and the solutions thereof are bounded.

2.2. Positivity of state variables and boundedness of solutions

Intuitively, model (5) is a representation of living organism and so it becomes necessary to ensure that all the state components are and remain non-negative with solutions bounded. The viability of the above condition ensued the mathematically invocation of the concept of derivative of function. Obviously, if the derivative of a function at any point is positive, the function is said to be increasing at that point. The reverse is also certain as a zero derivative implies a constant function.

Therefore, from for the concept of derivative of function, it can be shown that there exist unique solutions $s_h(t), i_h(t), r_h(t), v_h(t), s_v(t), i_v(t), r_v(t), v_v(t)$ of model (4) with initial values, (Hale et al. (1993), Bassey (2017), Zhu et al. (2009)),

$$(s_h(\theta), i_h(\theta), r_h(\theta), v_h(\theta), s_v(\theta), i_v(t), r_v(\theta), v_v(\theta)) \in C\,. \tag{7}$$

Biologically, these initial value functions are assumed to be non-negative i.e.,

$$\left\{s_h(\theta), i_h(\theta), r_h(\theta), v_h(\theta), s_v(\theta), i_v(\theta), r_v(\theta), v_v(\theta) \in C \setminus C \geq 0 \;\; \forall \theta \in [t_0, t_f]\right\}. \tag{8}$$

Then, the non-negativity of model (5) and certification of initial conditions (7) and (8) is defined by the following theorem.

Theorem 1.

Let

$$\eta = \begin{Bmatrix} \left(s_h(t), i_h(t), r_h(t), v_h(t), s_v(t), i_v(t), r_v(t), v_v(t)\right) \in \Re_+^8 \\ : (s_h(0), i_h(0), r_h(0), v_h(0), s_v(0), i_v(0), r_v(0), v_v(0)) > 0 \end{Bmatrix},$$

then the solution $\{(s_h(t), i_h(t), r_h(t), v_h(t), s_v(t), i_v(t), r_v(t), v_v(t))\}$ are non-negative for all $t \geq 0$.

Proof:

By definition, if

$s_h(0), i_h(0), r_h(0), v_h(0), s_v(0), i_v(0), r_v(0), v_v(0)$ are non-negative,

then

$s_h(t), i_h(t), r_h(t), v_h(t), s_v(t), i_v(t), r_v(t), v_v(t)$,

are also non-negative for all $t > 0$.

First, taken on the human population from the model when time $t > 0$, the total human population is given by

$$N_h(t) = s_h(t) + i_h(t) + r_h(t) + v_h(t),$$

i.e.,

$$\frac{dN_h}{dt} = \frac{ds_h}{dt} + \frac{di_h}{dt} + \frac{dr_h}{dt} + \frac{dv_h}{dt}. \tag{9}$$

The initial and terminal transmission dynamics of Equation (9) can be interpreted as

$$\frac{dN_h}{dt} = b_h + \sigma_h r_h - \mu_h N_h - \alpha_h i_h + \tau_1 v_h.$$

In the absence of mortality due to listeriosis infection,

$$\frac{dN_h}{dt} \le b_h - \mu_h N_h. \tag{10}$$

Solving the above differential Equation, we have

$$b_h - \mu_h N_h \ge De^{-\mu_h t},$$

where D is a constant. Applying initial condition, $N_h(0) = N_{h(0)}$, we obtain

$$b_h - \mu_h N_{h(0)} = D.$$

Therefore,

$$b_h - \mu_h N_h \ge \left(b_h - \mu_h N_{h(0)}\right)e^{-\mu_h t} \text{ and } N_h \le \frac{b_h}{\mu_h} - \left(\frac{b_h - \mu_h N_{h(0)}}{\mu_h}\right)e^{-\mu_h t}.$$

As $t \to \infty$, the population $N_h \to \frac{b_h}{\mu_h}$. This implies that $0 \le N_h \le \frac{b_h}{\mu_h}$ and $N_h(t) \le \frac{b_h}{\mu_h}$. Also, if $N_h(0) \le \frac{b_h}{\mu_h}$, then $N_h(t) \le \frac{b_h}{\mu_h}$. This implies the following:

$$\eta_h = \{(s_h, i_h, r_h, v_h) \in \Re_+^4 : s_h + i_h + r_h + v_h \le \frac{b_h}{\mu_h}\}. \tag{11}$$

Similarly, for the vector population with $t > 0$, we have,

$$N_v(t) = s_v(t) + i_v(t) + r_v(t) + v_v(t),$$

that is,

$$\frac{dN_v}{dt} = \frac{ds_v}{dt} + \frac{di_v}{dt} + \frac{dr_v}{dt} + \frac{dv_v}{dt}. \tag{12}$$

The biological interpretation of Equation (12) gives

$$\frac{dN_v}{dt} = b_v + \sigma_v r_v - \mu_v N_v - \alpha_v i_v + \tau_2 v_v.$$

In the absence of mortality due to listeriosis infection,

$$\frac{dN_v}{dt} \le b_v - \mu_v N_v. \tag{13}$$

Solving the above differential Equation, we have $b_v - \mu_v N_v \ge De^{-\mu_v t}$, where D is a constant.

Applying initial condition, $N_v(0) = N_{v(0)}$, we obtain $b_v - \mu_v N_{v(0)} = D$. Therefore,

$$b_v - \mu_v N_v \ge \left(b_v - \mu_v N_{v(0)}\right)e^{-\mu_v t} \text{ and } N_v \le \frac{b_v}{\mu_v} - \left(\frac{b_v - \mu_v N_{v(0)}}{\mu_v}\right)e^{-\mu_v t}.$$

As $t \to \infty$, the population $N_v \to \frac{b_v}{\mu_v}$. This implies that $0 \le N_v \le \frac{b_v}{\mu_v}$ and $N_h(t) \le \frac{b_h}{\mu_h}$. Also,

$$\text{if } N_v(0) \le \frac{b_h}{\mu_v}, \text{ then } N_v(t) \le \frac{b_v}{\mu_v}.$$

Therefore,

$$\eta_v = \{(s_v, i_v, r_v, v_v) \in \Re_+^4 : s_v + i_v + r_v + v_v \le \frac{b_v}{\mu_v}\}. \tag{14}$$

Thus, the feasible region for the system of ordinary differential Equations of model (5) is given by the product of Equations (11) and (14) respectively, i.e.,

$$\eta = \eta_h \times \eta_v \subset \Re_+^4 \times \Re_+^4 . \tag{15}$$

Hence, η is positively invariant. This completes the result. W

2.3. Stability analysis of untreated listeriosis model

It is obvious that, following the complexity of both the state variables and accompanying parameters, model (5) is a complex non-linear system and as such, the model is bound to encounter somewhat complex yet basic stability analysis. Nonetheless, the ability of the model to exhibit multiple locally asymptomatically stable states will be established. Equivocally, disease-free equilibrium for system (5) exists if $u_1, u_2 = 0$ and all other controls held constant. In computing the

DFE, we let E_0 denote the DFE such that each of the Equations of model (5) is equated to zero, i.e., at disease-free equilibrium, no infection and no recovery. This implies that

$$i_h^* = 0, r_h^* = 0, i_v^* = 0, r_v^* = 0, \tag{16}$$

and

$$E_0 = (s_h^*, i_h^*, r_h^*, v_h^*, s_v^*, i_v^*, r_v^*, v_v^*) = 0\,. \tag{17}$$

From the first Equation of model (5),

$$\dot{s}_h = b_h + \sigma_h r_h - [(1+u_1) + B_h]s_h - \mu_h s_h + \tau_1 v_h\,,$$

i.e.,

$$s_h^* = \frac{b_h}{\mu_h}\,. \tag{18}$$

The vaccinated human population is obtain from:

$$\dot{v}_h = (1-u_1)s_h - (\tau_1 + \mu_h)v_h - (1+\Lambda_h)\gamma_h \beta_m^1 v_h = 0\,. \tag{19}$$

Equation (19) implies that

$$(1-u_1)s_h - (\tau_1 + \mu_h)v_h = 0\,,$$

i.e.,

$$v_h^* = \frac{(1-u_1)s_h}{\tau_1 + \mu_h}\,. \tag{20}$$

But, $u_1 = 0$ and $s_h^* = \frac{b_h}{\mu_h}$. Then, Equation (20) becomes

$$v_h^* = \frac{b_h \mu_h^{-1}}{\tau_1 + \mu_h}\,. \tag{21}$$

Similarly, for the vector population, we have,

$$\dot{s}_v = b_v + \sigma_v r_v - [(1+u_2) + B_v]s_v - \mu_v s_v + \tau_2 v_v\,,$$

i.e.,

$$s_v^* = \frac{b_v}{\mu_v}\,. \tag{22}$$

The vaccinated human population is obtained from:

$$\dot{v}_v = (1-u_2)s_v - (\tau_2 + \mu_v)v_v - (1+\Lambda_v)\gamma_v \beta_m^2 v_v = 0\,, \tag{23}$$

which implies that

$$(1-u_2)s_v - (\tau_2 + \mu_v)v_v = 0\,,$$

i.e.,

$$v_v^* = \frac{(1-u_2)s_v}{\tau_2 + \mu_v}. \tag{24}$$

But, $u_2 = 0$ and $s_v^* = \frac{b_v}{\mu_v}$. Then, Equation (24) becomes

$$v_v^* = \frac{b_v \mu_v^{-1}}{\tau_2 + \mu_v}. \tag{25}$$

Therefore, substituting Equations (16), (18), (21), (22) and (25) into Equation (17), we obtain

$$E_0 = \left(\frac{b_h}{\mu_h}, 0, 0, \frac{b_h \mu_h^{-1}}{\tau_1 + \mu_h}, \frac{b_h}{\mu_h}, 0, 0, \frac{b_v \mu_v^{-1}}{\tau_2 + \mu_v} \right). \tag{26}$$

Equation (26) is the DFE when no infection and no recovery occur.

Next, is to establish the system basic reproduction number. Here, the concept of Next Generation matrix is invoked in deriving a linear stability of the DFE. By definition, the basic reproduction number is the rate of secondary infections produced by one infected human/animal upon interaction with a completely susceptible population. This reproduction number is necessary as it accentuate the biological infection in relation to the social and behavioral factors associated with rate of contact. Moreso, the basic reproduction is the threshold parameter that governs the spread of a disease, (Murray et al. (1926), Osman et al. (2018)). General, the next-generation matrix is defined as:

$$K = FV^{-1} \text{ and } R_{0(h,v)} = \Omega(FV^{-1}),$$

where $\Omega(FV^{-1})$ denotes the spectral radius of FV^{-1}.

Applying the Next-Generation matrix, only the infectious subgroups of the system (4) will be considered i.e.,

$$\begin{cases} \frac{di_h}{dt} = B_h s_h + (1 - \Lambda_h)\gamma_h v_h - (\lambda + \mu_h + \alpha_h) i_h, \\ \frac{di_v}{dt} = B_v s_v + (1 - \Lambda_v)\gamma_v v_v - (\rho + \mu_v + \alpha_v) i_v, \end{cases} \tag{27}$$

where B_h and B_v are as defined by Equation (6). Then,

$$f = \begin{bmatrix} B_h s_h + (1-\Lambda_h)\gamma_h v_h \\ B_v s_v + (1-\Lambda_v)\gamma_v v_v \end{bmatrix}, \; v = \begin{bmatrix} (\lambda + \mu_h + \alpha_h) i_h \\ (\rho + \mu_v + \alpha_v) i_v \end{bmatrix},$$

where f define the number of new infection infiltrating the system and v, representing the clearance rate of infections in the system. The Jacobian matrix of f and v at DFE are derived as:

$$F = \begin{bmatrix} \frac{\partial f_1}{\partial i_h} & \frac{\partial f_1}{\partial i_v} \\ \frac{\partial f_2}{\partial i_h} & \frac{\partial f_2}{\partial i_v} \end{bmatrix} = \begin{bmatrix} (c_h^1 + c_h^2)\gamma_h\beta_h s_h^* & (c_h^1 + c_h^2)\gamma_h\beta_v s_h^* \\ (c_v^1 + c_v^2)\gamma_v\beta_h s_v^* & (c_v^1 + c_v^2)\gamma_v\beta_v s_v^* \end{bmatrix}, \tag{28}$$

and

$$V = \begin{bmatrix} \frac{\partial v_1}{\partial i_h} & \frac{\partial v_1}{\partial i_v} \\ \frac{\partial v_2}{\partial i_h} & \frac{\partial v_2}{\partial i_v} \end{bmatrix} = \begin{bmatrix} (\lambda + \mu_h + \alpha_h) & 0 \\ 0 & (\rho + \mu_v + \alpha_v) \end{bmatrix}. \tag{29}$$

By computing the product of FV^{-1}, we have,

$$FV^{-1} = \begin{bmatrix} (c_h^1 + c_h^2)\gamma_h\beta_h s_h^* & (c_h^1 + c_h^2)\gamma_h\beta_v s_h^* \\ (c_v^1 + c_v^2)\gamma_v\beta_h s_v^* & (c_v^1 + c_v^2)\gamma_v\beta_v s_v^* \end{bmatrix} \begin{bmatrix} \frac{1}{(\lambda + \mu_h + \alpha_h)} & 0 \\ 0 & \frac{1}{(\rho + \mu_v + \alpha_v)} \end{bmatrix},$$

i.e.,

$$FV^{-1} = \begin{bmatrix} \frac{(c_h^1 + c_h^2)\gamma_h\beta_h s_h^*}{(\lambda + \mu_h + \alpha_h)} & \frac{(c_h^1 + c_h^2)\gamma_h\beta_h s_h^*}{(\rho + \mu_v + \alpha_v)} \\ \frac{(c_v^1 + c_v^2)\gamma_v\beta_v s_v^*}{(\lambda + \mu_h + \alpha_h)} & \frac{(c_v^1 + c_v^2)\gamma_v\beta_v s_v^*}{(\rho + \mu_v + \alpha_v)} \end{bmatrix}. \tag{30}$$

Now, letting D denote the eigenvalue of the matrix, then the eigenvalues of FV^{-1} can be computed as follows:

$$\begin{vmatrix} \frac{(c_h^1 + c_h^2)\gamma_h\beta_h s_h^*}{(\lambda + \mu_h + \alpha_h)} - D & \frac{(c_h^1 + c_h^2)\gamma_h\beta_h s_h^*}{(\rho + \mu_v + \alpha_v)} \\ \frac{(c_v^1 + c_v^2)\gamma_v\beta_v s_v^*}{(\lambda + \mu_h + \alpha_h)} & \frac{(c_v^1 + c_v^2)\gamma_v\beta_v s_v^*}{(\rho + \mu_v + \alpha_v)} - D \end{vmatrix} = 0. \tag{31}$$

Expanding and rearranging, we have,

$$D^2 - \left[\left(\frac{(c_v^1 + c_v^2)\gamma_v\beta_v s_v^*}{(\rho + \mu_v + \alpha_v)} \right) + \left(\frac{(c_h^1 + c_h^2)\gamma_h\beta_h s_h^*}{(\lambda + \mu_h + \alpha_h)} \right) \right] D = 0. \tag{32}$$

Solving the above quadratic, $D_1 = 0$ and

$$D_2 = \left[\left(\frac{(c_v^1 + c_v^2)\gamma_v\beta_v s_v^*}{(\rho + \mu_v + \alpha_v)} \right) + \left(\frac{(c_h^1 + c_h^2)\gamma_h\beta_h s_h^*}{(\lambda + \mu_h + \alpha_h)} \right) \right].$$

Therefore, the dominant eigenvalue is D_2, which implies that the reproduction number $R_{0(h,v)}$ is

$$R_{0(h,v)} = \left[\left(\frac{(c_h^1 + c_h^2)\gamma_h \beta_h s_h^*}{(\lambda + \mu_h + \alpha_h)} \right) + \left(\frac{(c_v^1 + c_v^2)\gamma_v \beta_v s_v^*}{(\rho + \mu_v + \alpha_v)} \right) \right]. \tag{33}$$

But from Equations (18) and (22), we have,

$$s_h^* = \frac{b_h}{\mu_h} \text{ and } s_v^* = \frac{b_v}{\mu_v}.$$

Then, Equation (33) becomes

$$R_{0(h,v)} = \left[\left(\frac{(c_h^1 + c_h^2)\gamma_h \beta_h b_h}{\mu_h(\lambda + \mu_h + \alpha_h)} \right) + \left(\frac{(c_v^1 + c_v^2)\gamma_v \beta_v b_v}{\mu_v(\rho + \mu_v + \alpha_v)} \right) \right]. \tag{34}$$

Thus, from Equation (34), the reproduction number for human population denoted by $R_{0(hq)}$ is obtained as:

$$R_{0(hq)} = \frac{(c_h^1 + c_h^2)\gamma_h \beta_h b_h}{\mu_h(\lambda + \mu_h + \alpha_h)},$$

and for the vectors, we have,

$$R_{0(vq)} = \frac{(c_v^1 + c_v^2)\gamma_v \beta_v b_v}{\mu_v(\rho + \mu_v + \alpha_v)}.$$

Therefore, it follows that vaccination of susceptible human and animal population will definitely amount to reduction in reproduction number $R_{0(h,v)}$. Then, the following proposition holds:

Proposition 1

The disease-free equilibrium (DFE) of model (4) is locally asymptotically stable provided $R_{0(h,v)} < 1$, otherwise, it is unstable if $R_{0(h,v)} > 1$.

Furthermore, in addition to DFE, model (5) in conjunction to tables (1 & 2) exhibits two other physical steady states and several non-physically steady states (omitted here for brevity). For related analysis, see models, (Schuchat et al. (1991), Jemmi et al. (2006)). More importantly, not going off the goal of this study, which is the derivation of a mathematical and quantitative approach geared towards the maximization of the performance index of the concentration of susceptible, recovered and vaccinated population via minimal chemotherapy cost, it becomes obvious to transform model (5) to an optimal control problem capable of accommodating desired treatment functions with defined objective functional.

3. Optimal Control Problem and Characterization

In this section, the process of chemotherapy application and observed treatment schedules is achievable by transforming the derived system to an optimal control problem from which the

characterization of the control is established. Also, to be determine in this section, is the existence of an optimal control.

3.1. Formulation of optimal control

For a system of model (5), which is established based on dual listeriosis infection and studied under multiple chemotherapy, the investigation seeks to maximize the levels of susceptible, the recovered and vaccinated population under minimized systemic cost and at the same time, suppressed infectious vectors. Therefore, if $u_1(t)$ and $u_2(t)$ are introduced such that there represent control functions (suppressive and immunostimulatory vaccinations) with domain for $u_{i=1,2}$ defined by the interval $a_i, b_i \in [0,1]_{i=1,2}$, then we say that chemotherapy is completely effective if $u_i = 1$ and off treatment if $u_i = 0$. Thus, the model seek an optimal control pair u_1^*, u_2^* defined by

$$J(u_1^*, u_2^*) = \max_{0 \le u_i \le 1} \{J(u_1, u_2) \setminus (u_1, u_2) \in Q\},$$

where $Q := \{(u_1, u_2) \setminus u_i$ is Lebesgue-measurable with $a_i \le u_i \le b_i$, $t \in [t_0, t_f], \forall i = 1, 2\}$ a control set. Mathematically, the objective functional for the control problem is formulated as:

$$J(u_1, u_2) = \int_{t_0}^{t_f} \{s_{h,v}(t) + r_{h,v}(t) + v_{h,v}(t) - [\varphi_1(u_1(t))^2 + \varphi_2(u_2(t))^2]\} dt, \tag{35}$$

subject to the state system

$$\begin{aligned}
\dot{s}_h &= b_h + \sigma_h r_h - [(1+u_1) + B_h] s_h - \mu_h s_h + \tau_1 v_h, \\
\dot{i}_h &= B_h s_h + (1-\Lambda_h)\gamma_h v_h - (\lambda + \mu_h + \alpha_h) i_h, \\
\dot{r}_h &= \lambda i_h + u_1 r_h - (\sigma_h + \mu_h) r_h, \\
\dot{v}_h &= (1-u_1) s_h - (\tau_1 + \mu_h) v_h - (1+\Lambda_h)\gamma_h \beta_m^1 v_h, \\
\dot{s}_v &= b_v + \sigma_v r_v - [(1+u_2) + B_v] s_v - \mu_v s_v + \tau_2 v_v, \\
\dot{i}_v &= B_v s_v + (1-\Lambda_v)\gamma_v v_v - (\rho + \mu_v + \alpha_v) i_v, \\
\dot{r}_v &= \rho i_v + u_2 r_v - (\sigma_v + \mu_v) r_v, \\
\dot{v}_v &= (1-u_2) s_v - (\tau_2 + \mu_v) v_v - (1+\Lambda_v)\gamma_v \beta_m^2 v_v,
\end{aligned} \tag{36}$$

where $u_1 r_h$ and $u_2 r_v$ depicts recovery of both human and animals under chemotherapy and $(1-u_1)s_h, (1-u_2)s_v$ are proportions of vaccinated human and animals at time t.

Remark 1

The introduction of optimal function $\varphi_{i=1,2} \ge 0$ as the optimal weight factors account for the fact that benefit on cost functional is nonlinear and thus, cases of drug side-effects are adequately under control, Pontello et al. (2012).

Proposition 2

Assume there exist drug hazardous side-effect, then the inequality on optimal weight factors $\varphi_{i=1,2}$ is such that $0 \le a_i \le u_i \le b_i < 1$ holds, (Rossi et al. (2008), Bassey (2018)).

3.2. Characterization of optimal control

For a realistic formulation of an optimal control, characterization of the penalty terms on constraints is necessary. Actualization of this requires the invocation of classical Pontryagin's Maximum Principle with which the objective functional is the Hamiltonian argument defined by the Lagrangian, Posfay-Barbe et al. (2004):

$$
\begin{aligned}
L\begin{pmatrix} s_h(t), i_h(t), r_h(t), v_h(t), s_v(t), i_v(t), r_v(t), v_v(t), u_1(t), u_2(t), \\ \delta_1(t), \delta_2(t), \delta_3(t), \delta_4(t), \delta_5(t), \delta_6(t), \delta_7(t), \delta_8(t) \end{pmatrix} \\
= s_{h,v}(t) + r_{h,v}(t) + v_{h,v}(t) - [\varphi_1(u_1(t))^2 + \varphi_2(u_2(t))^2] \\
+\delta_1[b_h + \sigma_h r_h - [(1+u_1) + B_h]s_h - \mu_h s_h + \tau_1 v_h] \\
+\delta_2[B_h s_h + (1-\Lambda_h)\gamma_h v_h - (\lambda + \mu_h + \alpha_h)i_h] \\
+\delta_3[\lambda i_h + u_1 r_h - (\sigma_h + \mu_h)r_h] \\
+\delta_4[(1-u_1)s_h - (\tau_1 + \mu_h)v_h - (1+\Lambda_h)\gamma_h \beta_m^1 v_h] \\
+\delta_5[b_v + \sigma_v r_v - [(1+u_2) + B_v]s_v - \mu_v s_v + \tau_2 v_v] \\
+\delta_6[B_v s_v + (1-\Lambda_v)\gamma_v v_v - (\rho + \mu_v + \alpha_v)i_v] \\
+\delta_7[\rho i_v + u_2 r_v - (\sigma_v + \mu_v)r_v] \\
+\delta_8[(1-u_2)s_v - (\tau_2 + \mu_v)v_v - (1+\Lambda_v)\gamma_v \beta_m^2 v_v] \\
+\phi_{11}(t)(b_1 - u_1) + \phi_{12}(t)(u_1 - a_1) \\
+\phi_{21}(t)(b_2 - u_2) + \phi_{22}(t)(u_2 - a_2),
\end{aligned}
\tag{37}
$$

where $\phi_{ij}(t) \ge 0 \ \forall i, j = 1,2$ are penalty multipliers satisfying

$$\phi_{11}(t)(b_1 - u_1) = 0, \ \phi_{12}(t)(u_1 - a_1) = 0, \qquad \text{at the optimal } u_1^*$$

and

$$\phi_{21}(t)(b_2 - u_2) = 0, \ \phi_{22}(t)(u_2 - a_2) = 0, \qquad \text{at the optimal } u_2^*.$$

These penalty multipliers ensures that $u_{i=1,2}^*$ is bounded in the domain $u_i \in [0,1]$, while the model adjoint variable are the $\delta_{j=1,\ldots,8}$, which determines the adjoint system. Of note, this adjoint system together with the state system determines the model optimality system. Therefore, the characteristics of the control system are achieved by examining all possible controls for u_i^* and including those on limit conditions $(0 \le u_i^* \le 1)$.

i) For the case $\{t / 0 < u_i(t) < 1\} : \phi_{ij} = 0, i = 1,2$: Pontryagin's maximum principle state that the unconstrained optimal control $u_i^*(t)$ satisfies

$$\frac{\partial L}{\partial u_1^*} = 0 \text{ and } \frac{\partial L}{\partial u_2^*} = 0.$$

Then, for $\frac{\partial L}{\partial u_i^*} = 0, i = 1, 2$, u_1^* and u_2^* can be solved by setting the partial derivative of L equal to zero, i.e.,

$$\frac{\partial L}{\partial u_1^*} = -2\varphi_1 u_1^*(t) + \delta_1 s_h + \delta_3 r_h - \delta_4 s_h - \phi_{11}(t) + \phi_{12}(t) = 0, \qquad \text{at } u_1^*.$$

Similarly,

$$\frac{\partial L}{\partial u_2^*} = -2\varphi_2 u_2^*(t) + \delta_5 s_v + \delta_7 r_v - \delta_8 s_v - \phi_{21}(t) + \phi_{22}(t) = 0, \qquad \text{at } u_2^*.$$

Now, solving for the optimal controls for u_1^* when $\phi_{ij} = 0$, we have,

$$u_1^*(t) = \frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h}{2\varphi_1} \tag{38}$$

and

$$u_2^*(t) = \frac{\delta_5 s_v + \delta_7 r_v - \delta_8 s_v}{2\varphi_2}. \tag{39}$$

Other characteristics of $u_i^*(t)$ are as follows:

ii) For case $\{t / u_i^*(t) = 0, i = 1, 2\} : \phi_{1j} \geq 0, \phi_{i2} = 0, i, j = 1$: The optimal control is given by

$$0 = \frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h - \phi_{1j}}{2\varphi_1},$$

which implies

$$\frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h}{2\varphi_1} \leq 0, \text{ since } \phi_{1j} \geq 0.$$

To ensure that u_1^* is non-negative, case (ii) is notated as:

$$u_1^*(t) = \left(\frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h}{2\varphi_1} \right)^+ = 0,$$

i.e.,

$$u_1^*(t) = \left(\frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h}{2\varphi_1} \right)^+.$$

Taking similar proceeding,

$$u_2^*(t) = \left(\frac{\delta_5 s_v + \delta_7 r_v - \delta_8 s_v}{2\varphi_2} \right)^+.$$

iii) For the case set $\{t / u_i^*(t) = 1, i = 1,2\} : \phi_{i1} = 0, \phi_{2j} \geq 0, i, j = 2$: The optimal control is obtained as:

$$1 = \frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h + \varphi_{2j}}{2\varphi_1}.$$

This implies that

$$0 \leq \varphi_{2j} = \delta_1 s_h + \delta_3 r_h - \delta_4 s_h - 2\varphi_1.$$

Therefore,

$$\left\{\left(\frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h}{2\varphi_1}\right) \geq 1\right\} = u_1^*.$$

Similarly,

$$\left\{\left(\frac{\delta_5 s_v + \delta_7 r_v - \delta_8 s_v}{2\varphi_2}\right) \geq 1\right\} = u_2^*.$$

Thus, on this set, we must choose

$$u_1^*(t) = \min\left\{\left(\frac{\delta_1 s_h + \delta_3 r_h - \delta_4 s_h}{2\varphi_1}\right), 1\right\} \text{and} \, u_2^*(t) = \min\left\{\left(\frac{\delta_5 s_v + \delta_7 r_v - \delta_8 s_v}{2\varphi_2}\right), 1\right\}.$$

Hence, a complete characterization of the optimal controls is defined by absorbing the three cases for $u_1^* \, u_2^*$. As compactly presented in the following proposition:

Proposition 3

The optimal control functions for the optimal control problem (36) and (37) with bounds $0 \leq a_i \leq u_i \leq b_i < 1$ is compatibly characterized by

$$u_1^*(t) = min\left\{max\left\{a_1, \tfrac{1}{2\varphi_1}(\delta_1 s_h + \delta_3 r_h - \delta_4 s_h)\right\}^+, b_1\right\}, \tag{40}$$

and

$$u_2^*(t) = \min\left\{\max\left\{a_2, \frac{1}{2\varphi_2}\left(\delta_5 s_v + \delta_7 r_v - \delta_8 s_v\right)\right\}^+, b_2\right\}. \tag{41}$$

Remark 2

Proposition 3 clearly depicts the fact that control functions $u_{i=1,2}^*$ are concurrently define in relation to circulating terms of healthy (susceptible) and recovered population and their adjoint variables. In this case, it becomes worthy at this moment to consider the existence of an optimal control pair for a dual infectious listeriosis.

3.3. Existence of an optimal control pair

Obviously, the model has been realistic with the imposition of restriction on the parameters as observed by Equations (35) and (36) respectively. For instance, if $s_{h,v(\max)}$ is the maximum limit of susceptible population and it is assumed that death rate at $s_{h,v}$ is to be greater than the source rate, then, an assumption of the form

$$\mu_{h,v} s_{h,v(\max)} > b_{h,v}, \tag{42}$$

holds. The implication is that a steady state population size that is below $s_{h,v(\max)}$ must be attained, such that any infiltration by infectious vector can be adequately accommodated. Moreover, population growth will be slow if population size ever gets near $s_{h,v(\max)}$ (Rossi et al. (2008), Posfay-Barbe et al. (2004)).

Notably, the existence of an optimal control and uniqueness proof for optimality system requires upperbounds. Therefore, for $s_{h,v}(t) < s_{h,v(\max)}$ the upperbounds on the solutions of actively infectious state components are determined as:

$$\frac{d\hat{i}_h}{dt} = Bs_h + (1-\Lambda_h)\gamma_h v_h, \qquad \hat{\imath}_h(t_0) = i_{(h)0},$$

and

$$\frac{d\hat{i}_v}{dt} = Bs_v + (1-\Lambda_v)\gamma_v v_v, \qquad \hat{\imath}_v(t_0) = i_{(v)0}.$$

If we invoke Equation (6), the above expression becomes

$$\frac{d\hat{i}_h}{dt} = [(c_h^1 + c_h^2)\gamma_h \beta_v i_v] s_{h(\max)} + (1-\Lambda_h)\gamma_h v_h, \qquad \hat{\imath}_h(t_0) = i_{(h)0},$$

and

$$\frac{d\hat{i}_v}{dt} = [(c_v^1 + c_v^2)\gamma_v \beta_h i_h] s_{v(\max)} + (1-\Lambda_v)\gamma_v v_v, \qquad \hat{\imath}_v(t_0) = i_{(v)0}.$$

or

$$\begin{pmatrix} \hat{i}_h \\ \hat{i}_v \end{pmatrix} = \begin{pmatrix} 0 & (c_h^1 + c_h^2)\gamma_h \beta_v i_v s_{h(\max)} \\ (c_v^1 + c_v^2)\gamma_v \beta_h i_h s_{v(\max)} & 0 \end{pmatrix} \begin{pmatrix} \hat{i}_h \\ \hat{i}_v \end{pmatrix}.$$

Therefore, the system is linear with bonded coefficient and supersolutions $\hat{i}_h, \hat{i}_v$ uniformly bounded as well. Thus, the existence is then established by taking a leap from models {Theorem. 2, pg. 26-27, Bassey (2018); Theorem. 4.1, pg. 68-69, Fleming et al. (1975)}.

Theorem 2.

Given proposition 2 and Equation (42), there exists an optimal control pair $(u_1^*, u_2^*) \in S$ that maximizes the objective functional $J(u_1, u_2)$ such that

$$\max_{(u_1,u_2)\in S} J(u_1, u_2) = J(u_1^*, u_2^*). \tag{43}$$

Proof:

Invoking the results of (Bassey (2018). Fleming et al. (1975), it can be shown that the following conditions are satisfied:

i. The control class $u_{i=1,2}(t)$ is Lebesgue-integrable functions on $[t_0, t_f]$ with values in the admissible control sets and that the corresponding state variables are satisfied and non-empty.
ii. The admissible control set S, is convex and closed.
iii. The right-hand side (RHS) of the state components is continuous and bounded by a linear function $u_{i=1,2}$ and having coefficient, which depends on proposition 2 and on the control variables.
iv. The integrand of the objective functional is concave on S.
v. There exist constants $k_1, k_2 > 0$ and ξ, such that the integrand $L(s_{h,v}, r_{h,v}, v_{h,v}, u_1, u_2)$ of the objective functional satisfies $L(s_{h,v}, r_{h,v}, v_{h,v}, u_1, u_2) \le k_2 - k_1(|u_1|^2 + |u_2|^2)^{\xi/2}$.

From Theorem. 9.2.1, page. 182, Perelson et al. (1993), the existence of solutions for Equation (36) is established and having bounded coefficients, which satisfies condition (i). Furthermore, it is seen here that the solutions are bounded and by definition, the control set is closed and convex, making condition (ii) obvious. Now, since the state system is bilinear in $u_{i=1,2}$ and RHS of Equation (37) satisfies condition (iii) and are bounded priori. Moreso, the integrand

$$\{s_{h,v}(t) + r_{h,v}(t) + v_{h,v}(t) - [\varphi_1(u_1(t))^2 + \varphi_2(u_2(t))^2]\} \le k_2 - k_1(|u_1|^2 + |u_2|^2)^{\xi/2},$$

where k_2 depends on the upper bound on $s_{h,v}, r_{h,v}, v_{h,v}$ and $k_1 > 0$, noting that $\{\varphi_1, \varphi_2\} > 0$. Hence, proof completed. W

4. Optimality System and Uniqueness

For a bilinear state system with existence of an optimal control pair, this section shall be devoted to the derivation of the system optimality theory and the establishment of uniqueness of the system.

4.1. Optimality system for an optimal control pair

Basically, optimality system is a vital component of the optimal control problem noting that it consists of the state variables couple with the adjoint system with the initial conditions and transversality conditions together with the derived optimal pair. Furthermore, it is a tool with which the biological behavior of the system is observed following the application of control

functions. It also serves as a mechanism for the determination of growth rate or clearance rate of state variables, (Rossi et al. (2008), Bassey (2018)).

Then, in line with the given description, the adjoint system of the model can be deduced as:

$$\frac{d\delta_i}{dt} = -\frac{\partial L}{\partial \Pi_i},$$

where $\Pi_{i=1,\ldots,8}$ are the state components. Thus, the final key components in the optimality system are the set of transversality conditions, which reduces and terminate the condition on the adjoint variables. Since our goal is that of maximization problem of the form

$$\max_{(u_1,u_2)\in S} J(u_1,u_2) = G(s_{h,v}(t) + r_{h,v}(t) + v_{h,v}(t)) + \int_{t_0}^{t_f} g_0(s_{h,v}, r_{h,v}, v_{h,v}, u_1, u_2)ds,$$

subject to

$$\frac{d\Pi_{s,r,v}}{dt} = g(t, \Pi_{s,r,v}, u_1, u_2),$$

such that, if $\Pi_{s,r,v}(t)$ belong to some target set $p(\Pi_{s,r,v}(t))$, then the following transversality conditions on the adjoint variables holds:

$$\delta_i(t) = \overline{v}G(\Pi_{s,r,v}(t)) + \sum_{i=1}^{n} c_i\, p_i(\Pi_{s,r,v}(t)), \tag{44}$$

where G is a function denoting terminal cost. But clearly, system control problem have no terminal cost. So, $G(\Pi_{s,r,v}(t)) = 0$. Also, no target set for the model, thus, the desired end result contains free-state variables. Therefore, the summation term is zero too. The implication is that the system transversality condition for the adjoint variables is

$$\delta_i(t_f) = 0, \forall i = 1, \cdots, 8. \tag{45}$$

From definition 2, if we sum the result of substitution of Equations (5), (40) and (41) into Equation (36), and Equation (37) after the differentiation of δ_i, then the following optimality system is obtained as:

$$\begin{aligned}
s_h' &= b_h + \sigma_h r_h - [(1+u_1) + B_h]s_h - \mu_h s_h + \tau_1 v_h,\\
i_h' &= B_h s_h + (1-\Lambda_h)\gamma_h v_h - (\lambda + \mu_h + \alpha_h)i_h,\\
r_h' &= \lambda i_h + u_1 r_h - (\sigma_h + \mu_h)r_h,\\
v_h' &= (1-u_1)s_h - (\tau_1 + \mu_h)v_h - (1+\Lambda_h)\gamma_h \beta_m^1 v_h,\\
s_v' &= b_v + \sigma_v r_v - [(1+u_2) + B_v]s_v - \mu_v s_v + \tau_2 v_v,\\
i_v' &= B_v s_v + (1-\Lambda_v)\gamma_v v_v - (\rho + \mu_v + \alpha_v)i_v,\\
r_v' &= \rho i_v + u_2 r_v - (\sigma_v + \mu_v)r_v,\\
v_v' &= (1-u_2)s_v - (\tau_2 + \mu_v)v_v - (1+\Lambda_v)\gamma_v \beta_m^2 v_v,
\end{aligned}$$

$$
\begin{aligned}
\delta_1' &= -1\begin{Bmatrix}\delta_1[-1(1+u_1^*)-(c_h^1+c_h^2)\gamma_h[\beta_h i_h+\beta_v i_v]-\mu_h]\\ +\delta_2[(c_h^1+c_h^2)\gamma_h[\beta_h i_h+\beta_v i_v]]+\delta_4(1-u_1^*)\end{Bmatrix},\\
\delta_2' &= -1\left\{\delta_1[-(c_h^1+c_h^2)\gamma_h\beta_h s_h]+\delta_2[-(c_h^1+c_h^2)\gamma_h\beta_h s_h-(\lambda+\mu_h+\alpha_h)]+\delta_3\lambda\right\},\\
\delta_3' &= -1\left\{\delta_1\lambda+\delta_3[u_1^*-(\sigma_h+\mu_h)]\right\},\\
\delta_4' &= -1\left\{\delta_1\lambda+\delta_2[(1-\Lambda_h)\gamma_h-\delta_4[(\tau_1+\mu_h)-(1+\Lambda_h)\gamma_h\beta_m^1\right\},\\
\delta_5' &= -1\begin{Bmatrix}\delta_5[-1(1+u_2^*)-(c_v^1+c_v^2)\gamma_v[\beta_h i_h+\beta_v i_v]-\mu_v]\\ +\delta_6[(c_v^1+c_v^2)\gamma_v[\beta_h i_h+\beta_v i_v]]+\delta_8(1-u_2^*)\end{Bmatrix},\\
\delta_6' &= -1\left\{\delta_5[-(c_v^1+c_v^2)\gamma_v\beta_v s_v]+\delta_6[-(c_v^1+c_v^2)\gamma_v\beta_v s_v-(\rho+\mu_v+\alpha_v)]+\delta_7\rho\right\},\\
\delta_7' &= -1\left\{\delta_5\sigma_v+\delta_7[u_2^*-(\sigma_v+\mu_v)]\right\},\\
\delta_8' &= -1\left\{\delta_5\tau_2+\delta_6[(1-\Lambda_v)\gamma_v-\delta_8[(\tau_2+\mu_v)-(1+\Lambda_v)\gamma_v\beta_m^2\right\},
\end{aligned}
\tag{46}
$$

where B_h and B_v are taken from Equation (6), with $\delta_i(t)=0, \forall i=1,...,8$ and u_1^*, u_2^* the optimal control functions designated by Equations (40) and (41), respectively.

4.2. Uniqueness of optimality system

Here, a simple proof is necessary for a small time interval to justify the uniqueness of solution of the system. From the point of existence of optimality system, since

$$s_{h,v} < s_{(h,v)\max},$$

then the system has a finite upperbounds. Of note, the uniqueness requires an upperbounds for its proof. The proof takes a leap from the following lemma.

Lemma 1.

The control pair functions $u_i^*(z)=(\min(\max(z,a,b)))$ is Lipschitz continuous in z, where $a<b$ are some fixed positive constants.

Theorem 3.

Let the time interval t_f be sufficiently small as possible, then bounded solutions of the optimality system are unique, (Bassey (2018), Joshi et al. (2002), Fister et al. (1998)).

Proof:

Suppose,

$$(s_h, i_h, r_h, v_h, s_v, i_v, r_v, v_v, \delta_1, \delta_2, \delta_3, \delta_4, \delta_5, \delta_6, \delta_7, \delta_8)$$

and

$$(\overline{s}_h, \overline{i}_h, \overline{r}_h, \overline{v}_h, \overline{s}_v, \overline{i}_v, \overline{r}_v, \overline{v}_v, \overline{\delta}_1, \overline{\delta}_2, \overline{\delta}_3, \overline{\delta}_4, \overline{\delta}_5, \overline{\delta}_6, \overline{\delta}_7, \overline{\delta}_8)$$

are two solutions of the model optimality system (46). Then, the values of the solution is obtain by letting

$$s_h = g^{\delta t}e, i_h = g^{\delta t}f, r_h = g^{\delta t}h, v_h = g^{\delta t}l, s_v = g^{\delta t}j, i_v = g^{\delta t}k, r_v = g^{\delta t}m, v_v = g^{\delta t}n,$$
$$\delta_1 = g^{\delta t}p, \delta_2 = g^{\delta t}q, \delta_3 = g^{\delta t}s, \delta_4 = g^{\delta t}t, \delta_5 = g^{\delta t}u, \delta_6 = g^{\delta t}w, \delta_7 = g^{\delta t}x, \delta_8 = g^{\delta t}y\ ,$$

and

$$\bar{s}_h = g^{\delta t}\bar{e}, \bar{i}_h = g^{\delta t}\bar{f}, \bar{r}_h = g^{\delta t}\bar{h}, \bar{v}_h = g^{\delta t}\bar{l}, \bar{s}_v = g^{\delta t}\bar{j}, \bar{i}_v = g^{\delta t}\bar{k}, \bar{r}_v = g^{\delta t}\bar{m}, \bar{v}_v = g^{\delta t}\bar{n},$$
$$\bar{\delta}_1 = g^{\delta t}\bar{p}, \bar{\delta}_2 = g^{\delta t}\bar{q}, \bar{\delta}_3 = g^{\delta t}\bar{s}, \bar{\delta}_4 = g^{\delta t}\bar{t}, \bar{\delta}_5 = g^{\delta t}\bar{u}, \bar{\delta}_6 = g^{\delta t}\bar{w}, \bar{\delta}_7 = g^{\delta t}\bar{x}, \bar{\delta}_8 = g^{\delta t}\bar{y}\ ,$$

where $\delta > 0$ is to be chosen. Furthermore, if the above variables are substituted into the derived optimal pair solutions (Equations (40), (41) and (46)), then the solutions becomes

$$u_1^*(t) = \min\left\{\max\left\{a_1, \frac{1}{2\varphi_1}\left(pe + sh + te\right)\right\}, b_1\right\},$$
$$u_2^*(t) = \min\left\{\max\left\{a_2, \frac{1}{2\varphi_2}\left(uj + xm + yi\right)\right\}, b_2\right\},$$

and

$$\bar{u}_1^*(t) = \min\left\{\max\left\{a_1, \frac{1}{2\varphi_1}\left(\bar{p}\bar{e} + \bar{s}\bar{h} + \bar{t}\bar{e}\right)\right\}, b_1\right\},$$
$$\bar{u}_2^*(t) = \min\left\{\max\left\{a_2, \frac{1}{2\varphi_2}\left(\bar{u}\bar{j} + \bar{x}\bar{m} + \bar{y}\bar{i}\right)\right\}, b_2\right\}.$$

Next, we substitute $s_h = g^{\delta t}e$ and all corresponding terms into the first ODE of Equation (46) and then differentiate to obtain

$$e' + \delta e = b_h + \sigma_h g^{\delta t}h - (1 + u_1^*(t))g^{\delta t}e - (c_h^1 + c_h^2)\gamma_h[\beta_h f + \beta_v k)g^{\delta t}]g^{\delta t}e - \mu_h g^{\delta t}e + \tau_1 g^{\delta t}l\ ,$$

$$f' + \delta f = (c_h^1 + c_h^2)\gamma_h[\beta_h f + \beta_v k)g^{\delta t}]g^{\delta t}e + (1 - \Lambda_h)\gamma_h g^{\delta t}l - (\lambda + \mu_h + \alpha_h)g^{\delta t}f\ ,$$

$$h' + \delta h = \lambda g^{\delta t}f + u_1^*(t)g^{\delta t}h - (\sigma_h + \mu_h)g^{\delta t}h\ ,$$

$$l' + \delta l = (1 - u_1^*(t)) - (\tau_1 + \mu_h)g^{\delta t}l - (1 + \Lambda_h)\gamma_h(\beta_h^1 g^{\delta t}l)\ ,$$

$$j' + \delta j = b_h + \sigma_v g^{\delta t}m - (1 + u_2^*(t))g^{\delta t}j - (c_v^1 + c_v^2)\gamma_v[\beta_v f + \beta_v k)g^{\delta t}]g^{\delta t}j - \mu_h g^{\delta t}j + \tau_2 g^{\delta t}n\ ,$$

$$k' + \delta k = (c_v^1 + c_v^2)\gamma_v[\beta_h f + \beta_v k)g^{\delta t}]g^{\delta t}j + (1 - \Lambda_v)\gamma_v g^{\delta t}m - (\rho + \mu_v + \alpha_v)g^{\delta t}j\ ,$$

$$m' + \delta m = \rho g^{\delta t}j + u_2^*(t)g^{\delta t}m - (\sigma_v + \mu_v)g^{\delta t}m\ ,$$

$$n' + \delta n = (1 - u_2^*(t)) - (\tau_2 + \mu_v) g^{\delta t} n - (1 + \Lambda_v)\gamma_v(\beta_v^1 g^{\delta t} n),$$

$$p' + \delta p = -1\begin{Bmatrix} g^{\delta t} p[-(1+u_1^*(t)) - (c_h^1 + c_h^2)\gamma_h[\beta_h f + \beta_v k) g^{\delta t}] - \mu_h] \\ +g^{\delta t} q[(c_h^1 + c_h^2)\gamma_h[\beta_h f + \beta_v k) g^{\delta t}] + g^{\delta t} t(1 - u_1^*(t)) \end{Bmatrix},$$

$$\vdots \qquad (48)$$

$$y' + \delta y = -1\left\{ g^{\delta t} u\tau_2 + g^{\delta t} w[(1 - \Lambda_v\gamma_v] - g^{\delta t} y[-(\tau_2 + \mu_2) - (1 + \Lambda_v)\gamma_v\beta_m^2 \right\}.$$

Next, we perform the subtraction of state solutions $\bar{s}_h$ from s_h, $\bar{i}_h$ from i_h, …, $\bar{v}_v$ from v_v, $\bar{\delta}_1$ from δ_1, …. and $\bar{\delta}_8$ from δ_8 and then multiply the result obtained by appropriate difference of functions and integrate from t_0 to t_f. Finally, the sixteen integral Equations are summed and uniqueness of system solution derived by using estimation approach. Thus, invoking lemma 1, the first result is obtained as:

$$|u_1^*(t) - \bar{u}_1^*(t)| \leq \frac{1}{2\varphi_1}\left|(pe - \bar{p}\bar{e}) + \left(sh - \bar{s}\bar{h}\right) + (te - \bar{t}\bar{e})\right|,$$

and

$$|u_2^*(t) - \bar{u}_2^*(t)| \leq \frac{1}{2\varphi_2}|(uj - \bar{u}\bar{j}) + (xm - \bar{x}\bar{m}) + (yj - \bar{y}\bar{j})|.$$

The explicit illustration of the estimate using $\left|u_1^* - \bar{u}_1^*\right|$ estimate is given for $s_h(t)$ as follows:

$$\frac{1}{2}(e-\bar{e})^2(t_f) + \delta_1\int_{t_0}^{t_f}(e-\bar{e})^2\,dt \leq \int_{t_0}^{t_f}\alpha_1|e-\bar{e}|\,dt + \left[\int_{t_0}^{t_f}|u_1^*e - \bar{u}_1^*e||e-\bar{e}|\,dt\right] + g^{\delta t}\int_{t_0}^{t_f}|f-\bar{f}||e-\bar{e}|\,dt$$

$$\leq \xi_1 g^{\delta t}\left[\int_{t_0}^{t_f}|e-\bar{e}|^2 + |p-\bar{p}|^2 + |h-\bar{h}|^2 + |l-\bar{l}|^2\right]dt$$

$$+\xi_2 g^{\delta t}\left[\int_{t_0}^{t_f}|e-\bar{e}|^2 + |p-\bar{p}|^2 + |h-\bar{h}|^2 + |l-\bar{l}|^2\right]dt,$$

where α_1 ξ_1 and ξ_2 are constants evaluated by coefficients and bounds on state adjoint of the optimality control system. Then, combining the sixteen estimates yields the following results:

$$\frac{1}{2}(t_f)\left[(e-\bar{e})^2 + (f-\bar{f})^2 + \cdots + (j-\bar{j})^2 + \cdots + (n-\bar{n})^2\right]$$

$$+\delta\int_{t_0}^{t_f}\left[(e-\bar{e})^2 + (f-\bar{f})^2 + \cdots + (j-\bar{j})^2 + \cdots + (n-\bar{n})^2\right]dt$$

$$\leq\left(\xi_1 + \xi_2 e^{3\delta t_f}\right)\int_{t_0}^{t_f}\left[(e-\bar{e})^2 + (f-\bar{f})^2 + \cdots + (j-\bar{j})^2 + \cdots + (n-\bar{n})^2\right]dt,$$

holds for all $t_0 = 0$. Hence, all terms involving t_0 have been ignored. Furthermore, it can be concluded from the above result that the inequality

$$\leq \left(\delta - \tilde{\xi}_1 - \tilde{\xi}_2 e^{3\delta t_f}\right) \int_{t_0}^{t_f} \left[(e-\bar{e})^2 + (f-\bar{f})^2 + \cdots + (j-\bar{j})^2 + \cdots + (n-\bar{n})^2 \right] dt \leq 0,$$

where $\tilde{\xi}_1$, $\tilde{\xi}_2$ functions are define by the coefficients and bounds on e, f, $\cdots$, n. Thus, for any chosen value of (δ), such that $\delta > \tilde{\xi}_1 + \tilde{\xi}_2$ and that $t_f < \frac{1}{3\delta} \ln\left(\frac{\delta - \tilde{\xi}_1}{\tilde{\xi}_2}\right)$, then the expressions $e = \bar{e}$, $f = \bar{f}$, $h = \bar{h}$, $\cdots$, $n = \bar{n}$ holds. Hence, the solution is unique for sufficiently small time t. W

Mathematical, the implication of the above result affirmed to the fact that uniqueness for small time interval is a two point boundary problem due to its opposite time orientation and state Equations, which is define base on initial and final time conditions. Also, the optimal controls u_1^* and u_2^* are characterized by the uniqueness of the system solutions.

Therefore, from epidemiological view point of Theorem. 3, if $\delta > \tilde{\varphi}_1 + \tilde{\varphi}_2$ and $t_f < \frac{1}{3\delta} \ln\left(\frac{\delta - \tilde{\varphi}_1}{\tilde{\varphi}_2}\right)$ such that $\tilde{\varphi}_2 \lhd 0$, then infection is insignificant (i.e., infection is asymptomatic). Otherwise, if $t_f > \frac{1}{3\delta} \ln\left(\frac{\delta - \phi\%_1}{\phi\%_2}\right)$ such that if $\delta < \phi\%_1 + \phi\%_2$ then prevalence of infection exist and could assume global dimension.

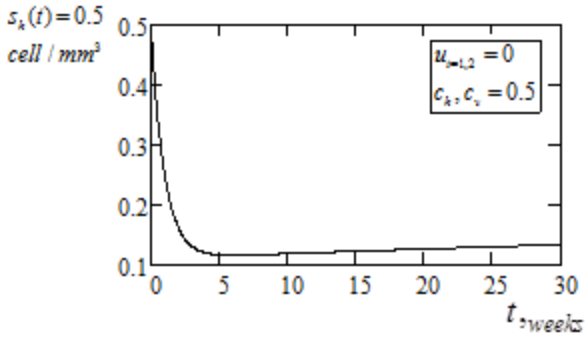
5. Numerical Simulations of Derived Optimality System

Here, we demonstrate numerically, the validity of the derived system, which includes the basic system model (5) for an untreated listeriosis infection scenario when $u_{i=1,2} = 0$ (i.e., no treatment/vaccination administered) and the derived optimality system (47). The entire simulation explore highly in-built Runge-Kutta of order 4 in a Mathcad surface. We note that the simulation of model (5) serves as leverage to our derived optimality system.

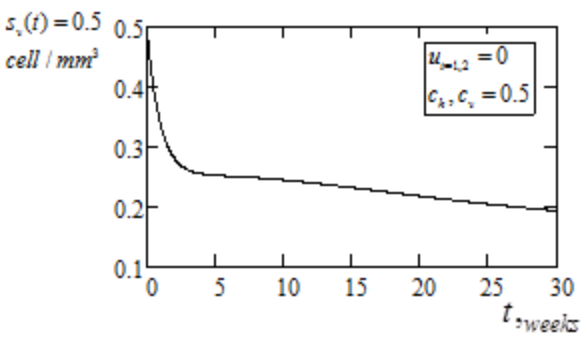
5.1. Model simulation without control function (i.e., $u_{i=1,2} = 0$)

By invoking model (5) and letting $u_{i=1,2} = 0$, we simulate using tables (3 & 4), the situation where no treatment (or vaccination) is administered. Interestingly, this serves as a control to the derived optimality system. Thus, Figure 2(a-h) illustrate listeriosis infection under off-treatment control scenario.

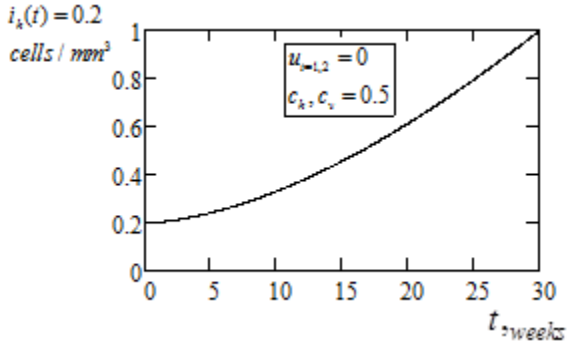
By invoking model (5) and letting $u_{i=1,2} = 0$, we simulate using tables (3 & 4), the situation where no treatment (or vaccination) is administered. Interestingly, this serves as a control to the derived optimality system. Thus, Figure 2(a-h) illustrates listeriosis infection under off-treatment control scenario.



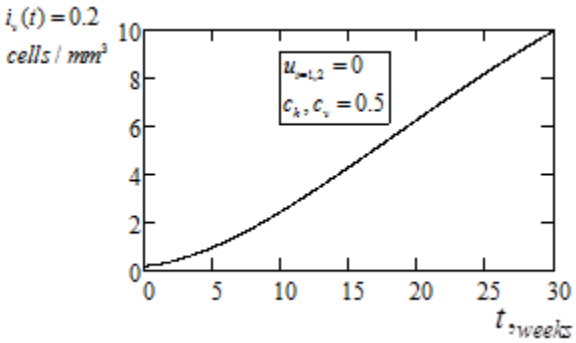
a) Simulation of susceptible human population, $b_k = 0.1\ cells mm^{-3} d^{-1}$



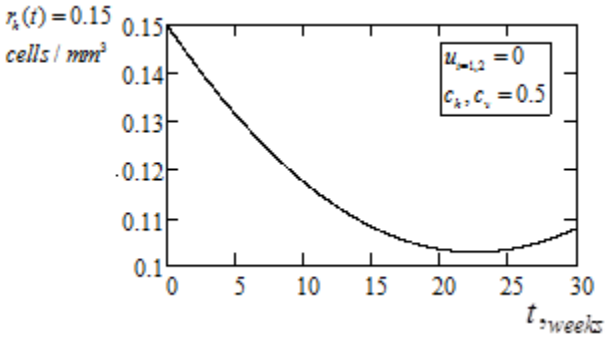
e) Simulation of susceptible vectors population, $b_v = 0.25\ cells mm^{-3} d^{-1}$



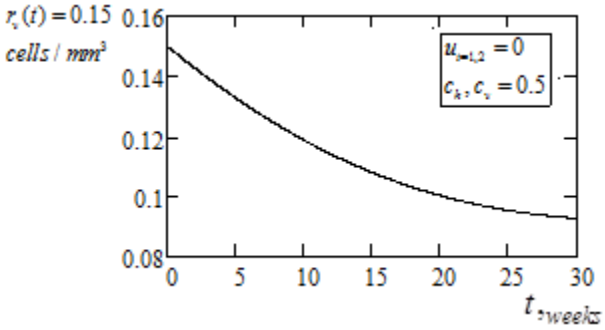
b) Simulation of infectious human Population, $\beta_k = 0.02 d^{-1}$



f) Simulation of infectious vector Population, $\beta_v = 0.27 d^{-1}$



c) Simulation of recovered human population, $\sigma_k = 0.03, \lambda = 0.005$



g) Simulation of recovered vector population, $\sigma_v = 0.005, \lambda = 0.0002$

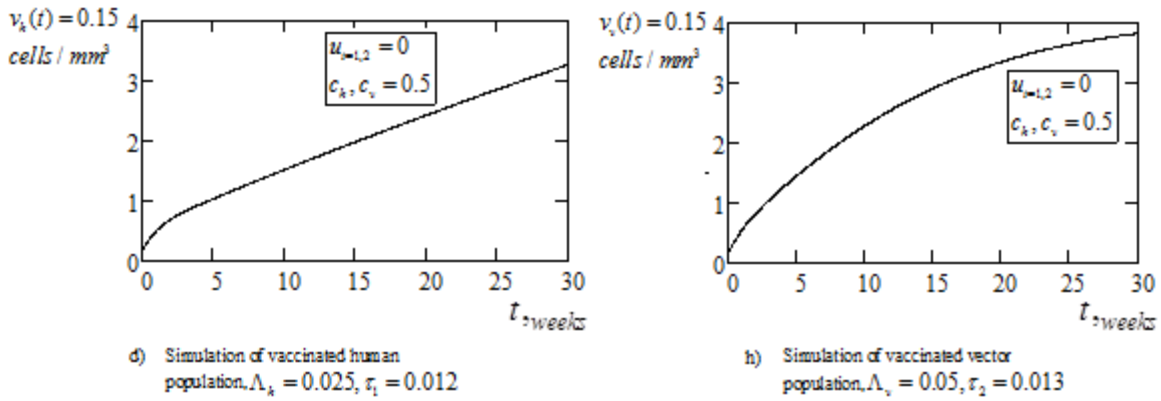
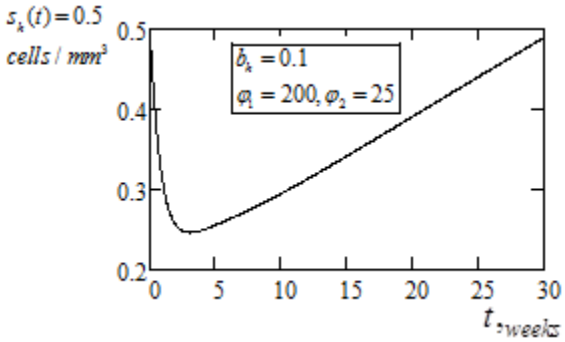


Figure 2(a - h): Graphical simulations of the dynamics of listeriosis infection on human and animal population for an untreated case

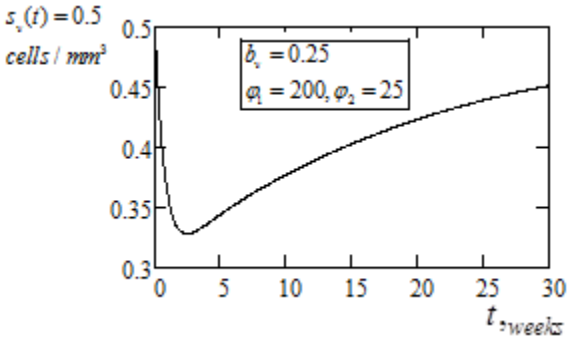
Figure 2(a-d) represent the infectious scenario for human population, while Figure 2(e-h) depicts for vector population for an untreated cases. We observe from here that the susceptible for both human and vector population exhibit rapid initial depletion at the onset of infection (i.e., the first 5-weeks). The population here continues to witness gradual decline to near zero stability after $5 \le t_f \le 30$ weeks – Figure 2(a and e). Appendix 1(a) shows the obtained results for the numerical simulation. Figure 5(b and f) denotes spontaneous inclination of infectious human and vector population following the invasion of listeriosis virus under an untreated situation. The results are as in appendix 1(b). From Figure 2(c and g) above, we investigate the dynamics of infected human and vector population that could recovered under off-treatment situation. Virtually, a concave-like declination of purportedly recovered population is observed by both human and vector population with that of the human decreasing to $r_h \le 0.13\ cells/mm^3$ and vector $r_v \le 0.093\ cells/mm^3$ $\forall t_h \le 30$ weeks. Details of the performance index are given by appendix 1(c). Furthermore, from Figure 2(d and h) the proportion of vaccinated human and vector population with acceptable loss of immunity indicates some considerable inclination with maximal values of $v_h \le 0.13\ cells/mm^3$ and vector $r_v \le 0.093\ cells/mm^3$ $\forall t_h \le 30$ weeks. Summary of results are contained in appendix 1(d).

5.2. Simulation of model optimality system

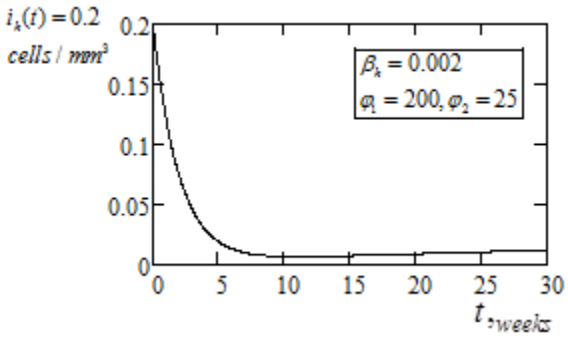
With the introduction of treatment control functions $u_{i-1,2} > 0$, which is subjected to clinical optimal weight factors $\varphi_{i=1,2} > 0$ and limit bounds $a_{i=1,2} \ge 0, b_{i=1,2} \ge 0$, we illustrate as in Figure 3(a-h) the dynamical behaviors of the model state variables. Notably, the inclusion of optimal weight factors allows the regulation of drug toxicity, such that if regularization of chemotherapies limits are given as $a_1 = 0, a_2 = 0.2, b_2 = 0.2, b_2 = 0.9$ and $\varphi_1 = 200, \varphi_2 = 25$, while other parameters remains as in tables (3 and 4), then the following structures are visible:



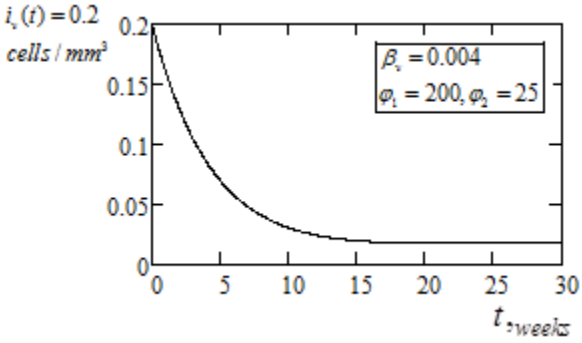
a) Simulation of susceptible human population under control function, $u_{i=1,2} = 0.8$



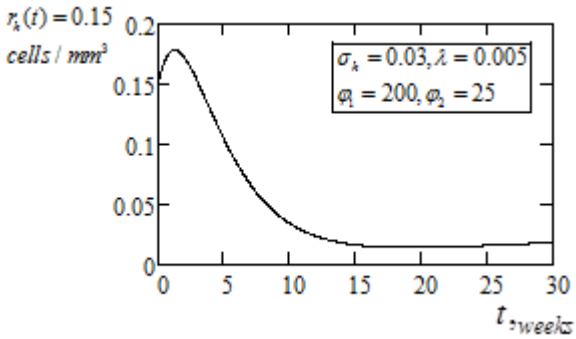
e) Simulation of susceptible vector population under control function, $u_{i=1,2} = 0.8$



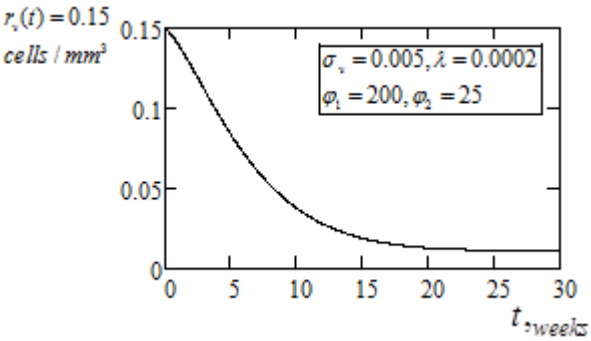
b) Simulation of infectious human population under control function, $u_{i=1,2} = 0.8$



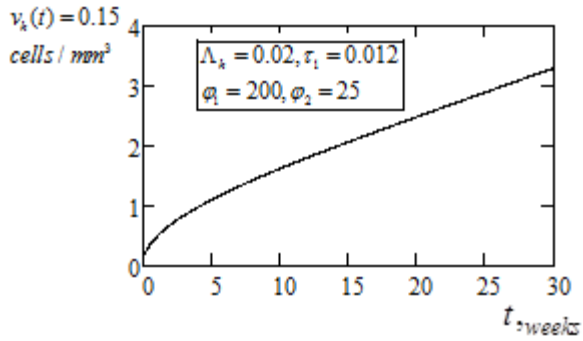
f) Simulation of infectious vector population under control function, $u_{i=1,2} = 0.8$



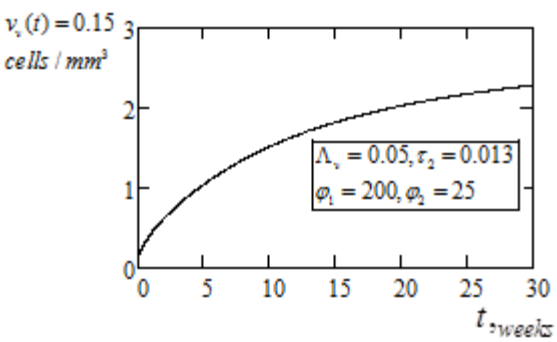
c) Simulation of recovered human population under control function, $u_{i=1,2} = 0.8$



g) Simulation of recovered vector population under control function, $u_{i=1,2} = 0.8$



d) Simulation of vaccinated human population under control function, $u_{i=1,2} = 0.8$



h) Simulation of vaccinated vector population under control function, $u_{i=1,2} = 0.8$

Figure 3(a - h) Graphical simulations of the dynamics of listeriosis infection on human and animal population under control functions

Considering Figure 3(a and e), the study demonstrated the effect of application of multiple treatment. Upsurge of susceptible human and vector population is seen, which can be attributed to three major factors: positive response to chemotherapies application, incremental rate of recovery $r_h(t), r_v(t)$ and $b_h(t), b_v(t)$ as well as vaccinated population with loss of immunity Λ_h, Λ_v. Appendix 2(a) gives the details of the dynamic flow. From Figure 3(b and f), we observed tremendous decline of infectious human and vector population, following coherent appreciation of choice dual chemotherapies. The dynamical values of the simulation are seen in appendix 2(b). The recovery population for both human and vectors as depicted by Figure 3(c and g) clearly indicated the effect of applied multiple chemotherapies following the rapid restoration of susceptible population as in Figure 3(a and e). The outcome of the recovery dynamics is define as in appendix 2(c). Finally, under induced multiple drugs, the vaccinated groups (human and vectors) exhibited rapid inclination in population size with detail of population proliferations as indicated by appendix 2(d).

6. Discussion

Guided by the model set goals and motivated by the optimal maximization of susceptible, recovered and vaccinated human and animal population from incessant fatality rate associated with *L. monocytogenes* infection, this study have been formulated to address the aforementioned cases, following the consequential effect of dual listeriosis virions interplay with the human and animal population. The study was conducted using multiple chemotherapies (trimethoprim-sulphamethoxazole in combination with either ampicillin and/or penicillin).

Achieving the set goals, an 8-Dimensional mathematical listeriosis virions dynamic model was derived and then transformed to an optimal control problem. In justifying the state variables as a representative of living organisms, the state positivity and boundedness of solutions was verified. Also, investigated by this study, were the system reproduction number and the accompanying stability analysis for the disease-free equilibrium for an untreated infectious scenario. Furthermore, appreciating the derived optimal control problem, the study employed classical Pontryagin's maximum principle for its analysis. An approach which led to the establishment of the system optimal control characterization, the existence of optimal control pair, the optimality system and the uniqueness of optimality system. Numerical simulation was thereafter conducted in consonant with validating the derived model.

The versatility of the model optimality system was adjudged by the simulation of the basic system model (4) for an untreated listeriosis infection scenario – see Figure 2(a-h). The results indicated contamination of both human and animal susceptible population (i.e., decline in both populations) after $5 \le t_f \le 30$ weeks of infestation. Here, infectious population was seen to decline rapidly with vectors highly affected. Recovery rate were also hampered due to off-treatment situation. However, vaccinated population sustained its incremental growth in population. Appendix 1(a-d) clearly defined the numerical results of Figure 2(a-h).

Further simulations following the introduction of multiple chemotherapies were conducted. With the incorporation of optimal weight factors and limit bounds on chemotherapies, rapid elimination of infectious listeriosis virions was significantly accomplished. Moreso, rapid restoration of

susceptible population, which is also attributed to the inflow of proliferated recovered and vaccinated population, vindicated this result. The numerical results of Figure 3(a-h) have been carefully presented in appendix 2(a-d). Of note, the early elimination of infection to near zero level implied reduction in the amount of chemotherapies required and the cost involvement.

7. Conclusion

The present study investigated the performance index for the maximization of susceptible, recovery and vaccinated human and animal population from dual infectious *L. monocytogenes* studied under the interface of multiple chemotherapies. The governing model was conceived as an 8-Dimensional mathematical model derived using ODEs. Against the innovative ideas of model, Osman et al. (2018), the novelty of this study is in the incorporation of vaccinated susceptible human population and the application of multiple chemotherapies as treatment factors. Classical Pontryagin's maximum principle was applied for the model analysis, which singled out the exclusive impact of the model. Results of the numerical simulations indicated that, following the application of multiple chemotherapies coupled with incorporation of vaccinated susceptible human population, rapid elimination of infectious *L. monocytogenes*, accelerated recovery of infected human and vector population was accomplished. This tremendous results is seen to translate into the enhancement and maximization of both susceptible human and animal population under notable minimized systemic cost. Furthermore, reduction in rate of contact of infectious listeriosis virus with susceptible population yields significant reduction in the system reproduction number. This clearly showed that infection and control dynamics is a function of system reproduction number. Therefore, the practicability of this study admits the overall intellectual proceeding of the technique applied. Thus, the application of the model to other related infectious disease is strongly suggested.

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APPENDICES

Appendix 1

1(a)	Figure 2(a & e) - Dynamics of susceptible population ($u_{i=1,2} = 0$)	
	Period (weeks)	**Results**
a)	$t_f \le 5$	$0.11 \le s_h \le 0.5$
	$t_f \le 30$	$0.11 \le s_h \le 0.14$
e)	$t_f \le 3$	$0.289 \le s_v \le 0.5$
	$t_f \le 30$	$0.193 \le s_v \le 0.289$

1(b)	Figure 2(b & f) - Dynamics of infectious population ($u_{i=1,2} = 0$)	
	Period (weeks)	**Results**
b)	$t_f \le 30$	$0.2 \le i_h \le 0.994$
f)	$t_f \le 30$	$0.2 \le i_v \le 9.971$

1(c)	Figure 2(c & g) - Dynamics of recovery population ($u_{i=1,2} = 0$)	
	Period (weeks)	**Results**
c)	$t_f \le 20$	$0.103 \le r_h \le 0.15$
	$t_f \le 30$	$r_h \le 0.107$
g)	$t_f \le 30$	$0.093 \le r_v \le 0.15$

1(d)	Figure 2(d & h) - Dynamics of vaccinated population ($u_{i=1,2} = 0$)	
	Period (weeks)	**Results**
d)	$t_f \le 30$	$0.15 \le v_h \le 3.27$ Smooth diagonal curve
h)	$t_f \le 30$	$0.289 \le s_v \le 0.5$ Smooth concave curve

Appendix 2

2(a)	Figure 3(a & e)- Dynamics of susceptible population ($u_{i=1,2} \geq 0$)	
	Period (weeks)	Results
a)	$t_f \leq 3$	$0.246 \leq s_h \leq 0.5$
	$t_f \leq 30$	$s_h \leq 0.5$
e)	$t_f \leq 3$	$0.328 \leq s_v \leq 0.5$
	$t_f \leq 30$	$0.328 \leq s_v \leq 0.447$

2(b)	Figure 3(b & f)- Dynamics of infectious population ($u_{i=1,2} \geq 0$)	
	Period (weeks)	Results
b)	$1 \leq t_f \leq 10$	$0.2 \leq i_h \leq 6.654\times10^{-3}$
	$10 \leq t_f \leq 30$	$6.654\times10^{-3} \leq i_h \leq 0$
f)	$1 \leq t_f \leq 10$	$0.2 \leq i_v \leq 0.018$
	$10 \leq t_f \leq 30$	$0.018 \leq i_v \leq 0$

2(c)	Figure 3(c & g)- Dynamics of recovery population ($u_{i=1,2} \geq 0$)	
	Period (weeks)	Results
c)	$t_f \leq 3$	$0.15 \leq r_h \leq 0.18$
	$3 \leq t_f \leq 30$	$0.18 \leq r_h \leq 0.014$
g)	$1 \leq t_f \leq 30$	$0.15 \leq r_v \leq 0.11$

2(d)	Figure 3(d & h)- Dynamics of vaccinated population ($u_{i=1,2} \geq 0$)	
	Period (weeks)	Results
d)	$t_f \leq 30$	$0.15 \leq v_h \leq 3.298$
h)	$t_f \leq 30$	$0.15 \leq v_v \leq 2.283$

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