Modelling the impact of Quarantine and Isolation-based control interventions on the transmission dynamics of Lassa fever

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Introduction

- Lassa fever is an acute viral hemorrhagic fever illness caused by Lassa virus.
- It is endemic in West African countries like Liberia, Sierra Leone, Guinea and Nigeria.
- There are about 100,000 to 300,000 infected cases that result in 5,000 deaths annually.
- Lassa virus transmission can also occur through contaminated medical equipment such as reused needles in health care settings.
- The incubation period of Lassa fever is about one to three weeks [1].
- The signs and symptoms of Lassa fever occurs within the incubation period of the virus after the patient comes in contact with the virus.

Introduction cont'd

- There is no vaccine against Lassa fever except non-pharmaceutical interventions such as prompt isolation of infected persons, quarantine of exposed persons and contact tracing.
- **Quarantine:** the restriction of movement or separation of susceptible people who are exposed to a communicable disease for a period of days that is equivalent to the incubation period of the disease.
- **Isolation:** the separation of symptomatic persons who have a communicable disease from the healthy.

Introduction cont'd

- Several researchers have developed mathematical models of Lassa fever in order to help eradicate the disease such as Obabiyi and Onifade [2], Omale and Edibo [3] and Innocent and Omo [4].

- Obabiyi and Onifade [2] considered early diagnosis of infected humans, hygiene environment maintenance and use of new needle when taking. Omale and Edibo [3] considered treatment as control measures. Innocent and Omo [4] advised that good health policy should be implemented in order to reduce the basic reproduction number less than one.

Research question

How can quarantine and isolation as control measures guide public health experts, infectious disease physicians, epidemiologists, and policy makers in eliminating Lassa fever virus in the population?

Model Formulation

- The Lassa fever model considers two populations, namely: human population, $N_h(t)$ and the rodent population, $N_r(t)$.

- The human population is sub-divided into six compartments; Susceptible human class, $S_h(t)$, Exposed human class, $E_h(t)$, Quarantined human class, $Q_h(t)$, Infected human class, $I_h(t)$, Isolated human class, $J_h(t)$ and Recovered human class,$R_h(t)$ such that

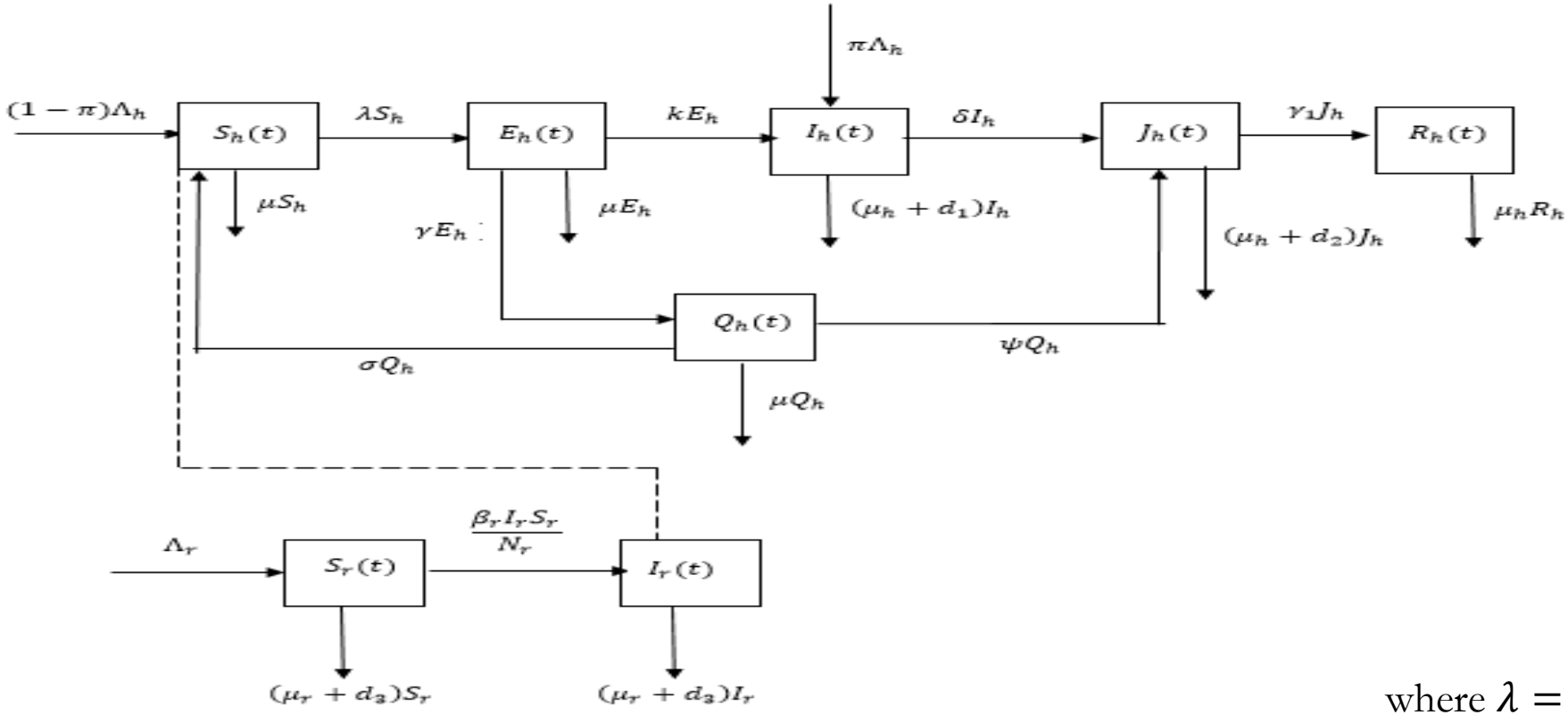
$$N_h(t) = S_h(t) + E_h(t) + I_h(t) + J_h(t) + R_h(t) + Q_h(t).$$

Model formulation cont'd

The rodent population, $N_r(t)$, is subdivided into susceptible rodent, $S_r(t)$, and infected rodent, $I_r(t)$ such that

$$N_r(t) = S_r(t) + I_r(t).$$

Model flow diagram



where $\lambda = \left(\frac{\beta_1 I_h + \beta_2 J_h + \beta_3 I_r}{N_h}\right)$

Model equations

$$\frac{dS_h}{dt} = (1-\pi)\Lambda_h + \sigma Q_h - \left(\frac{\beta_1 I_h + \beta_2 J_h + \beta_3 I_r}{N_h}\right) S_h - \mu_h S_h$$

$$\frac{dE_h}{dt} = \left(\frac{\beta_1 I_h + \beta_2 J_h + \beta_3 I_r}{N_h}\right) S_h - \mu_h E_h - \gamma E_h - k E_h$$

$$\frac{dQ_h}{dt} = \gamma E_h - \sigma Q_h - \mu_h Q_h - \psi Q_h$$

$$\frac{dI_h}{dt} = \pi\Lambda_h + k E_h - \mu_h I_h - d_1 I_h - \delta I_h$$

$$\frac{dJ_h}{dt} = \delta I_h + \psi Q_h - \mu_h J_h - d_2 J_h - \gamma_1 J_h$$

$$\frac{dR_h}{dt} = \gamma_1 J_h - \mu_h R_h$$

$$\frac{dS_r}{dt} = \Lambda_r - \beta_r \frac{I_r}{N_r} S_r - \mu_r S_r - d_3 S_r$$

$$\frac{dI_r}{dt} = \beta_r \frac{I_r}{N_r} S_r - \mu_r I_r - d_3 I_r$$

where $S_h(0) > 0, E_h(0) \geq 0, Q_h(0) \geq 0, I_h(0) \geq 0, J_h(0) \geq 0, R_h(0) \geq 0, S_r(0) > 0$, and $I_r(0) \geq 0$ are the initial conditions.

Parameter descriptions for the Lassa fever model

Parameters	Parameter description and their dimensions	Parameters	Parameter description and their dimensions
Λ_h	Human recruitment rate, Human × Day^{-1}	δ	Isolation rate for infected persons, Day^{-1}
β_1	Effective contact rate for infected individuals, dimensionless	d_1	Disease-induced rate for infected persons, Day^{-1}
β_2	Effective contact rate for isolated individuals, dimensionless	d_2	Disease-induced rate for isolated persons, Day^{-1}
β_3	Effective contact rate for infected rodents, dimensionless	γ_1	Recovery rate, Day^{-1}
π	Proportion of people born by infected mothers, dimensionless	μ_h	Natural death rate for human population, Day^{-1}
γ	Quarantine rate, Day^{-1}	Λ_r	Rodents recruitment rate, Human × Day^{-1}
k	Progression from Exposed to infected class, Day^{-1}	β_r	Contact rate for susceptible rodent getting infected, Day^{-1}
σ	Susceptible rate for quarantine persons without symptoms, Day^{-1}	μ_r	Natural death rate for rodents population, Day^{-1}
φ	Isolation rate for quarantine persons with symptoms, Day^{-1}	d_3	Hunting or pesticide or other predator rate population, Day^{-1}

Boundedness and positivity of the solutions

- The Lassa fever model of equations has solutions which are contained in the feasible region and is bounded in Ω;

$$\Omega = \left\{ \left(S_h(t), E_h(t), Q_h(t), I_h(t), J_h(t), R_h(t), S_r(t), I_r(t) \right) \in \mathbb{R}_+^8 : N_h \leq \frac{\Lambda_h}{\mu_h}, \; N_r \leq \frac{\Lambda_r}{\mu_r + d_3} \right\}.$$

- Assume that the initial solution set $\{(S_h(0), E_h(0), Q_h(0), I_h(0), J_h(0), R_h(0), S_r(0), I_r(0)) \geq 0\}$. The solution set $(S_h(t), E_h(t), Q_h(t), I_h(t), J_h(t), R_h(t), S_r(t), I_r(t)) \in \mathbb{R}_+^8$ of the model equations are non-negative.

Disease-free equilibrium

- The disease-free equilibrium point, E_0, is given by

$$E_0 = [S_{h0}, E_{h0}, Q_{h0}, I_{h0}, J_{h0}, R_{h0}, S_{r0}, I_{r0}] = \left(\frac{\Lambda_h}{\mu_h}, 0,0,0,0,0, \frac{\Lambda_r}{\mu_r + d_3}, 0\right)$$

Effective reproduction number

- The effective reproduction number, R_e, is computed using the next generation approach described by Van den Driessche and Watmough [5].

- The effective reproduction number, R_e is

$$R_e = \max(R_{eh}, R_{er}) = \left(\frac{\delta\beta_2 gk + \gamma\varphi\beta_2 h + kgp\beta_1}{fghp}, \frac{\beta_r}{q}\right),$$

where $f = \mu_h + \gamma + k$, $g = \sigma + \mu_h + \psi$, $h = \mu_h + d_1 + \delta$, $p = \mu_h + d_2 + \gamma_1$, $q = \mu_r + d_3$, R_{eh} : the effective reproduction number of human population, R_{er} : the effective reproduction number of the rodent population.

Stability of the disease-free equilibrium state

Theorem. The DFE, E_0, of the model equations is locally and globally asymptotically stable if $R_{eh}, R_{er} < 1$ and unstable if $R_{eh}, R_{er} > 1$ in Ω.

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Existence stability of the endemic equilibrium

Solving the model equations at the steady-state in terms of λ gives

$$S_h^* = \frac{fg\Lambda_h}{fg\mu_h+\lambda\left(g(\mu_h+k)+\gamma(\mu_h+\varphi)\right)}, E_h^* = \frac{\lambda g\Lambda_h}{fg\mu_h+\lambda\left(g(\mu_h+k)+\gamma(\mu_h+\varphi)\right)}, \; Q_h^* = \frac{\lambda\gamma\Lambda_h}{fg\mu_h+\lambda\left(g(\mu_h+k)+\gamma(\mu_h+\varphi)\right)}$$

$$I_h^* = \frac{\lambda kg\Lambda_h}{fgh\mu_h+\lambda h\left(g(\mu_h+k)+\gamma(\mu_h+\varphi)\right)}, \; J_h{}^* = \frac{\lambda\Lambda_h(\delta gk+\gamma h\varphi)}{fghp\mu_h+\lambda hp\left(g(\mu_h+k)+\gamma(\mu_h+\varphi)\right)},$$

$$R_h^* = \frac{\gamma_1\lambda\Lambda_h(\delta gk+\gamma h\varphi)}{fghp\mu_h^2+\lambda hp\mu_h\left(g(\mu_h+k)+\gamma(\mu_h+\varphi)\right)}, \; S_r^* = \frac{\Lambda_r}{q\mathrm{R}_{er}}, \quad I_r{}^* = \frac{(\mathrm{R}_{er}-1)\Lambda_r}{q\mathrm{R}_{er}}$$

where λ is the solution of the polynomial $A\lambda^2 + B\lambda + C = 0$,

Existence stability of the endemic equilibrium contd.

with

$$A = q\Lambda_h R_{er}\mu_h(\gamma hp + \gamma h\varphi + ghp + gkp) + q\Lambda_h R_{er}\gamma_1(\gamma h\varphi + \delta gk),$$

$$B = fghpq\Lambda_h R_{er}\mu_h(1 - R_{eh}) + ph\Lambda_h\beta_3\mu_h\big(g(\mu_h + k) + \gamma(\mu_h + \varphi)\big)(1 - R_{er}),$$

$$C = fghp\Lambda_r\beta_3\mu_h^2(1 - R_{er}).$$

A is positive. Applying Descarte's rule of signs to determine the sign of λ, a unique endemic equilibrium exists for any sign of B if $R_{eh} > 1$ and $R_{er} > 1$.

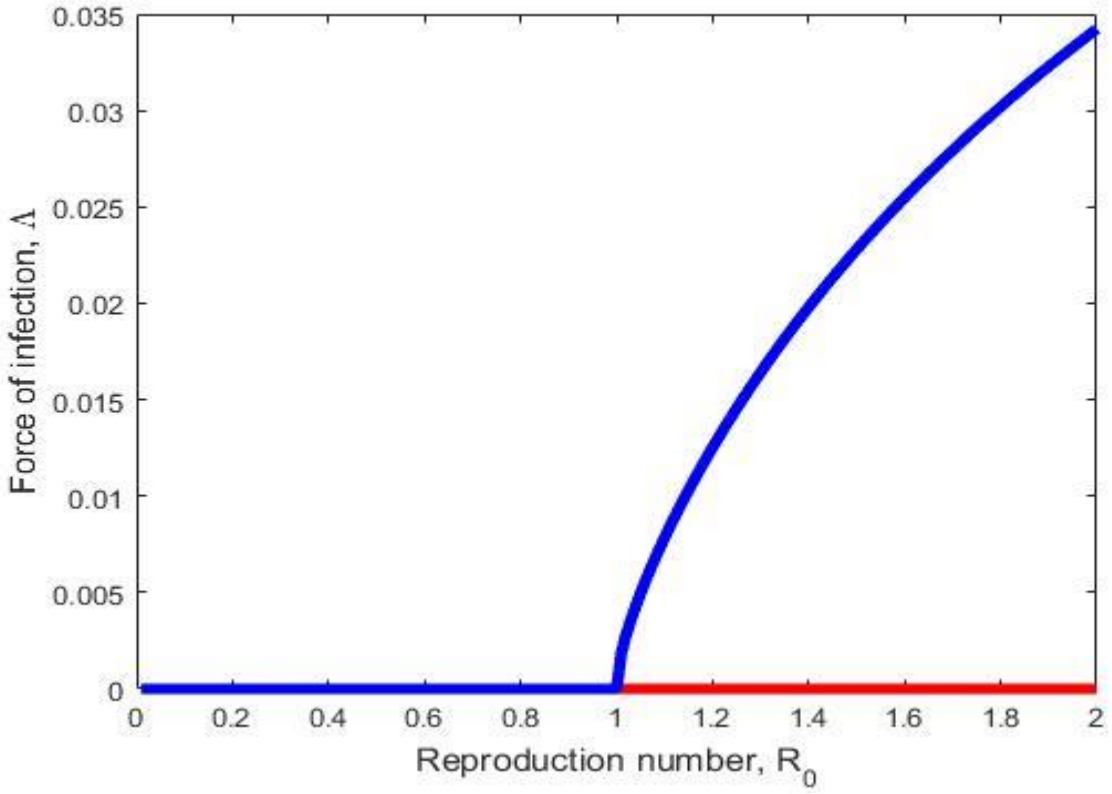
- **Theorem.** The model equations has a unique (positive) equilibrium whenever $R_{eh} > 1$, and $R_{er} > 1$ otherwise none.

Bifurcation analysis

The approach of centre manifold theory described by Castillo - Chavez and Song is used to investigate the existence of forward bifurcation at $R_e = 1$

The Lassa fever virus model exhibits a forward bifurcation.

It is observed that as R_e decreases to less than 1, which is $R_e < 1$ no endemic exist, the disease continues to reduce in the presence of quarantine and isolation and as R_e increases, that is $R_e > 1$ Lassa fever invades the population.



Numerical Simulation

- Numerical Simulations of the model are carried out using the initial conditions, $S_h(0) = 1000, E_h(0) = 250, Q_h(0) = 150, I_h(0) = 50, J_h(0) = 30, R_h(0) = 5, S_r(0) = 500, I_r = 30$ and parameter values in Table 1 except where specified otherwise.

Numerical simulation cont'd

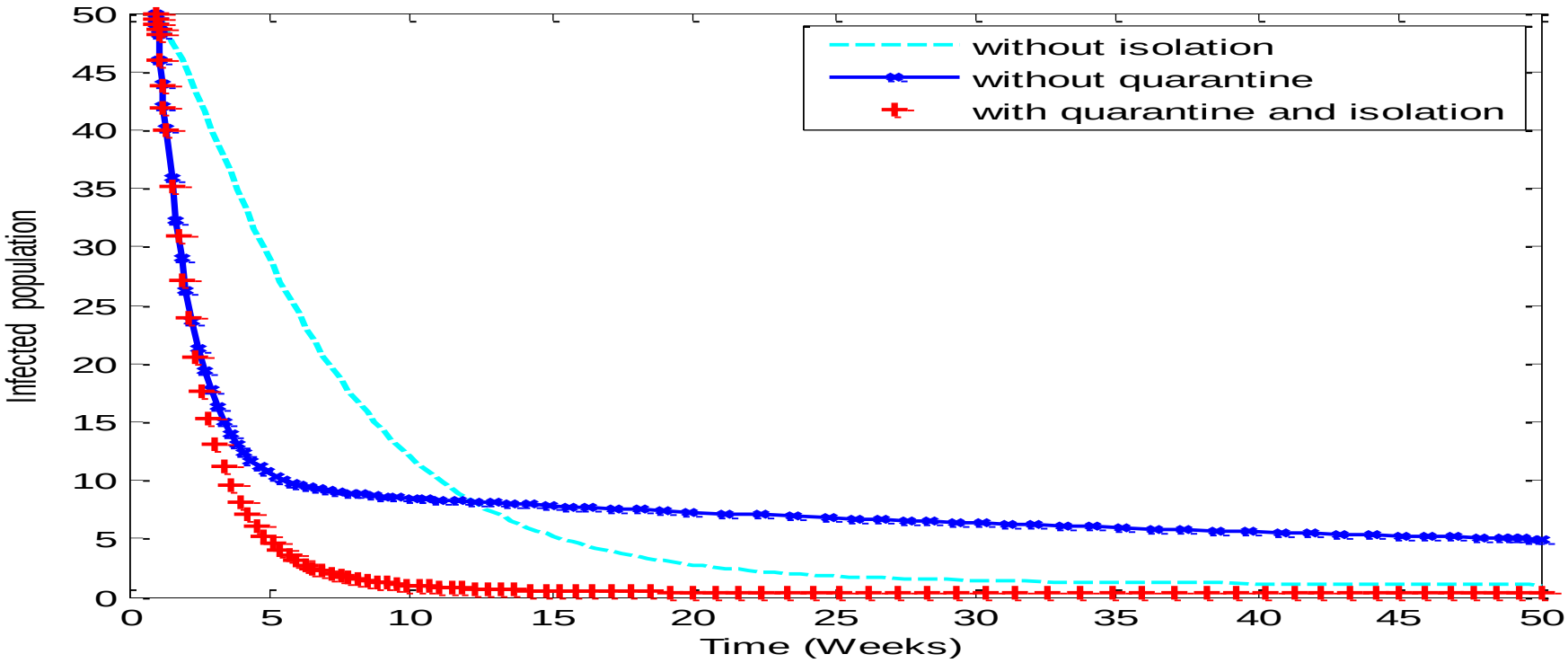


Figure 1. Simulation showing the effect of quarantine and isolation on infected population.

Numerical simulation cont'd

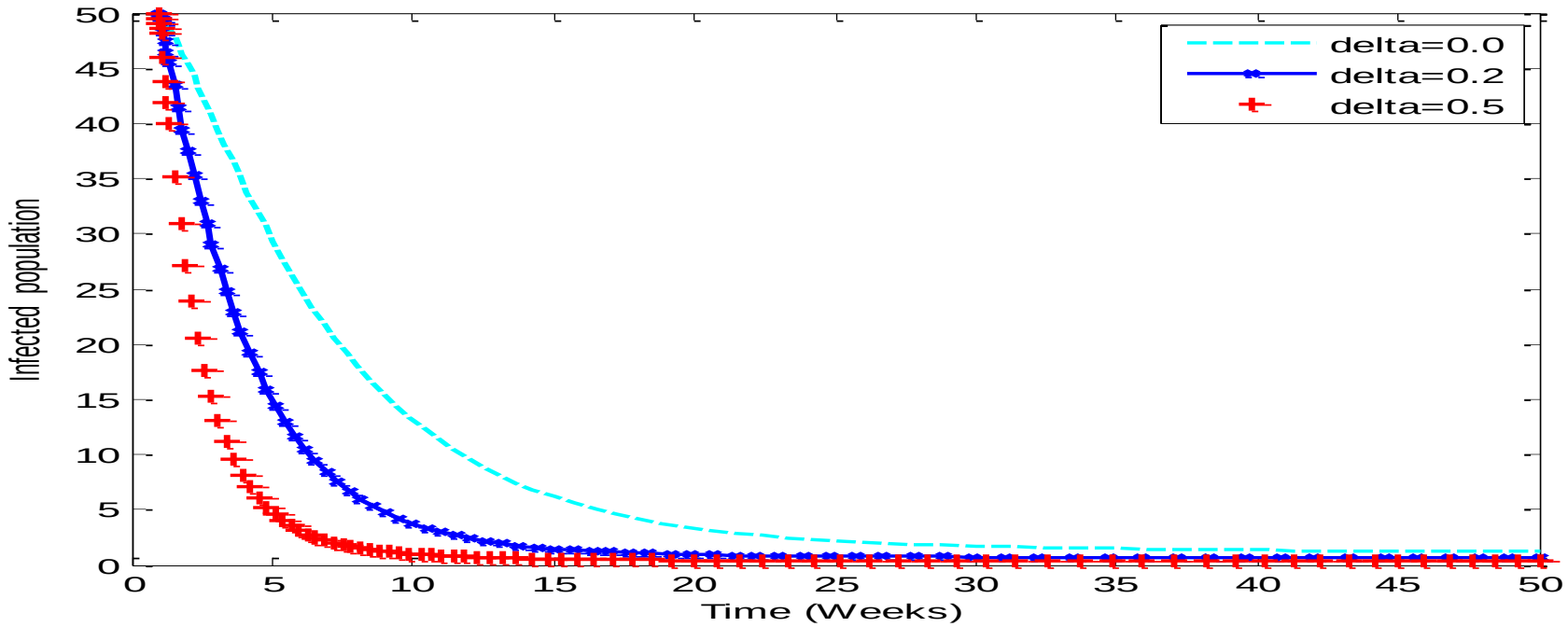


Figure 2. Simulation showing the effect of isolating the infected persons on infected population.

Numerical simulation cont'd

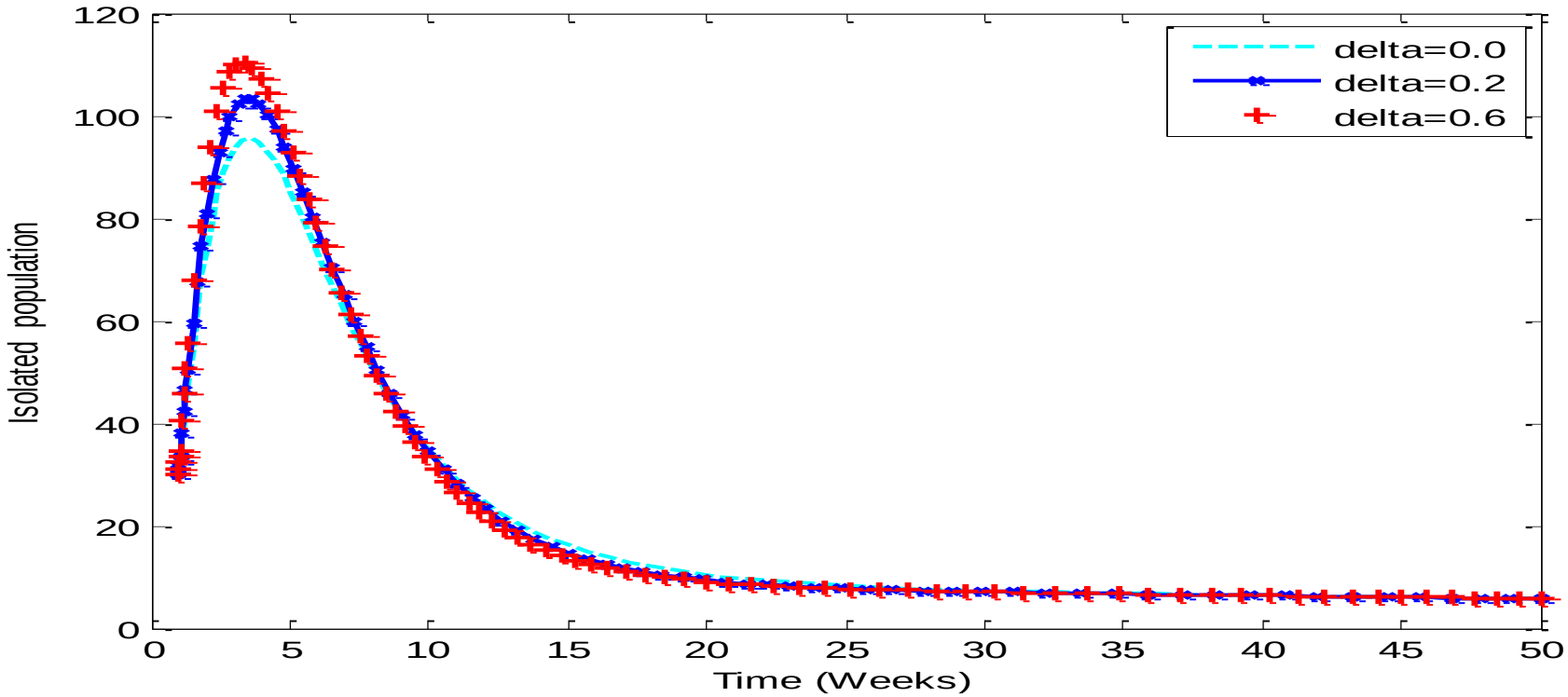


Figure 3. Simulation showing the effect of isolating the infected persons on isolation population.

Numerical simulation cont'd

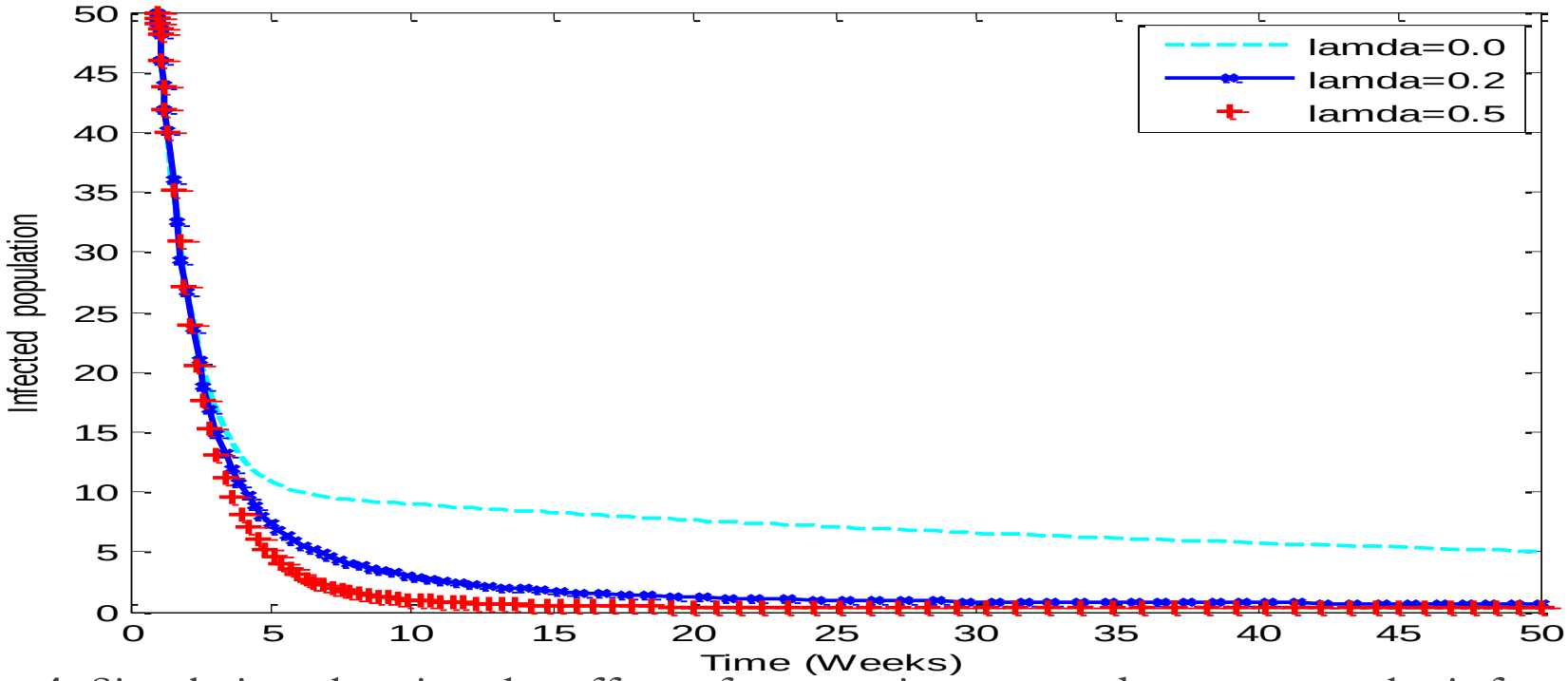


Figure 4. Simulation showing the effect of quarantine exposed persons on the infected population.

Numerical simulation cont'd

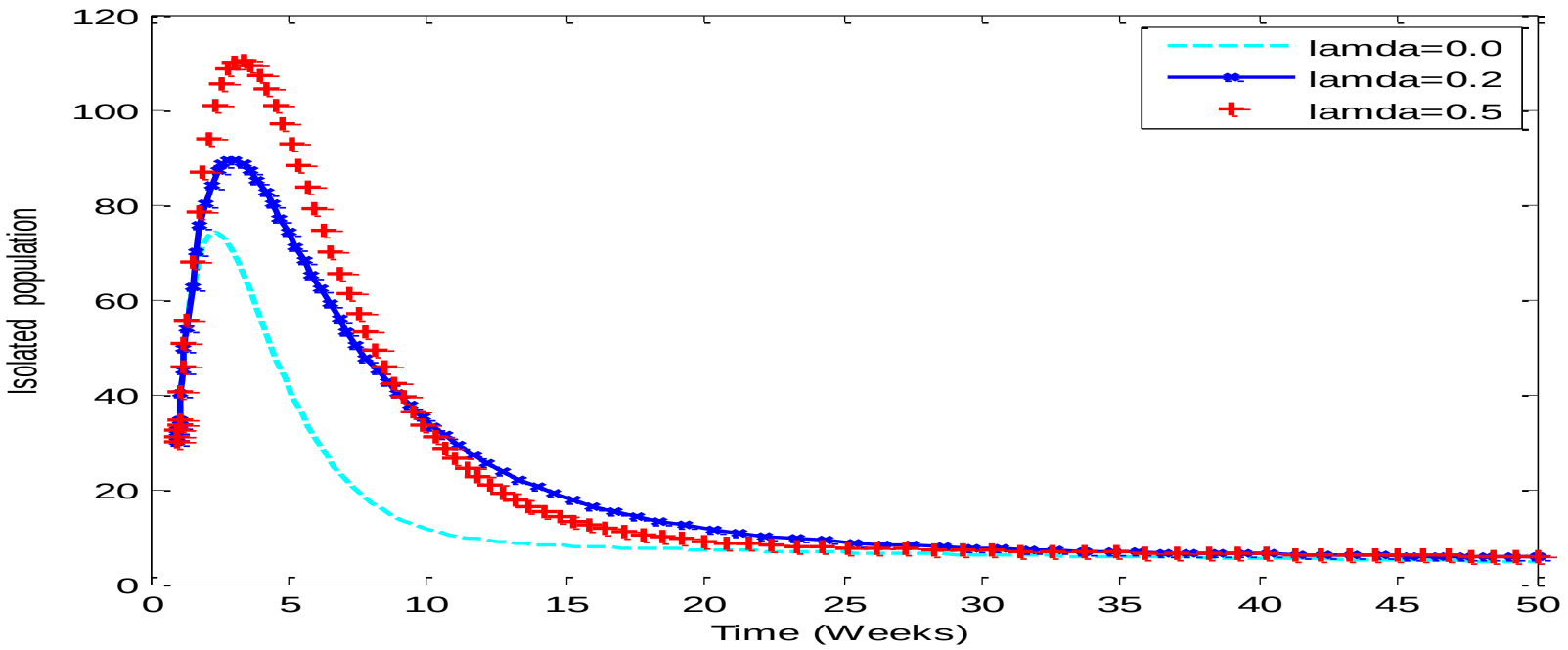


Figure 5. Simulation showing the effect of quarantine exposed persons on the isolation population.

Discussion and conclusion cont'd

- Our study is limited by some of the assumptions made to develop the model.

- We have assumed in the model that some individuals in the population were quarantined and isolated, which is considered reasonable in many cases [Cetron *et al (2004)* , Yan and Zou, (2008)], although this assumption can produce confounding effects in some circumstances.

Discussion and conclusion cont'd

- The results revealed that the use of quarantine and isolation as control interventions against Lassa fever have great impact in control/curtailing Lassa fever transmission and it may eventually leads to its elimination eventually.
- In other words, the use of quarantine and isolation may be a prohibitive drain on resources unless the number of cases is small.

References

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[2] Obabiyi, O. S. & Onifade, A. A. (2017). Mathematical Model for Lassa Fever Transmission Dynamics with Variable Human and Reservoir Population. International Journal of Differential Equations and Applications, 16(1): 67 – 91.

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[5] Driessche, P. V., and Watmough, J. (2002). Reproduction Numbers and Sub-Thresholds Endemic Equilibrium for Compartmental Models of Disease Transmission. Mathematical Bioscience, **180** (2002): 29 – 48.

Thank you