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Mathematical Modeling and Optimal Control Strategies of Lassa Fever Disease Model with Cost effectiveness analysis in Bauchi State

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ABSTRACT
In this study, we proposed a mathematical model of Lassa fever disease incorporating three control measures consisting of preventive measures (through the use of mass campaign and sanitation of the environment), treatment of infected persons and the use of rodenticide to eradicate the host reservoir of the virus mainly known as Mastomys natelenses.The transmission dynamics of the disease was investigated via a system of non - linear differential equations. We have established the threshold parameter R_0 *using the next generation matrix approach. Sensitivity analysis of all the parameters in* R_0 *was carried-out to ascertain the impact of each parameter on the transmission of Lassa fever. The most sensitive parameters were* $\beta_H, \beta_V,$ *and* μ_V*. The Lassa fever free equilibrium is locallyasymptotically stable when* $R_0 < 1,$ *and unstable when* $R_0 > 1.$ *The global stability is proved using Castillo-Chavez conditions. Result of the analysis indicate that, the Lassa fever free equilibrium is globally asymptotically stable when* $R_0 < 1$ *. The Pontryagin's maximum principle was used to determine the conditions necessary for obtaining the optimality of the system. If the marginal benefit is greater than the marginal cost involves for a particular control measure, then the purpose of such intervention is achieved.*

Key words: Lassa fever, Basic reproduction number, Control strategies, invariant region
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I. Introduction

Lassa fever is a viral disease that attacks the liver, nervous system, spleen and kidney. It is an acute viral hemorrhagic fever (VHF) first isolated in a town called Lassa in the *Yedseram* River Valley in the present Borno State of Northern Nigeria in 1969 [25] and [1]. It can also be defined as a zoonotic disease caused by Lassa virus (LASV), and is endemic in several West African countries, including Guinea, Liberia, Nigeria, and Sierra Leone; disease occurs both sporadically and as outbreaks [26]. However, some Lassa fever cases have been imported in the U.S and U.K through travelers who acquire the disease elsewhere [25]. Population studies demonstrating serologic evidence of LASV infection and the presence of occasional sporadic Lassa fever cases in additional West African countries (i.e., Benin, Burkina Faso, Ghana, the Ivory Coast, Mali, and Togo) indicate that other areas of the region also may be at risk.*Mastomys natalensis* (i.e., the multimammate mouse which also is known as the multimammate rat) has long been considered the sole natural reservoir of LASV, but additional rodent reservoirs (*M. erythroleucus* and *H. pamfi*) recently have been discovered and may affect the distribution of Lassa fever. Primary transmission of the virus from animal hosts to humans typically occurs via exposure to excreta (urine or feces) or blood from LASV-infected rodents. Person-to-person and laboratory transmissions occur to a lesser extent and result from direct contact with the blood, tissue, urine, feces, or bodily secretions of an LASV-infected individual or reuse of contaminated medical equipment [26].

Although public health officials often cite annual case estimates of 100,000 to 300,000 LASV infections and up to 5,000 deaths, these numbers are extrapolations from a single longitudinal study conducted over 30 years ago in Sierra Leone. The true public health burden of Lassa fever is unknown and represents a crucial gap in understanding the relative impact of Lassa fever in the affected West African countries [26].

Existing Lassa fever surveillance data are limited and/or biased because they typically have been collected in conjunction with biomedical research projects located in areas where the disease already is recognized to be endemic. In contrast, seroprevalence studies in non-endemic areas have suggested high

numbers of previously unrecognized infections, and more recent surveillance reports have observed substantial increases in the number and geographic spread of cases. Thus, the true incidence and spatial distribution of Lassa fever may be significantly underestimated. LASV infection causes a wide spectrum of clinical manifestations; an estimated 80% of people with LASV infections have no or mild symptoms (and often are unrecognized and unreported), while the remaining 20% may progress to severe and life-threatening disease requiring hospitalization. Among survivors, the most common long-term *sequela* of Lassa fever is sensor neural hearing loss. The onset of Lassa fever is gradual and nonspecific with an incubation period ranging from 2 to 21 days; thus, it is clinically difficult to distinguish Lassa fever from other febrile illnesses that occur in West Africa such as malaria, typhoid, yellow fever, dengue, and Ebola virus disease (EVD) [26].

The onset of the disease, when it is symptomatic, is usually gradual, starting with fever, general weakness, and malaise. After a few days, headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhea, cough, and abdominal pain may follow. In severe cases facial swelling, fluid in the lung cavity, bleeding from the mouth, nose, vagina or gastrointestinal tract and low blood pressure may develop. Clinical diagnosis is often difficult, especially early in the course of the disease [26].

Lassa virus infections can only be diagnosed definitively in the laboratory using RT-PCR, ELISA, Antigen detection tests, or virus isolation. None of those tests are currently licensed. Early supportive care with rehydration and symptomatic treatment improves survival. Ribavirin has been widely used off-label to treat patients with LF based on the results of one clinical study performed in Sierra Leone in the 80's. Lastly, there is no licensed vaccine [26].

In Nigeria, sporadic outbreaks of Lassa fever have been documented since 1969. The infection is endemic in several states including Edo, Ebonyi, Onitsha, Jos, Taraba, Nasarawa, Yobe, Rivers and Ondo states. In 2012 for example, 623 suspected cases (108 Laboratory confirmed), including 70 deaths were recorded from 19 states in Nigeria [15]; [28]. A total of 11 confirmed cases of Lassa were recorded in Nigeria with high prevalence in Oyo State in 2014. Between January 1st and 8th of March 2015, the Nigerian Center for Disease Control (NCDC) reported 21 cases of Lassa fever (4Lab. Confirmed) and 1death due to Lassa [29]; [6]. Between August 2015 and January 2016, there were 239 suspected cases of LF (44 Lab. Confirmed), including 82 deaths, across 19 states including; Bauchi, Nasarawa, Niger, Delta, Ekiti, Ondo, Kogi, Ebonyi, Lagos, Osun, FCT, Taraba, Kano, Rivers, Edo, Plateau, Gombe, Oyo States etc. [16]; [30]. Similarly, the year 2016, 2017, 2018 and 2019 were also affected by Lassa fever in Nigeria with outbreaks across several states [2].

For instance, in early 2018, Nigeria has witnessed an unprecedented LF outbreak, whereby the usual annual observed LF burden has been concentrated into one trimester. From 1st January to 29th April 2018, a total of 1878 suspected cases have been reported from 21 states. Of these, 420 were confirmed positive [26]. Similarly, there were 1374 suspected with 420 confirmed cases and 93 confirmed deaths from week 1 to week 9 of 2019 from 21 states across 66 L. G. A, while around the same period in 2020, there were 3054 suspected cases, 775 confirmed positive cases and 132 confirmed deaths from 27 states across 118 L. G. A. [17].In 2021, the cumulative suspected cases were 1508, 233 confirmed and 49 deaths across 14 states and 51 LGA(s). This indicate a sharp decline when compared with cases in the year 2020 [18]. However, in 2022, the epidemic of Lassa fever moves up to 3746 suspected cases, 691 confirmed and 132 deaths across 23states and 91 LGA(s). Of all the confirmed cases in 2022, 67% were fromOndo (28%), Edo (24%) and Bauchi being the 3rd most endemic and first in the north eastern sub-region (15%) [19]. From week 1-15 (16th April, 2023), the suspected cases in Nigeria reach a peak of 4702, with 877 confirmed cases and 152 deaths across 101 LGA(s), wide spread in 26 state(s) of the Federation. 72% of all cases in week1-15 of 2023 were from Ondo (32%), Edo (29%) and Bauchi (11%) [20]. This shows that there is a significant increase in suspected cases, confirmed casesand death almost every year, hence the need for more research in order to curtail the spread of Lassa fever in Bauchi state in particular and Nigeria at large, therefore, the emergence for this study is crucial at this moment.

Mathematical modeling of Lassa fever has been employed by various researchers to study the dynamics of the disease transmission. [9] presents a mathematical model that tracks the transmission dynamics of Lassa fever in a two-interacting human host and rodent vector populations. The model in-corporates a non-drug compliance rate in the parameters for the human population. The basic reproduction number is derived and the stability of the disease-free and endemic equilibrium points were analyzed. [2] presented a periodically-forced seasonal non-autonomous system of a non-linear ordinary differential equation developed to captures the dynamics of Lassa fever transmission and seasonal variation in the birth of *mastomys* rodents where time was measured in days to capture seasonality. It was shown that the model is epidemiologically meaningful and mathematically well-posed by using the results from the qualitative properties of the solution of the model. [1] formulated a Lassa fever disease model with sensitivity analysis. The equilibrium states, basic reproduction number were obtained using generation matrix and their stabilities were analyzed using Descartes' rule of sign and comparison test. Their results show that the disease free equilibrium is locally and globally asymptotically stable when $\beta\pi y < \mu\left(y+\mu+\theta_1\right)\left(\mu+\delta+\theta_2\right)$. Finally, they carried out sensitivity analysis and it is

shown that the parameter β is the most sensitive. [11] presented a deterministic model for Lassa fever transmission in the presence of quarantine and permanent immunity. The model was validated for existence and uniqueness of solution. The threshold parameter for disease eradication R_0, was computed and used to investigate its global stability using Lyapunov function such that whenever $R_0 < 1$, the disease can be eradicated.[4] developed a deterministic model for Lassa fever disease in a population with vital dynamics, incorporating standard incidence rate, disease induced death and infection due to humans, reservoirs and aerosol (airborne) transmissions. They obtained the basic reproduction number, R_0, which can be used to control the transmission dynamics of the disease and thus, established the conditions for local and global stability of the disease-free equilibrium.A deterministic mathematical model is presented by [21] to study the dynamics of Lassa fever in Nigeria. The model describes the transmission between the human and rodent populations. The cumulative number of cases reported by the Nigerian Centre for Disease Control within the first week of January 2020 through the eleventh week in 2021 was used to performed the model fitting and parameterization by the nonlinear least square method. The reproduction number R_0, which measures the potential spread of Lassa fever in the population was use to investigate the local and global stability of the system. The result shows that the model system is locally and globally asymptomatically stable whenever $R_0 < 1$, otherwise it is unstable. Furthermore, the endemic equilibrium stability is investigated and the criteria for the existence of the phenomenon of bifurcation was presented.The sensitivity analysis of each reproduction number parameter and solutions of the developed model were derived through an iterative numerical technique, a six-stage fith-order Runge–Kutta method. Numerical simulations of the total infected human population $(E_h + I_h)$ under different numerical values (controlled parameters) were presented. The result from the study shows that combined controlled parameters made the total infected human population decline faster and thus reduces Lassa fever's burden on the population.

In this paper, we complement and extend on the work of [1] by incorporating vector-to-human, vector-to-vector transmission and standard incidence rate, disease induced death and isolation of the infected class in to the Lassa fever model with a view to study the optimal control strategies that will help in curtailing the spread of the disease and to determine its cost effectiveness.

II. Lassa fever model description

The human population N_H, is partitioned into six compartments of susceptible human population S_H, Latently infected human population L_H, infected human population I_H, isolated human population I_{SH}, treated human population $T_{H,}$ and the population of recovered human R_H. Thus, the total human population is

$$N_H = S_H + L_H + I_H + I_{SH} + T_H + R_H \qquad (1)$$

The susceptible human population S_H, grow through birth at the rate Λ_H, and due to loss of immunity from human recovery class R_H. at the rate α . Some individuals are prevented from the disease through mass campaign for personal hygiene and proper environmental sanitation $u_1(t) \in [0,1]$, while those individuals that are exposed to the disease for lack of awareness and poor sanitations get in to contact directly with infected vector (rodents), faeces, urine or saliva or indirectly with infected person, hence, can acquire the disease at the force of infection

$$\lambda_H(t) = \frac{\beta_H I_V(t) + \beta_H I_H(t)}{N_H} \qquad (2)$$

Where β_H, is the probability of vector-to-human and human-to-human transmission.

The latently infected human L_H, increase as a result of the transfer of newly infected individuals who do not show symptoms from the susceptible population at the rate $\lambda_H(t)$. This population is reduce due to migration of individuals to isolation I_{SH} for proper care at the rate γ_1. Those individuals who recover at this stage due to

treatment of early symptoms moved to recovery class R_H, at the rate η, while those who developed other symptoms such asheadache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhea, cough, and abdominal pain moved to infected class I_H, at rate φ. Individuals in this category receives treatment $u_2(t) \in [0,1]$ using Ribavirin where ϕ_1 is the medication parameter for the use of treatment u_2.

The infected human population I_H, grows by the transfer of latently infected persons at the rate φ, and is reduce due to migration of individual in this class to isolation at the rate ρ. Individuals treated in this class $u_2(t) \in [0,1]$ with ϕ_2 as modification parameter would move to treatment class T_H. This population is reduce due to death from Lassa fever at rate δ_H.

The Isolated human population I_{SH}, grow due to transfer of latently infected persons L_H, and infected individuals I_H, at the rate γ_1 and ρ respectively. This population is reduce as a result of migration of individuals who received treatment $u_2(t) \in [0,1]$ with ϕ_3 as modification parameter for the use of treatment u_2 and moved to treatment class T_H.

The population of treated human is increased due to transfer of individuals who received treatment $u_2(t) \in [0,1]$ from latent class L_H, infected human I_H, and Isolated human populations I_{SH}. Those who fully recovered from Lassa fever disease are moved to recovered class at the rate θ.

The recovered human population with temporary immunity R_H, is increase due to the transfer of individuals from treated population at the rate θ and is reduce by the migration of individual who loss immunity at the rate α. Natural death μ_H, is assumed in all the human populations.

The total vector (rodents) population N_V, is subdivided in to three sub-populations of susceptible vector S_V, latently infected vector L_V, and infected vector I_V. Thus, the total vector population is

$$N_V = S_V + L_V + I_V \tag{3}$$

The susceptible vector population S_H, is increase through birth of new offspring at the rate Λ_V, and is reduce due to migration in to the latently infected vector L_V, due to interaction with infected vector I_V or infected human I_H, at the force of infection

$$\lambda_V(t) = \frac{\beta_V I_H(t) + \beta_V I_V(t)}{N_V(t)} \tag{4}$$

Where β_V is the probability of vector-to-vector and human-to-vector transmission. The population is further reduced due to the use of rodenticide $u_3(t) \in [0,1]$ where τ is the modification parameter for the use of the control u_3.

The population of latently infected vector L_V, is increase by the transfer of individuals from the susceptible vector population S_H, at a rate $\lambda_V(t)$ and same population is reduce by the transfer of individual in to infected vector population at the rate γ_2. The population is also reduce due the use of control u_3, where τ is the modification parameter.

The population of infected vector is increase by the transfer of latently infected vector at the rate γ_2 and is decrease by the use of rodenticide u_3, with τ being the modification parameter. Natural death μ_V, is assumed in all the vector sub-populations.

2.2 The model diagram of Lassa fever disease

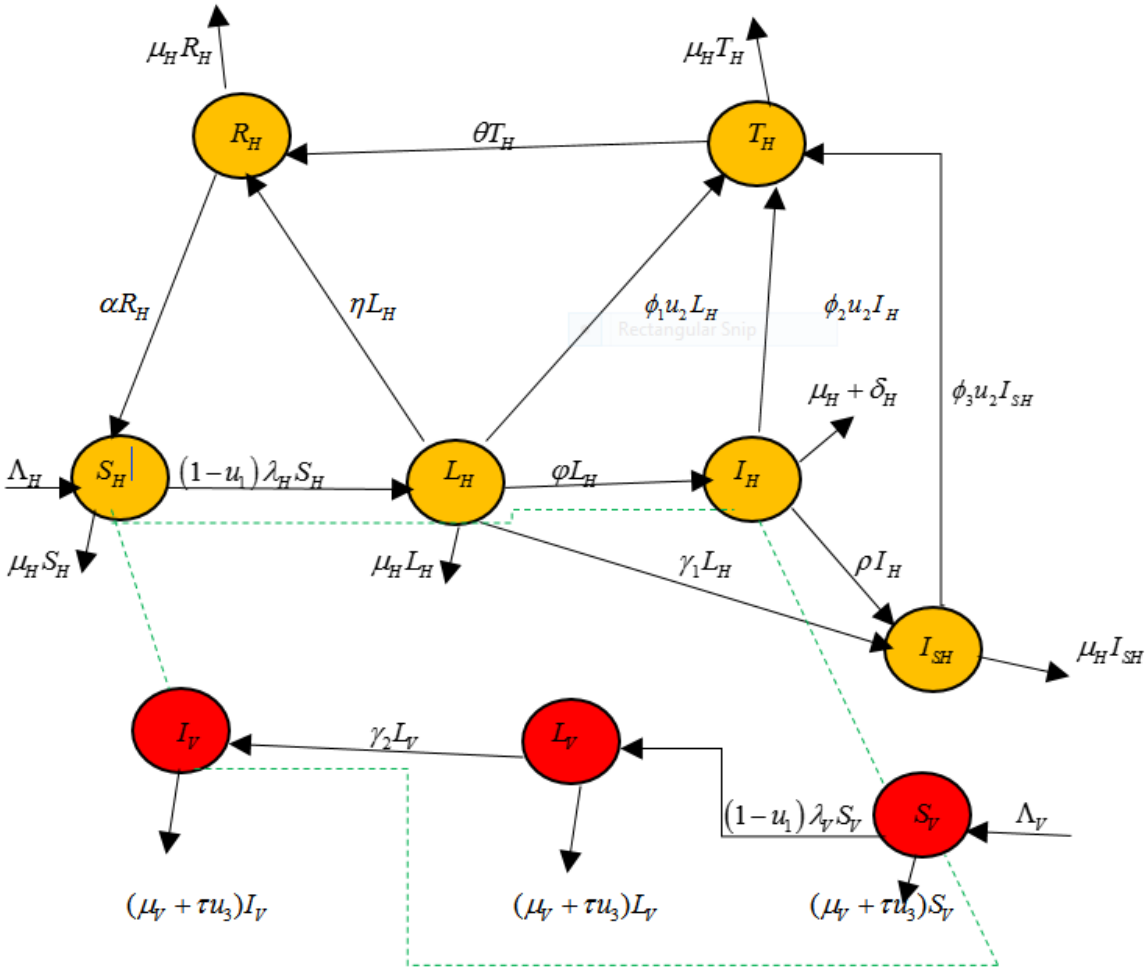

Figure 1.1The schematic diagram of the Lassa fever model

2.3 The model equations

$$\frac{dS_H}{dt} = \Lambda_H + \alpha R_H - (1-u_H)\lambda_H S_H - \mu_H S_H$$

$$\frac{dL_H}{dt} = (1-u_1)\lambda_H S_H - \gamma_1 L_H - \varphi L_H - \eta L_H - \phi_1 u_2 L_H - \mu_H L_H$$

$$\frac{dI_H}{dt} = \varphi L_H - \rho I_H - \phi_2 u_2 I_H - (\mu_H + \delta_H) I_H$$

$$\frac{dI_{SH}}{dt} = \gamma_1 L_H + \rho I_H - \phi_3 u_2 I_{SH} - \mu_H I_{SH} \quad (5)$$

$$\frac{dT_H}{dt} = \phi_1 u_2 L_H + \phi_2 u_2 I_H + \phi_3 u_2 I_{SH} - (\theta + \mu_H) T_H$$

$$\frac{dR_H}{dt} = \eta L_H + \theta T_H - (\alpha + \mu_H) R_H$$

$$\frac{dS_V}{dt} = \Lambda_V - (1-u_1)\lambda_V S_V - (\mu_V + \tau u_3) S_V$$

$$\frac{dL_V}{dt} = (1-u_1)\lambda_V S_V - \gamma_2 L_V - (\mu_V + \tau u_3) L_V$$

$$\frac{dI_V}{dt} = \gamma_2 + L_V - (\mu_V + \tau u_3) I_V$$

With initial conditions

$S_H(0) = S_{H_0}, L_H(0) = L_{H_0}, I_H(0) = I_{H_0}, I_{SH}(0) = I_{SH_0}, T_H(0) = T_{H_0}, R_H(0) = R_{H_0},$

$S_V(0) = S_{V_0}, L_V(0) = L_{V_0}, I_V(0) = I_{V_0},.$

By setting the control parameters $u_1 = u_2 = u_3 = 0,$ we obtain equation (6)

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= \Lambda_H + \alpha R_H - \lambda_H S_H - \mu_H S_H \\
\frac{dL_H}{dt} &= \lambda_H S_H - (\gamma_1 + \varphi + \mu_H) L_H \\
\frac{dI_H}{dt} &= \varphi L_H - (\rho + \mu_H + \delta_H) I_H \\
\frac{dI_{SH}}{dt} &= \gamma_1 L_H + \rho I_H - \mu_H I_{SH} \\
\frac{dR_H}{dt} &= \eta L_H - (\alpha + \mu_H) R_H \\
\frac{dS_V}{dt} &= \Lambda_V - \lambda_V S_V - \mu_V S_V \\
\frac{dL_V}{dt} &= \lambda_V S_V - (\gamma_2 + \mu_V) L_V \\
\frac{dI_V}{dt} &= \gamma_2 L_V - \mu_V I_V
\end{aligned}\right\} \quad (6)$$

III. Basic properties of the model

3.1Positivity of the solution

Since we are dealing with human population, the system (6) have a non-negative solution. The following theorem will demonstrate this assertion.

Theorem1: Let the initial solution set be

$S_H(0) = S_{H_0}, L_H(0) = L_{H_0}, I_H(0) = I_{H_0}, I_{SH}(0) = I_{SH_0}, R_H(0) =$

$R_{H_0}, S_V(0) = S_{V_0}, L_V(0) = L_{V_0}, I_V(0) = I_{V_0},.$

$\{S_H > 0, L_H > 0, I_H > 0, I_{SH} > 0, R_H > 0, S_V > 0, L_V > 0, I_H > 0\} \in R_+^8$, then,the solution set $\{S_H(t), L_H(t), I_H(t), I_{SH}(t), R_H(t), S_V(t), L_V(t), I_V(t)\}$ is positive for all time t.

Proof:

From the first differential equationin model (6)

$$\frac{dS_H}{dt} = \Lambda_H + \alpha R_H - \lambda_H S_H - \mu_H S_H$$

$$\frac{dS_H}{dt} \geq -\lambda_H S_H - \mu_H S_H \quad (7)$$

$$\frac{dS_H}{dt} \geq -(\lambda_H + \mu_H) S_H \quad (8)$$

by separating the variables and integrating we have,

$$\ln(S_H) \geq \int -(\lambda_H + \mu_H) dt + c \quad (9)$$

Taking the exponential of both sides we have

$$S_H(t) \geq Ae^{-(\lambda_H + \mu_H)t} \quad \text{where} \quad A = e^c \text{ is a constant} \quad (10)$$

Applying the initial condition $t = 0$ in (10), we get

$$S_H(t) \geq S_H(0)e^{-(\lambda_H+\mu_H)t} > 0 \qquad (11)$$

However, in the same fashion, we can also demonstrate that the remaining equations in our system (6) have non-negative solutions at time $t = 0$.

3.2 Invariant region

The system of equation (6) is analyzed in a biologically-feasible region. The total human populations:

$$N_H = S_H + L_H + I_H + I_{SH} + R_H$$

which lead to the differential equations

$$\frac{dN_H}{dt} \geq \Lambda_H - \delta_H I_H - \mu_H N_H \qquad (12)$$

the total vector populations:

$$N_V = S_V + L_V + I_V$$

which also result inthe differential equation

$$\frac{dN_V}{dt} \geq \Lambda_V - \mu_V N_V \qquad (13)$$

Theorem 2: suppose that the solution set of system (6) with given initial conditions in a feasible biological region is $w_1 \times w_2 \in R_+^5 \times R_+^3 \subset W$ with

$$w_1 = \left\{ S_H, L_H, I_H, I_{SH}, R_H \in R_+^5 : N_H \leq \frac{\Lambda_H}{\mu_H} \right\} \text{ and (14)}$$

$$w_2 = \left\{ S_V, L_V, I_V \in R_+^3 : N_V \leq \frac{\Lambda_V}{\mu_V} \right\}, \qquad (15)$$

Hence, W is positively invariant region.

Proof: following the procedure of [22] we established the result;

$$\frac{dN_H}{dt} \geq \Lambda_H - \mu_H N_H \qquad (16)$$

Letting $\delta_H = 0$ in(12)we get

$$\frac{dN_V}{dt} \geq \Lambda_V - \mu_V N_V \qquad (17)$$

By solving the differential equations (16) and (17) we arrived at

$N_H(t) \leq \frac{\Lambda_H}{\mu_H} - \frac{\left(\Lambda - \mu_H N_H(0)\right)}{\mu_H} e^{-\mu t}$ and $N_V(t) \leq \frac{\Lambda_V}{\mu_V} - \frac{\left(\Lambda_V - \mu_V N_V(0)\right)}{\mu_V} e^{-\mu t}$. It suffices to say that as $t \to \infty$ the population under study $N_H \to \frac{\Lambda_H}{\mu_H}$ and $N_V \to \frac{\Lambda_V}{\mu_V}$ for both humans and vector populations at any given initial time. This simply indicate that, the feasible solution set of our model (6) is a positive invariant region, hence, it is sufficient enough to investigate the behavior of the model in W. Therefore, it's epidemiologically and mathematicallywell-posed to study the model (6).

3.3 Lassa fever-free equilibrium state

At Lassa fever free equilibrium state, we set the system (6) to zero and solved.

$$\frac{dS_H}{dt} = \frac{dL_H}{dt} = \frac{dI_H}{dt} = \frac{dI_{SH}}{dt} = \frac{dR_H}{dt} = \frac{dS_V}{dt} = \frac{dL_V}{dt} = \frac{dI_V}{dt} = 0 \qquad (18)$$

Thus, $E^* = \left(S_H, L_{H,}, I_{H,}, I_{SH,} R_H, S_V, L_V, I_V\right) = \left(\frac{\Lambda_H}{\mu_H}, 0, 0, 0, 0, \frac{\Lambda_V}{\mu_V}, 0, 0\right)$ (19)

3.4Basic Reproduction Number R_0

The next generation matrix is used to obtain the basic reproduction number R_0 which is the secondary infection that can be generated by an infectious person during his or her life time as an infected individual. Thus,

$R_0 = \rho(FV^{-1})$, where $F = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]$ for $i \geq 1$, $1 \leq j \leq m$ for the infected compartments only. $\rho(FV^{-1})$ denoted the spectral radius of the matrix A. F and V are $m \times m$ matrices, where m is the number of infected classes[8].Therefore, the infected classes of system (6) are:

$$\begin{aligned} F_1 &= \lambda_H S_H - (\gamma_1 + \varphi + \eta + \mu_H) L_H \\ F_2 &= \varphi_1 L_H - (\rho + \mu_H) I_H \\ F_3 &= \lambda_V S_V - (\gamma_2 + \mu_V) L_V \\ F_4 &= \gamma_2 L_V - \mu_V I_V \end{aligned} \tag{20}$$

$$F_i = \begin{bmatrix} F_1 \\ F_2 \\ F_3 \\ F_4 \end{bmatrix} = \begin{bmatrix} \lambda_H S_H \\ 0 \\ \lambda_V S_V \\ 0 \end{bmatrix} V_i = \begin{bmatrix} V_1 \\ V_2 \\ V_3 \\ V_4 \end{bmatrix} = \begin{bmatrix} (\gamma_1 + \varphi + \eta + \mu_H) L_H \\ (\rho + \mu_H + \delta_H) I_H - \varphi L_H \\ (\gamma_2 + \mu_V) L_V \\ \mu_V I_V - \gamma_2 L_V \end{bmatrix} \tag{21}$$

Therefore, according to[8], the basic reproduction number is the dominant eigenvalue, $\rho(FV^{-1})$ where ρ is the spectral radius, thus,

$$R_0 = \frac{(\varphi q_3 \beta_H \mu_V + q_1 q_2 \gamma_2 \beta_V)}{\mu_V q_1 q_2 q_3} \tag{22}$$

where $q_1 = (\gamma_1 + \varphi + \eta + \mu_H)$, $q_2 = (\rho + \mu_H + \delta_H)$, $q_3 = (\gamma_2 + \mu_V)$

By substituting the values of q_1, q_2, q_3 in (22) we obtained

$$R_0 = \frac{(\varphi \beta_H \mu_V (\gamma_2 + \mu_V) + \gamma_2 \beta_V (\gamma_1 + \varphi + \eta + \mu_H)(\rho + \mu_H + \delta_H))}{\mu_V (\gamma_1 + \varphi + \eta + \mu_H)(\rho + \mu_H + \delta_H)(\gamma_2 + \mu_V)} \tag{23}$$

The dynamics of the transmission of the Lassa fever disease depends largely on the basic reproduction number (23). The spread of Lassa fever in the population is determine by the number of secondary infection that can be produce by one infectious person. If the secondary infection is less than one person per infected individual then, the spread of Lassa fever can be controlled, but if otherwise the disease will persist and continued to be endemic in the region. This lead to the formulation of the following theorem:

Theorem3: The Lassa fever-free equilibrium is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1.$

3.5Global stability of the Lassa fever-free equilibrium

To prove the global asymptotic stability of (6) the method by [5] is used. Therefore, system (6) are re-write in the following form;

$$\left.\begin{aligned} \frac{dX}{dt} &= F(X, Z) \\ \frac{dZ}{dt} &= G(X, Z), G(X, 0) = 0 \end{aligned}\right\} \tag{24}$$

Where $X = (S_H, R_H, S_V)$ represents the number of uninfected populations, $X \in R_+^3$, and $Z = (L_H, I_H, L_V, I_V)$ stand for the number of infected populations, $Z \in R_+^4$.

The Lassa fever-free state is $Q^0 = (X^0, 0)$ .The conditions H_1 and H_2 must be met to guarantee a global asymptotic stability:

H_1: *for* $\frac{dX}{dt} = F(X, 0)$, X^0 is globally asymptotically stable

$H_2 : G(X, Z) = CZ - G(X, Z)$, where $G(X, Z) \geq 0$, *for* $(X, Z) \in W$

Where $C = D_Z G\left(X^0, 0\right)$ is an M-matrix (the off diagonal of C are non-negative) and W is the biological feasible region.

Lemma 1: The point $Q^0 = \left(X^0, 0\right)$ is called stable global asymptotic equilibrium point, if in addition $R_0 < 1$ and the conditions H_1 and H_2 are satisfied. Hence, we established the below theorem:

Theorem 4: Let $R_0 < 1$. Then the Lassa fever-free equilibrium is globally asymptotically stable.

Proof:

Let $X = \left(S_H, R_H, S_V\right), Z = \left(L_H, I_H, L_V, I_V\right)$ and $Q^0 = \left(X^0, 0\right)$ where $X^0 = \left(\frac{\Lambda_H}{\mu_H}, 0, \frac{\Lambda_V}{\mu_V}\right)$

$$\left.\begin{aligned} &\Rightarrow X \in R_+^3 \\ &\frac{dS_H}{dt} = \Lambda_H + \alpha R_H - \left(1-u_1\right)\left(\frac{\beta_H I_V + \beta_H I_H}{N_H}\right) S_H - \mu_H S_H \\ &\frac{dR_H}{dt} = \eta L_H - \alpha R_H - \mu_H R_H \\ &\frac{dS_V}{dt} = \Lambda_V - \left(1-u_1\right)\left(\frac{\beta_V I_H + \beta_V I_V}{N_V}\right) S_V - \mu_V S_V \end{aligned}\right\} \quad (25)$$

$$F\left(X, 0\right) = \begin{pmatrix} \Lambda_H - \mu_H S_H \\ 0 \\ \Lambda_V - \mu_V S_V \end{pmatrix} \quad (26)$$

It is pertinent to state that, $X^0 = \left(\frac{\Lambda_H}{\mu_H}, 0, \frac{\Lambda_V}{\mu_V}\right)$ is globally asymptotically stable (GAS).

By solving $\frac{dS_H}{dt} = \Lambda_H - \mu_H S_H$ (27)

We obtained $S_H(t) = \frac{\Lambda_H}{\mu_H} + \left(S_H(0) - \frac{\Lambda_H}{\mu_H}\right) e^{-\mu_H t}$ (28)

This show that, $S_H \to \frac{\Lambda_H}{\mu_H}$ as $t \to \infty$.

It is also easy to demonstrate in the same fashion that $S_V \to \frac{\Lambda_V}{\mu_V}$ as $t \to \infty$. Therefore, we deduced from the solution that it converges globally in the region W.

$$\left.\begin{aligned}
&\Rightarrow X \in R_+^4 \\
&\frac{dL_H}{dt} = (1-u_1)\left(\frac{\beta_H I_V + \beta_H I_H}{N_H}\right) S_H - \varphi L_H - \gamma_1 L_H - \eta L_H \\
&\frac{dI_H}{dt} = \varphi L_H - \rho I_H - (\mu_H + \delta_H) I_H \\
&\frac{dL_V}{dt} = (1-u_1)\left(\frac{\beta_V I_H + \beta_V I_V}{N_V}\right) S_V - \gamma_2 L_V - \mu_V L_V \\
&\frac{dI_V}{dt} = \gamma_2 L_V - \mu_V I_V
\end{aligned}\right\} \quad (29)$$

$$C = \begin{bmatrix} -(\varphi + \gamma_1 + \eta + \mu_H) & \beta_V & 0 & \beta_H \\ \varphi & -(\rho + \mu_H + \delta_H) & 0 & 0 \\ 0 & \beta_V & -(\gamma_2 + \mu_V) & \beta_H \\ 0 & 0 & \gamma_2 & -\mu_V \end{bmatrix} \quad (30)$$

$$G(X,Z) = \begin{pmatrix} G_1(X,Z) \\ G_2(X,Z) \\ G_3(X,Z) \\ G_4(X,Z) \end{pmatrix} = \begin{pmatrix} (1-u_1)(\beta_H I_V + \beta_H I_H)\left(1 - \frac{S_H}{N_H}\right) \\ 0 \\ (1-u_1)(\beta_V I_H + \beta_V I_V)\left(1 - \frac{S_V}{N_V}\right) \\ 0 \end{pmatrix} \begin{pmatrix} L_H \\ I_H \\ L_V \\ I_V \end{pmatrix} \quad (31)$$

Obviously, since $S_H \geq 0,$ and $S_V \geq 0,$ certainly $G(X,Z) \geq 0$. It is also shown that C is an M-matrix. Hence all the two conditions H_1 and H_2 are fulfilled, then, by lemma 1, the Lassa fever-free equilibrium Q^0 is globally asymptotically stable when $R_0 < 1.$

3.6Estimation of parameter values

A very important aspect in modeling is using a real-data to validate a proposed model for clear understanding of its ability to predict with some degree of precision a feasible result that would make the model more relevance. In this regard, we have obtained a real data of reported cases of Lassa fever in Bauchi state from January 2022 up to week 27 in 2023 from the Nigerian center for disease control (NCDC) data based. Using the procedureof [21], we estimate the parameter values as follows: the natural human mortality rateis $\mu_H = \frac{1}{\mu_0}$ where μ_0 is the mean of life-expectancy of the human population. The value of μ_0 is estimated to be 60.45(see [21]. The population of Bauchi state is estimated to be about 8,308,800 by 2023 at 3.7% annual growth rate [3]. The total population in our model (6) is denoted by N_H and we established that the human population is bounded by $N_H = \frac{\Lambda_H}{\mu_H}$. Hence, the recruitment rate is computed as $N_H \times \mu_H$. Also, the natural mortality rate in the vector population (rodents) is $\mu_V = \frac{1}{\mu_0}$ and the mean life-expectancy of the *Mastomys natalensis rat*is one year i.e $\mu_0 = 1$ [10], [7] and [21]. Therefore, the total vector population is assumed to be $N_V = 30000$

and the recruitment rate is obtained by $N_V \times \mu_V$ [21]. The spread of Lassa fever is done through contact between susceptible human and infected vector, or susceptible vector and infected human. The onset of the disease is gradual, usually begins with fever, general weakness and malaise. Exposure to the disease is between 6-21days [27]. We estimated the progression from the latent stage (asymptomatic) to infectious(symptomatic) population based on this fact. Therefore, the average progression from latent to infected in Bauchi state is $\varphi = 0.00225$. The reported cases of death due to Lassa fever δ_H and confirmed infected I_H were used to estimate the death rate as $\delta_H = 0.159$. The recovery of human from the disease is estimated to be between 2-21days [31]; [7].The remaining parameters were obtained from available literature based on the cumulative weekly reports from the NCDC. We plot the number of monthly death and confirmed casesin Bauchi state (from January 2022 to June 2023) of Lassa fever using excel as depicted in figure 1.2 and figure 1.3 respectively.

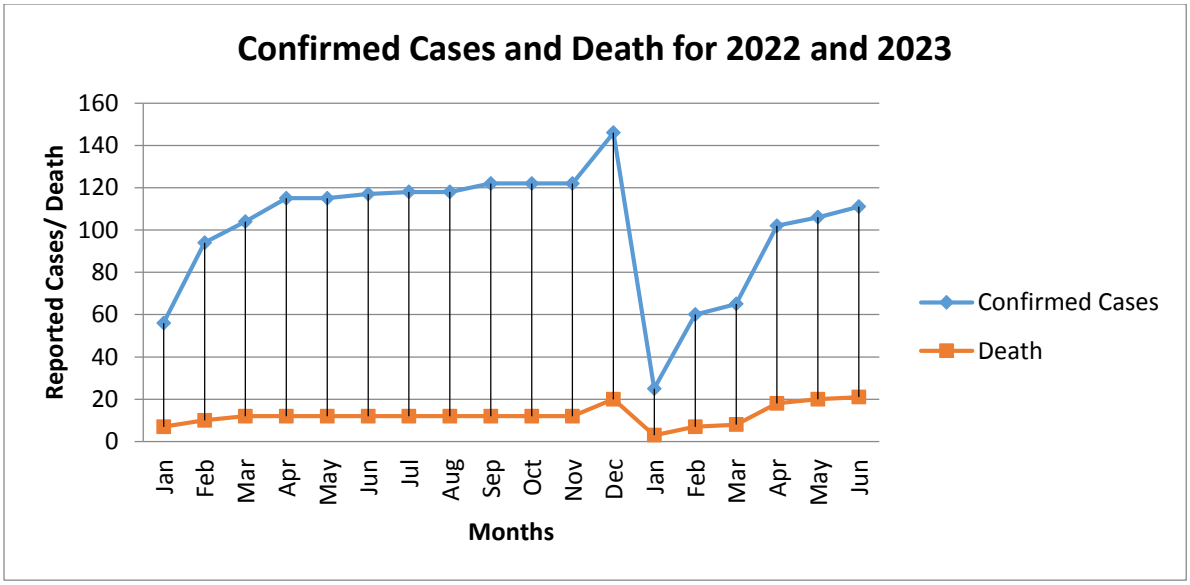

Figure 1.2: represent the number of confirmed cases and death in Bauchi state from January 2022 to June 2023.

Table 1.1 Parameter values and description for model (6)

Parameter	Description	values	source
Λ_H	Human recruitment rate	1740	Estimated
Λ_V	Vector recruitment rate	380	Estimated
β_H	Transmission probability in human	0.0015	Estimated
β_V	Transmission probability in vector	0.00001	Estimated
α	Progression rate from recovery	0.1	[31]
γ_1	Progression rate from latent to Isolation class	0.80	Assumed
γ_2	Progression rate from latent vector to infected vector	0.333	[7]
η	progression rate from latent human to recovery class	0.001	Assumed
φ	Progression rate from latent human to infectious class	0.0025	Estimated
ρ	Progression rate from infected human to isolation class	0.75	Assumed
μ_H	Natural human mortality rate	0.002	Estimated
μ_V	Natural vector mortality rate	0.126	Estimated
δ_H	Lassa fever induced date rate	0.159	Estimated
δ_V	Vector death rate due to Lassa virus	0.00027	[7]

A_1	Weight constant associated with infectious human population	1	[23]
A_2	Weight constant associated with vector population	1.5	[23]
θ	Progression rate from treated to temporary recovery	0.05	Assumed
ψ	Discount rate	0.396	Assumed
τ	The vector death rate due to the use rodenticide	0.01	Assumed
$\phi_i \ (i=1,2,3)$	Modification parameter for the use of treatment	0.123	Assumed
C_1	Cost associated with control measure u_1	0.2	[23]
C_2	Cost associated with control measure u_2	0.2	[23]
C_3	Cost associated with control measure u_3	0.15	[23]
C_{tr}	Unit cost of treatment of an infected person	\$9	Assumed
C_R	Unit cost of using rodenticide/pesticide	\$12	Assumed
C_p	Unit cost of using prevention	\$7	Assumed

The following initial values of variables were used in the numerical solution $S_H = 8,308,744,\ L_H = 52,$ $I_H = 4,\ I_{SH} = 3,\ T_H = 0,\ R_H = 0,\ S_V = 30000,\ L_V = 1200,$ and $I_V = 400.$

3.7 Sensitivity analysis of the Lassa fever model

The effect of each parameter of system (6) on the basic reproduction number R_0, is investigated to determine the impact of these parameters on the transmission of Lassa fever. The formula employed to carry out this task is $\alpha_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0}$, where R_0 is the basic reproduction number and P is a parameter of interest. The result obtained is presented in table 1.2 below.

It is clearly seen that, the parameters β_H, β_V and μ_V have positive sensitivity indices which indicates that R_0 increase with these parameters while the remaining parameters $\gamma_1, \gamma_2, \varphi, \mu_H, \rho, \eta$ and δ_H, have negative values and R_0 decrease with these parameters. For, example, the positive values means there's direct relationship between β_H, β_V μ_V and R_0 while there's an inverse relationship between negative parameters and R_0. Meanwhile, a unit increase in the value of say β_H, will lead to a unit increase in the value of R_0 and the vice-versa.

Table 1.2 Sensitivity indices of the Lassa fever model

Parameter	Description	Sensitivity index
β_H	Transmission probability in human	+1
β_V	Transmission probability in vector	+1
γ_1	Progression rate from latent to Isolation class	–0.80
γ_2	Progression rate from latent vector to infected vector	–0.459
μ_V	Natural vector mortality rate	+0.126
μ_H	Natural human mortality rate	–1
φ	Progression rate from latent human to infectious class	–1
ρ	Progression rate from infected human to isolation class	–0.75

η	progression rate from latent human to recovery class	–0.001
δ_H	Lassa fever induced date rate	–0.159

4.1 The model equations with optimal control

We have incorporated optimal control strategies in to our system (5) with the view to identify the optimal level of each strategy proposed required to halt the spread of Lassa fever in the study area (Bauchi State). Three control measures were introduced, namely, the use of prevention strategy $u_1(t)$ through the use of mass campaign for awareness on the personal hygiene and sanitation of the environmentetc., the use of treatment $u_2(t)$ on the infected person(s) and the use of rodenticide $u_3(t)$ to eradicate or decrease the vector population in the affected region. The force of infection with Lassa virus will be decrease by a factor of $(1-u_1(t)),$ and $u_2(t)$ in the human population. While, it will be decrease by a factor of $(1-u_1(t)),$ and $u_3(t)$ in the vector population. However, the system with control measures is governed by system (5).

The objective functional is defined as follow:

$$J(u)=\int_0^{t_f}\left[(A_1(L_H+I_H)+A_2N_V)+\frac{1}{2}(C_1u_1^2+C_2u_2^2+C_3u_3^2)\right]dt \qquad (34)$$

where t_f is the final time and the coefficients $A_1,\ A_2,\ C_1,\ C_2,\ C_3,$ are positive weights to balance the factors. The aim is to minimized the number of individuals with Lassa fever at latent stage of infections $L_H,$ the number of infected and infectious individuals, $I_H,$ and the population of the vector (rodents) $N_V,$ while minimizing the cost of controls $u_1(t),u_2(t),u_3(t)$. The cost of implementing each of the three controls are represented by $\frac{1}{2}C_1u_1^2,\frac{1}{2}C_2u_2^2\ and\ \frac{1}{2}C_3u_3^2$. The cost related to the first control measure signifies the expenses that might be made in the course of using mass campaign for awareness on prevention from Lassa infection throughpersonal hygiene, sanitation etc. The second cost is on the expenses that might be made on treatment of infected individuals, while, the last cost is on the expenses of using pesticide to free the environment from the vector/reservoir of the virus.Thus, we seek an optimal controls $u_1^*,u_2^*,\ u_3^*$ such that

$$J\left(u_1^*,u_2^*,u_3^*\right)=\min_{u_1,u_2,u_3}\left\{J\left(u_1,u_2,u_3\right)\ni u_1,u_2,u_3\in U\right\}$$

Where U is the set of measurable functions defined from $[0,t_f]$ onto$[0,1]$.The necessary conditions that an optimal control must satisfy were derived from Pontryagin's Maximum Principle by [24], andthe existence result for optimal control from the adjoint variable of the state variables satisfy the following set of differential equations. This principle converts (26) into a problem of minimizing point wise a Hamiltonian H, with respect to$(u_1,u_2,u_3).$

Theorem 6: There exists an optimal control set $u_1,u_2,u_3$and the corresponding state system (5) that minimizes $J(u_1,u_2,u_3)$over$U$. Moreover, there exists adjoint functions $\lambda_{S_H},\lambda_{L_H},\lambda_{I_H},\lambda_{I_{SH}},\lambda_{T_H},\lambda_{R_H},\lambda_{S_V},\lambda_{L_V},\lambda_{I_V}$ such that our Hamiltonian is

$$H=A_1L_H+A_2I_H+A_3N_V+\frac{1}{2}(C_1u_1^2+C_2u_2^2+C_3u_3^2)e^{-\psi t}$$

$$
\begin{aligned}
&+\lambda_{S_H}[\Lambda_H+\alpha R_H-\frac{1}{N_H}(1-u_1)(\beta_H I_V+\beta_H I_H)S_H-\mu_H S_H]\\
&+\lambda_{L_H}[\frac{1}{N_H}(1-u_1)(\beta_H I_V+\beta_H I_H)S_H-\gamma_1 L_H-\mu_H L_H-\varphi L_H-\eta L_H-\phi_1 u_2 L_H]\\
&+\lambda_{I_H}[\varphi L_H-\rho I_H-\phi_2 u_2 I_H-(\mu_H+\delta_H)I_H]\\
&+\lambda_{I_{SH}}[\gamma_1 L_H+\rho I_H-\phi_3 u_2 I_{SH}-\mu_H I_{SH}]\\
&+\lambda_{T_H}[\phi_1 u_2 L_H+\phi_2 u_2 I_H+\phi_3 u_2 I_{SH}-\theta T_H-\mu_H T_H]\\
&+\lambda_{R_H}[\eta L_H+\theta T_H-\alpha R_H-\mu_H R_H]\\
&+\lambda_{S_V}[\Lambda_V-\frac{1}{N_V}(1-u_1)(\beta_V I_H+\beta_V I_V)S_V-(\mu_V+\tau u_3)S_V]\\
&+\lambda_{L_V}[\frac{1}{N_V}(1-u_1)(\beta_V I_H+\beta_V I_V)S_V-\gamma_2 L_V-(\mu_V+\tau u_3)L_V]\\
&+\lambda_{I_V}[\gamma_2 L_V-(\mu_V+\tau u_3)I_V]\\
&+\lambda_{C_f}[C_p u_1 S_H+C_{tr}u_2 L_H+C_{tr}u_2 I_H+C_R\tau u_3 S_V+C_R\tau u_3 L_V+C_R\tau u_3 I_V
\end{aligned}
\tag{35}
$$

Where $\lambda_{S_H},\lambda_{L_H},\lambda_{I_H},\lambda_{I_{SH}},\lambda_{T_H},\lambda_{R_H},\lambda_{S_V},\lambda_{L_V},\lambda_{I_V}$ are the adjoint variables or co-state variables with transversality conditions:

$\lambda_{S_H}(t_f)=\lambda_{L_H}(t_f)=\lambda_{I_H}(t_f)=\lambda_{I_{SH}}(t_f)=\lambda_{T_H}(t_f)=\lambda_{R_H}(t_f)=\lambda_{S_V}(t_f)=\lambda_{L_V}(t_f)=\lambda_{I_V}(t_f)=0$ and the controls u_1^*,u_2^*,u_3^* satisfy the optimality conditions.

Proof

The adjoint system were obtained by differentiating the Hamiltonian function in (35)evaluated at the optimal control which lead to:

$$
\begin{aligned}
\frac{\partial H}{\partial S_H}&=\frac{1}{N_H}(1-u_1)(\beta_H I_V+\beta_H I_H)S_H(\lambda_{S_H}-\lambda_{L_H})+\mu_H\lambda_{S_H}-C_p S_H u_1\lambda_{C_f}\\
\frac{\partial H}{\partial L_H}&=(\lambda_{L_H}-\lambda_{I_H})\varphi+\mu_H\lambda_{L_H}+\gamma_1(\lambda_{L_H}-\lambda_{I_{SH}})+\eta(\lambda_{L_H}-\lambda_{R_H})+\phi_1 u_2(\lambda_{L_H}-\lambda_{T_H})-C_{tr}u_2\lambda_{C_f}-A_1\\
\frac{\partial H}{\partial I_H}&=(\lambda_{I_H}-\lambda_{T_H})\phi_2 u_2+\rho(\lambda_{I_H}-\lambda_{I_{SH}})+(\mu_H+\delta_H)\lambda_{I_H}-C_{tr}u_2\lambda_{C_f}-A_2\\
\frac{\partial H}{\partial I_{SH}}&=\phi_3 u_2(\lambda_{I_{SH}}-\lambda_{T_H})+\mu_H\lambda_{I_{SH}}-C_{tr}u_2\lambda_{C_f}-A_2\\
\frac{\partial H}{\partial T_H}&=(\lambda_{L_H}-\lambda_{R_H})\theta+\mu_H\lambda_{T_H}+\theta\lambda_{T_H}\\
\frac{\partial H}{\partial R_H}&=(\lambda_{R_H}-\lambda_{S_H})\alpha+\mu_H\lambda_{R_H}\\
\frac{\partial H}{\partial S_V}&=\frac{1}{N_V}(1-u_1)(\beta_V I_H+\beta_V I_V)(\lambda_{S_V}-\lambda_{L_V})+\mu_V\lambda_{S_V}+\tau u_3(\lambda_{S_V}-\lambda_{L_V}-\lambda_{I_V})C_{S_R}\tau u_3\lambda_{C_f}-A_3\\
\frac{\partial H}{\partial L_V}&=(\lambda_{L_V}-\lambda_{I_V})\gamma_2+\mu_V\lambda_{L_V}-C_{S_R}\tau u_3\lambda_{C_f}-A_3\\
\frac{\partial H}{\partial I_V}&=\mu_V\lambda_{I_V}-C_{S_R}\tau u_3\lambda_{C_f}-A_3
\end{aligned}
\tag{36}
$$

With transversality conditions:

$$\lambda_{S_H}(t_f)=\lambda_{L_H}(t_f)=\lambda_{I_H}(t_f)=\lambda_{I_{SH}}(t_f)=\lambda_{T_H}(t_f)=\lambda_{R_H}(t_f)=\lambda_{S_V}(t_f)=\lambda_{L_V}(t_f)=\lambda_{I_V}(t_f)=0 \quad (37)$$

We obtain the characterization of the controls by solving for $u_i\ (i=1,2,3)$ in

$$\frac{\partial H}{\partial u_i}=0 \ \ (i=1,2,3) \quad (38)$$

Solving for u_i with $i=1,2,3$ we obtained

$$\left\{\begin{array}{l} u_1^*=\max\left\{0,\min\left(1,\dfrac{\frac{1}{N_H}(\beta_H I_V+\beta_H I_H)S_H(\lambda_{L_H}-\lambda_{S_H})+\frac{1}{N_V}(\beta_V I_H+\beta_V I_V)S_V(\lambda_{L_V}-\lambda_{S_V})}{C_1 e^{-\psi t}}\right)\right. \\ u_2^*=\max\left\{0,\ \min\left(1,\dfrac{\phi_1 L_H(\lambda_{T_H}-\lambda_{L_H})+\phi_2 I_H(\lambda_{T_H}-\lambda_{I_H})+\phi_3 I_{SH}(\lambda_{T_H}-\lambda_{I_{SH}})+C_{tr}L_H\lambda_{C_f}}{C_2 e^{-\psi t}}\right)\right. \\ u_3^*=\max\left\{0,\ \min\left(1,\dfrac{\tau(S_V\lambda_{S_V}+L_V\lambda_{L_V}+I\lambda_{I_V})-\tau C_{S_R}\lambda_{C_f}(S_V+L_V+I_V)}{C_3 e^{-\psi t}}\right)\right. \end{array}\right\} \quad (38)$$

4.2 Cost effectiveness analysis

To determine the cost analysis, we set the following objective functional:

$$C_f=\int_0^{t_f}(C_P u_1(t)S_H+C_{tr}\phi u_2(t)I_H+\iota C_{S_V}u_3(t)S_V+L_V(t)+I_V(t))e^{-\psi t}dt\,. \quad (39)$$

The objective functional (39) is subject to our system (35). We developed the Hamiltonian H as

$$\left.\begin{array}{l} +\lambda_{S_H}[\Lambda_H+\alpha R_H-\frac{1}{N_H}(1-u_1)(\beta_H I_V+\beta_H I_H)S_H-\mu_H S_H] \\ +\lambda_{L_H}[\frac{1}{N_H}(1-u_1)(\beta_H I_V+\beta_H I_H)S_H-\gamma_1 L_H-\mu_H L_H-\eta L_H-\varphi L_H-\phi_1 u_2 L_H] \\ +\lambda_{I_H}[\varphi L_H-\rho I_H-\phi_2 u_2 I_H-(\mu_H+\delta_H)I_H] \\ +\lambda_{I_{SH}}[\gamma_1 L_H+\rho I_H-\phi_3 u_2 I_{SH}-\mu_H I_{SH}] \\ +\lambda_{T_H}[\phi_1 u_2 L_H+\phi_2 u_2 I_H+\phi_3 u_2 I_{SH}-\theta T_H-\mu_H T_H] \\ +\lambda_{R_H}[\eta L_H+\theta T_H-\alpha R_H-\mu_H R_H] \\ +\lambda_{S_V}[\Lambda_V-\frac{1}{N_V}(1-u_1)(\beta_V I_H+\beta_V I_V)S_V-(\mu_V+\tau u_3)S_V] \\ +\lambda_{L_V}[\frac{1}{N_V}(1-u_1)(\beta_V I_H+\beta_V I_V)S_V-\gamma_2 L_V-(\mu_V+\tau u_3)L_V] \\ +\lambda_{I_V}[\gamma_2 L_V-(\mu_V+\tau u_3)I_V] \end{array}\right\} \quad (40)$$

Where $\lambda_{S_H},\lambda_{L_H},\lambda_{I_H},\lambda_{I_{SH}},\lambda_{T_H},\lambda_{R_H},\lambda_{S_V},\lambda_{L_V},\lambda_{I_V}$ are the shadow prices associated with their respective classes. The changes in the objective value of the optimal solution of an optimization problem are obtained by relaxing the constraint by one unit. We use Pontryagin's Maximum Principle to obtain

$$-\frac{d\lambda_{S_H}}{dt}=\frac{\partial H_C}{dS_H},-\frac{d\lambda_{L_H}}{dt}=\frac{\partial H_C}{dL_H},-\frac{d\lambda_{I_H}}{dt}=\frac{\partial H_C}{dI_H},-\frac{d\lambda_{I_{SH}}}{dt}=\frac{\partial H_C}{dI_{SH}},-\frac{d\lambda_{T_H}}{dt}=\frac{\partial H_C}{dT_H},-\frac{d\lambda_{R_H}}{dt}=\frac{\partial H_C}{dR_H},$$
$$-\frac{d\lambda_{S_V}}{dt}=\frac{\partial H_C}{dS_V},-\frac{d\lambda_{L_V}}{dt}=\frac{\partial H_C}{dL_V},-\frac{d\lambda_{I_V}}{dt}=\frac{\partial H_C}{dI_V} \quad (41)$$

$$\left.\begin{aligned}
-\frac{d\lambda_{S_H}}{dt}&=-[C_p u_1(t)e^{-\psi t}-\frac{1}{N_H}(1-u_1)\left(\beta_H I_V+\beta_H I_H\right)\lambda_{S_H}-\mu_H\lambda_{S_H}+\frac{1}{N_H}(1-u_1)\left(\beta_H I_V+\beta_H I_H\right)\lambda_{L_H}]\\
-\frac{d\lambda_{L_H}}{dt}&=-[C_{tr}u_2(t)e^{-\psi t}(\gamma_1-\mu_H+\varphi+\phi_1u_2)\lambda_{L_H}+\varphi\lambda_{I_H}+\gamma_1\lambda_{I_{SH}}+\eta\lambda_{L_H}+\phi_1u_2\lambda_{T_H}]\\
-\frac{d\lambda_{I_H}}{dt}&=-[C_{tr}u_2(t)e^{-\psi t}-(\rho+\phi_2u_2+\mu_H+\delta_H)\lambda_{I_H}+\rho\lambda_{I_{SH}}+\phi_2u_2\lambda_{T_H}]\\
-\frac{d\lambda_{I_{SH}}}{dt}&=-[-(\phi_3u_2+\mu_H)\lambda_{I_{SH}}+\phi_3u_2\lambda_{T_H}]\\
-\frac{d\lambda_{T_H}}{dt}&=-[(\theta+\mu_H)\lambda_{T_H}]\\
-\frac{d\lambda_{R_H}}{dt}&=-[-(\eta+\alpha+\mu_H)\lambda_{R_H}]\\
-\frac{d\lambda_{S_V}}{dt}&=-[C_{S_V}u_3(t)e^{-\psi t}-\frac{1}{N_V}(1-u_1)\left(\beta_V I_H+\beta_V I_V\right)\lambda_{S_V}-(\mu_V+\iota u_3)\lambda_{S_V}+\frac{1}{N_V}(1-u_1)\left(\beta_V I_H+\beta_V I_V\right)\lambda_{L_V}]\\
-\frac{d\lambda_{L_V}}{dt}&=-[C_{S_V}u_3(t)e^{-\psi t}-(\gamma_2+(\mu_V+\tau u_3)\lambda_{L_V}+\gamma_2\lambda_{I_V}]\\
-\frac{d\lambda_{I_V}}{dt}&=-[C_{S_V}u_3(t)e^{-\psi t}-(\mu_V+\tau u_3)\lambda_{I_V}]
\end{aligned}\right\} \quad (42)$$

4.2.1Assessment of the cost of using the first control measure (Mass campaign);

Differentiating (40) partially with respect to u_1,

$$\frac{dH_C}{du_1}=C_P S_H(t)e^{-\psi t}+\lambda_H(\lambda_{S_H}-\lambda_{L_H})+\lambda_V(\lambda_{S_V}-\lambda_{L_V}) \quad (43)$$

The expression $\frac{1}{N_H}\left(\beta_H I_V+\beta_H I_H\right)(\lambda_{S_H}-\lambda_{L_H})+\frac{1}{N_V}\left(\beta_V I_H+\beta_V I_V\right)(\lambda_{S_V}-\lambda_{L_V})$ in (43), is the total marginal benefit of the use of mass campaign against the spread of Lassa fever disease and $C_P S_H(t)e^{-\psi t}$ is the marginal cost. If the marginal cost of the mass campaign is equal to the marginal benefit, then the optimal policy is achieved.

$$\left.\begin{aligned}
u_1(t)=0 \quad if \quad C_P S_H e^{-\psi t}&>\frac{1}{N_H}\left(\beta_H I_V+\beta_H I_H\right)(\lambda_{S_H}-\lambda_{L_H})+\frac{1}{N_V}\left(\beta_V I_H+\beta_V I_V\right)(\lambda_{S_V}-\lambda_{L_V})\\
u_1(t)\in(0,1) \ if \ C_P S_H e^{-\psi t}&=\frac{1}{N_H}\left(\beta_H I_V+\beta_H I_H\right)(\lambda_{S_H}-\lambda_{L_H})+\frac{1}{N_V}\left(\beta_V I_H+\beta_V I_V\right)(\lambda_{S_V}-\lambda_{L_V})\\
u_1(t)=1 \quad if \quad C_P S_H e^{-\psi t}&<\frac{1}{N_H}\left(\beta_H I_V+\beta_H I_H\right)(\lambda_{S_H}-\lambda_{L_H})+\frac{1}{N_V}\left(\beta_V I_H+\beta_V I_V\right)(\lambda_{S_V}-\lambda_{L_V})
\end{aligned}\right\} \quad (44)$$

The use of mass campaign as prevention against the spread of Lassa fever disease will be cost optimal only when the anticipated marginal benefit is greater than the marginal cost.

4.2.2 Assessment of the cost of using the second control measure (treatment of infected human population);

Again, differentiating (40) partially with respect to u_2,

$$\frac{dH_C}{du_2} = C_{tr} I_H(t) e^{-\psi t} + \phi_1(\lambda_{L_H} - \lambda_{T_H}) + \phi_2(\lambda_{I_H} - \lambda_{T_H}) + \phi_3(\lambda_{I_{SH}} - \lambda_{T_H})$$

(45)

where $C_{tr} I_H(t) e^{-\psi t}$ represent the marginal cost of treatment and $\phi_1(\lambda_{L_H} - \lambda_{T_H}) + \phi_2(\lambda_{I_H} - \lambda_{T_H}) + \phi_3(\lambda_{I_{SH}} - \lambda_{T_H})$ stands for the marginal benefit of the treatment. However, if the marginal benefit is higher than the marginal cost it simply implied that the control target is achieved. Therefore,

$$\left.\begin{aligned} u_2(t) = 0 \quad if \quad & C_{tr} I_H e^{-\psi t} > \phi_1(\lambda_{L_H} - \lambda_{T_H}) + \phi_2(\lambda_{I_H} - \lambda_{T_H}) + \phi_3(\lambda_{I_{SH}} - \lambda_{T_H}) \\ u_2(t) \in (0,1) \quad if \quad & C_{tr} I_H e^{-\psi t} = \phi_1(\lambda_{L_H} - \lambda_{T_H}) + \phi_2(\lambda_{I_H} - \lambda_{T_H}) + \phi_3(\lambda_{I_{SH}} - \lambda_{T_H}) \\ u_2(t) = 1 \quad if \quad & C_{tr} I_H e^{-\psi t} < \phi_1(\lambda_{L_H} - \lambda_{T_H}) + \phi_2(\lambda_{I_H} - \lambda_{T_H}) + \phi_3(\lambda_{I_{SH}} - \lambda_{T_H}) \end{aligned}\right\} \quad (46)$$

4.2.3 Assessment of the cost of using the third control measure (pesticide to reduce/annihilate the vector population);

Also, differentiating (40) partially with respect to u_3,

$$\frac{dH_C}{du_3} = C_{S_V} S_V(t) e^{-\psi t} + \tau(\lambda_{L_V} + \lambda_{I_V} - \lambda_{S_V}) \quad (47)$$

$C_{S_V} S_V(t) e^{-\psi t}$ is the marginal cost of using pesticide to reduce the vector population, while, $\tau(\lambda_{L_V} + \lambda_{I_V} - \lambda_{S_V})$ is the marginal benefit of using u_3 as intervention for controlling the spread of Lassa virus in the population.Thus,

$$\left.\begin{aligned} u_3(t) = 0 \quad if \quad & C_{S_V} S_V e^{-\psi t} > \tau(\lambda_{L_V} + \lambda_{I_V} - \lambda_{S_V}) \\ u_3(t) \in (0,1) \quad if \quad & C_{S_V} S_V e^{-\psi t} = \tau(\lambda_{L_V} + \lambda_{I_V} - \lambda_{S_V}) \\ u_3(t) = 1 \quad if \quad & C_{S_V} S_V e^{-\psi t} < \tau(\lambda_{L_V} + \lambda_{I_V} - \lambda_{S_V}) \end{aligned}\right\} \quad (48)$$

If the marginal benefit is higher than the marginal cost of using pesticide to reduce/annihilate the vector population, then, the control target is attained.

V. Conclusion

A model of Lassa fever that incorporates vector-to- human, human-to –human, vector-to- vector transmission and optimal control strategies is developed and investigated.Three control measures namely, prevention through mass campaign and sanitation of the environment, isolation and treatment of infected individuals and the use of rodenticide to reduce the vector population were considered. A system of non-linear ordinary differential equations was formulated to understand the dynamics of the disease transmission. The positivity of solution and boundedness of the system was proved. The disease free equilibrium of the Lassa-fever model is established. The basic reproduction number R_0 of the model is obtained using the technique of next generation matrix. Sensitivity analysis of the threshold R_0 is performed using the data in Table 1.1. It's found that the most sensitive parameters are; β_H, β_V and μ_V. The global stability analysis of Lassa-free equilibrium is obtained by Castillo-Chavez approach. The result of the analysis revealed that, the Lassa-free equilibrium is globally asymptotically stable if $R_0 < 1.$ The Pontryagin's maximum principle was used to determine the optimality of the system. The assessment of cost effectiveness of all the three control measures is performed to identify if the marginal benefit of a particular control is greater than the marginal cost or otherwise. This can be explain further in our subsequent study when the numerical analysis is performed.

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