Mikailalsys Journal of Mathematics and Statistics

e-ISSN : 3030-816X
p-ISSN : 3030-8399

Index : Harvard, Boston, Sydney University, Dimensions, Lens, Scilit, Semantic, Google, etc

https://doi.org/10.58578/MJMS.v3i2.5205

Optimal Control Analysis of the Dynamical Spread of Malaria/Cholera Co-Infection

G. A. Adeniran[1], M. O. Alabi[2], I. A. Olopade[3], V. A. Akinrinmade[4]
[1,2]Chrisland University, Ogun State, Nigeria; [3]Federal University Wukari, Taraba State, Nigeria; [4]Osun State College of Technology, Osun State, Nigeria
gbadeniran@chrislanduniversity.edu.ng; moolaalabi@yahoo.com

Article Info:

Submitted:	Revised:	Accepted:	Published:
Feb 20, 2025	Mar 6, 2025	Mar 18, 2025	Mar 23, 2025

Abstract

In this paper, a fourteen (14) non-linear compartmental model is presented to study the transmission dynamics of Malaria/Cholera co-infection in a population at any point in time. The model is rigorously analyzed to gain insight into the dynamical features of Malaria/Cholera co-infection in order to know the effect of each control and which of the diseases should be treated before the other when all the controls are to be implemented. Optimal control analysis was carried out with different control strategies, Malaria Prevention (Mosquitoes treated bed net (u_1)), Malaria Treatment (u_2), Malaria-Cholera Prevention (u_3), Cholera Prevention (u_4), Cholera Treatment (u_5) and Boosting of Immune System (u_6) were introduced as the control strategy for the spread of Malaria-Cholera Co-infection and also, optimal control theory is applied to give an optimality system which we used to minimize the number of infected individuals and propose the most suitable control strategy for the spread of malaria/cholera co-infection. It is shown that the model has a diseases free equilibrium which is globally asymptotically stable (GAS). Also, there exists a unique endemic equilibrium point which is locally stable

MJMS Journal is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License

whenever the associated threshold is less than unity i.e $(R_o < 1)$ and become unstable whenever the associated threshold quantity exceeds unity i.e $(R_o > 1)$. It was also shown that there exists a solution for the optimality system. Numerical Simulation was performed using Differential Transformation Method (DTM). From the result, it was observed that the prevention control and treatment control strategies were more efficient in reducing the number of malaria/cholera infected individuals as compared to other control strategies.

Keywords: Malaria, Cholera, Reproduction Number, Optimal Control, Stability, Malaria/Cholera Co-infection

Introduction

One of the most dangerous infectious diseases is malaria, which is mostly brought on by plasmodium parasites. In 104 countries, about 3.3 billion people, or half of the world's population, are at risk of contracting malaria (Tumwiine *et al.*, 2014; WHO, 2013a). According to estimates, the infection affects between 300 and 500 million people of all ages each year and between 1.5 and 2.7 million of those people pass away from it (Mahalanabis *et al.*, 2008).

Malaria disease is spread widely across tropical and subtropical regions, which includes Africa, Despite being preventable and curable, malaria has long been an endemic disease in Nigeria. One major barrier to the management of malaria in Nigeria is treatment failure (Zuckerman *et al.*, 2007). (Zuckerman *et al.*, 2007) state that one of the main causes of malaria treatment failure in Nigeria is non-compliance with medication. Malaria treatment failures have been linked to parasite resistance or insufficient dosages (Yusuf *et al.*, 2005). Another significant obstacle to the control of malaria is drug resistance to antimalarials (Tumwiine *et al.*, 2014).

The disease remains one of the most deadly diseases across the globe, it is caused by infection with single-celled (Protozoans) parasite of genus *Plasmodium* which is characterized by Vomiting, fever, chills, pain and headache (WHO, 2013b).

Malaria can be cured and prevented within 48 hours; it causes total complication if not treated on time. This deadly disease can be prevented by the use of spraying with residual insecticides and treated bed nets particularly the malaria caused by the *Plasmodium falciparum*

is normally treated with Arteminisinin-based Combination Therapy (ACT) (Adewale et al, 2017a).

Cholera is an infectious disease that spreads quickly and causes severe vomiting, watery diarrhea, and leg pain. It is primarily transmitted through contaminated food or drinking water. As of 2010, there were an estimated 3-5 million cases of cholera worldwide and 100,000–130,000 deaths from the disease. The incubation period for cholera ranges from a few hours to five days (WHO, 2012).

In many developing nations, cholera, a deadly water-borne infectious disease caused by the vibrio cholera bacterium, becomes a major issue as a result of inadequate access to clean drinking water supplies, improper reservoir treatment, and inadequate sanitation. According to WHO data from 2012, there were 245, 393 cases of cholera worldwide in 48 countries, with 67% of those cases occurring in African nations (WHO, 2011).

The bacteria called *Vibrio cholerae* is a highly virulent cause of severe diarrheal infections of the small intestine. Those who are untreated suffer greatly from frequent, watery diarrhea and vomiting. It is transmitted by consuming food or water contaminated with the virus called *vibrio cholerae*. The individuals with this virus can quickly result in electrolyte imbalance and dehydration if not treated in time and can be fatal (Castillo-Chavez *et al.,* 2002; Chitnis *et al.,* 2006; Wurtz *et al.,* 2012).The spread of cholera is directly related to poor access to sanitary facilities and clean water. Peri-urban slums and camps for internally displaced people or refugees are examples of typical at-risk places where basic needs like clean water and sanitation are not being provided. Multiple interactions between the pathogen, the human host, and the environment are involved in the dynamics of cholera, and these interactions comprise both direct and indirect channels of transmission from the environment to humans (Wurtz *et al.,* 2012).

In the early part of 20th century, a virus that attacks bacterial cells and cause bacteria to be destroyed called Bacteriophage was applied as the prophylaxis and treatment of cholera disease before the use of antibiotics. In the recent time, much attention has been given on the use of bacteriophages as an alternative method for treating infections or as an antibiotic, because some specific phages can be used to control or attack specific bacteria which are likely to be resistance to them. However there has been controversy about the effectiveness of the bacteriophages in treating cholera disease (Politzer, 1995; Sarkar, 2002; Shaima *et al*., 2024; Sulyman *et al*., 2014).

Classical control strategy for the spread of cholera disease is attributed to improvement in food/personal hygiene, safer water treatment and sanitation system. Another means of cholera control is the giving of vaccine, but so far the effective vaccine to be used for the control is still under processed (Magambedze, *et al.*, 2011; Ochoche, 2013; Saymov, 1963; Seidlein, 2007).

However, some works have been done in order to investigate the transmission dynamics of Malaria with cholera co-infection. Tumwiine *et al.*, 2014, Developed and analyze a mathematical model for the control of cholera in Nigeria with modifications as compared to previous cholera models. In their model was incorporated treatment, water hygiene and environmental sanitation in curtailing the disease. The model studied shows that with proper combination of control measures the spread of cholera could be reduced. Numerical simulation of the full model using maple shows clearly that improvement in treatment, water hygiene and the environmental sanitation offered to about fifty percent is effective to eradicate cholera epidemic. Shaima *et al.*, 2024 developed a compartmental model for the transmission of the co-infection of cholera and malaria and was analyzed, a set of seven variables' controlling strategies, ranging from vector control to water sanitation and treatment, were added to the model; and their effect have been studied using the optimal control technique. Numerical simulations show the impact of these controlling strategies on the reduction of the new infections in humans and vectors as well as the reduction of the Cholera vibrio concentration in the environment. The numerical results show that the most cost-effective controlling strategy in reducing the number of new infection is the vector control strategy.

Mathematical model formulation

A non-linear mathematical model is formulated and analyzed to study the sensitivity of parameters involved in the basic reproduction number (R_0) on the dynamical spread of Malaria/Cholera Co-infection. In modeling the dynamics, the total homogeneously mixing population at time t, denoted by $N(t)$ is divided into compartments of susceptible individuals $S_h(t)$, exposed malaria individuals $E_M(t)$, infected malaria individuals $I_M(t)$, recovered malaria individuals $R_M(t)$, exposed malaria/cholera individuals $E_{MC}(t)$, infected malaria/cholera individuals $I_{MC}(t)$, recovered malaria/cholera individuals

$R_{MC}(t)$, exposed cholera individuals $E_C(t)$, infected cholera individuals $I_C(t)$, recovered cholera individuals $R_C(t)$. So that

$$N_h = S_h + E_M + I_M + R_M + E_{MC} + I_{MC} + R_{MC} + E_C + I_C + R_C. \qquad (2.1)$$

The total vector population denoted by N_V is sub-divided into susceptible mosquito $S_V(t)$, Exposed mosquito to malaria parasite $E_V(t)$, infected mosquito with malaria parasite $I_V(t)$. Thus

$$N_V = S_V + E_V + I_V \qquad (2.2)$$

The model is given by the following system of ordinary differential equations with the flow diagram given in fig 1.

$$\begin{aligned}
S_h^1 &= \pi_h - \lambda_M S_h - \lambda_C S_h - \lambda_{MC} S_h - \mu_h S_h + \phi R_M + \omega R_C + \psi R_{MC} \\
E_M^1 &= \varepsilon_1 \lambda_M S_h - (\kappa_M + \mu_h) E_M - \tau_1 E_M \\
I_M^1 &= (1-\varepsilon_1)\lambda_M S_h + \kappa_M E_M - (\tau_2 + r + \delta_M + \mu_h) I_M \\
R_M^1 &= \tau_1 E_M + \tau_2 I_M + r I_M - (\phi + \mu) R_M + \gamma(1-\rho)\theta I_{MC} \\
E_{MC}^1 &= \varepsilon_3 \lambda_{MC} S_h - (\kappa_{MC} + \mu_h + \delta_{MC}) E_{MC} \\
I_{MC}^1 &= (1-\varepsilon_3)\lambda_{MC} S_h + \kappa_{MC} E_{MC} - (\tau_4 + \mu_h + \delta_{MC} + \theta) I_{MC} \\
R_{MC}^1 &= \theta\rho I_{MC} + \tau_4 I_{MC} - (\psi + \mu_h) R_{MC} \\
E_C^1 &= \varepsilon_2 \lambda_C S_h - (\kappa_C + \mu) E_C \\
I_C^1 &= (1-\varepsilon_2)\lambda_C S_h + \kappa_C E_C - (\tau_3 + \mu_h + \delta_C) I_C \\
R_C^1 &= \tau_3 I_C - (\omega + \mu_h) R_C + (1-\gamma)(1-\rho)\theta I_{MC} \\
B_C^1 &= g B_C + \alpha(I_C + \eta_5 I_{MC}) - \mu_b B_C \\
S_V^1 &= \pi_V - \lambda_V S_V - \mu_V S_V \\
E_V^1 &= \lambda_V S_V - (\sigma_V + \mu_V) E_V \\
I_V^1 &= \sigma_V E_V - \mu_V I_V
\end{aligned} \qquad (2.3)$$

The Susceptible Population is increased by the recruitment of individuals (either by birth or immigration) into the population at the rate π_h. The Population decreases by natural death rate μ_h and both singly and dually-infected transmission individuals which later increase by both singly and dually-recovered individuals due to loss of immunity at the rates ϕ, ω and ψ. Both singly and dually-infected individuals transmit either malaria or cholera infection

as follows (note that we split the disease transmission process into those generated by singly-infected and dually-infected individuals to make the formulation easier to follow).

Susceptible individuals acquire Malaria infection following effective contact with malaria infected mosquitoes (via their bites) which is actually the I_V class the at the rate λ_M given by

$$\lambda_M = \frac{\beta_M a I_V}{N_V} \tag{2.4}$$

Where β_M is the probability of transmission from mosquito to human, provided that there is a contact between the mosquito and the human. "a" is the number of mosquito bites that one person has per unit time.

$$\lambda_v = \frac{\beta_V (E_M + \eta_1 I_M)}{N_h} \tag{2.5}$$

Where β_v are the effective contact rates of Malaria from vector to human and from human to vector.

Similarly, Susceptible individuals acquire Cholera infection from individuals with Cholera only i.e (E_C, $\eta_2 I_C$ and $\eta_3 B_C$) Classes at a rate λ_C given by

$$\lambda_C = \frac{\beta_C (E_C + \eta_2 I_C + \eta_3 B_C)}{N_h} \tag{2.6}$$

Where β_c the effective contact is rate of Cholera, η_2 and η_3 are the modification parameters.

Dually-infected individuals are assumed capable of transmitting either Malaria or Cholera, but not the mixed infection, then the transmission rate is Assumed to be

$$\lambda_{MC} = \frac{\beta_{MC} (E_{MC} + \eta_4 I_{MC})}{N_h} \tag{2.7}$$

Where β_{mC} is the effective Contact rate of Malaria-Cholera.

Then,

$$\frac{dS_h}{dt} = \pi_h - \lambda_m S_h - \lambda_C S_h - \lambda_{mc} S_h - \mu_h S_h + \phi R_m + \omega R_C + \psi R_{mC} \quad (2.8)$$

A fraction ε_1 of the newly infected individuals with high immunity are assumed to show no disease symptoms initially. These individuals are moved to the exposed class. The remaining fraction (1-ε_1) of the newly infected individuals with very low immunity are assumed to displayed disease symptoms and are moved to Malaria infected class (I_m). The population of exposed class is decreased by the progression exposed malaria individual to infected malaria at the rate (κ_m) and also reduced by natural death rate (μ_h) and finally decreased by the treatment of exposed malaria individuals at the rate (τ_1). Thus,

$$\frac{dE_M}{dt} = \varepsilon_1 \lambda_M S_h - (\kappa_M + \mu_h) E_M - \tau_1 E_M \quad (2.9)$$

The population of infected malaria individuals is increased by the infection due to low immunity at the rate ((1-ε_1)λ_M) and the progression of exposed malaria individuals at the rate (κ_M). The population is decreased by the treatment of infected malaria individuals at the rate (τ_2), the recovered malaria individuals at the rate (r), the disease induced death at the rate (δ_M) and the natural death of malaria at the rate (μ_h). Thus,

$$\frac{dI_M}{dt} = (1-\varepsilon_1)\lambda_M S_h + \kappa_M E_M - (\tau_2 + r + \delta_M + \mu_h) I_M \quad (2.10)$$

The population of Recovered malaria individuals is increased by the treatment of exposed malaria individuals at the rate (τ_1), the treatment of infected malaria individuals at the rate (τ_2) and the recovery rate of infected malaria individuals by (r). This population is decreased by loss of immunity of an individuals at the rate (ϕ) and the natural death rate μ_h. This population is further increased by the fraction of an individuals who recovered of malaria only at the rate $\gamma(1-\rho)\theta$. Thus,

$$\frac{dR_M}{dt} = \tau_1 E_M + \tau_2 I_M + r I_M - (\phi + \mu_h) R_M + \gamma(1-\rho)\theta I_{MC} \quad (2.11)$$

The population of Malaria infected Cholera is increased by infection which can be acquired by following effective contact rate with infectious individuals in the dually

Exposed Malaria -Cholera (E_{MC}) and dually Infected Malaria – Cholera ($\eta_4 I_{MC}$) categories at a rate

$$\lambda_{MC} = \frac{\beta_{MC}(E_{MC} + \eta_4 I_{MC})}{N_h} \tag{2.12}$$

Where λ_{MC} represents the force of infection for Malaria-Cholera co-infection.

The population of dually Exposed Malaria – Cholera is increased by the fraction ε_3 of newly infected individuals high immunity are moved to the dually Exposed Malaria – Cholera Population. The remaining fraction (1-ε_3) of the newly infected individuals are assumed to displayed disease symptoms with low immunity and are moved to dually Infected Malaria- Cholera (I_{MC}) population. The population of dually Exposed Malaria – Cholera is decreased by the progression of dually Exposed Malaria – Cholera at the rate (κ_{MC}), the natural death rate (μ_h) and the induced death rate of dually Exposed Malaria – Cholera (δ_{MC}). Thus,

$$\frac{dE_{MC}}{dt} = \varepsilon_3 \lambda_{MC} S_h - (\kappa_{MC} + \mu_h + \delta_{MC})\, E_{MC} \tag{2.13}$$

The population of dually Infected Malaria -cholera is increased by the infection due low immunity of an individual at the rate ((1-ε_3)λ_{MC}) and the progression of dually Exposed Malaria-cholera individuals at the rate (κ_{MC}).

The population is decreased by the treatment of dually Infected Malaria – Cholera individuals at the rate (τ_4), the natural death rate (μ_h), dually Infected Malaria-Cholera Induced death rate (δ_{MC}) and the fraction of an individuals who recovered fully from both diseases at the rate (θ). Thus,

$$\frac{dI_{MC}}{dt} = (1-\varepsilon_{\backslash 3})\lambda_{MC} S_h + \kappa_{MC} E_{MC} - (\tau_4 + \mu_h + \delta_{MC} + \theta) I_{MC} \tag{2.14}$$

The population of dually Recovered Malaria - Cholera is increased by individual who recovered from both diseases at the rate ($\theta\rho$) and the treatment of dually Infected Malaria-Cholera individuals at the rate (τ_4). The population is decreased by loss of immunity of an individuals at the rate (ψ) and the natural death rate (μ_h). Thus,

$$\frac{dR_{MC}}{dt} = \theta\rho I_{MC} + \tau_4 I_{MC} - (\psi + \mu_h)\,\mathrm{R}_{MC} \tag{2.15}$$

A fraction ε_2 of the newly infected individuals are due to high immunity of an individual are assumed to show no disease symptoms initially. These individuals are moved to the exposed Cholera population. The remaining fraction $(1-\varepsilon_2)$ of the newly infected individuals are assumed to displayed disease symptoms due to their low immunity are moved to the infected population. The population of exposed Cholera individuals is decreased by the progression of exposed Cholera individuals to the infected Cholera at the rate (κ_C) and also reduced by natural death rate (μ_h).

Thus,

$$\frac{dE_C}{dt} = \varepsilon_2\lambda_C S_h - (\kappa_C + \mu_h)E_C \tag{2.16}$$

The population of Infected Cholera individuals is increased by the infection of an individual with low immunity at the rate $((1-\varepsilon_2)\lambda_c)$ and the progression of exposed cholera individuals at the rate (k_C). The population is decreased by the treatment of infected cholera individuals at the rate (τ_3), the natural death rate (μ_h) and the cholera induced death rate (δ_c). Thus,

$$\frac{dI_C}{dt} = (1-\varepsilon_2)\lambda_C S_h + \kappa_C E_C - (\tau_3 + \mu_h + \delta_C)I_C \tag{2.17}$$

The population of Recovered Cholera individuals is increased by the treatment of infected Cholera individuals at the rate (τ_3). The population is decreased by loss of immunity of an individuals after recovery at the rate (ω) and the natural death rate (μ_h). The population later increased by the fraction of an individuals that recovered from Cholera only at the rate $(1-\gamma)(1-\rho)\theta$. Thus,

$$\frac{dR_C}{dt} = \tau_3 I_C - (\omega + \mu_h)R_C + (1-\gamma)(1-\rho)\theta I_{MC} \tag{2.18}$$

The population of the Cholera bacteria is increased by the growth rate of the bacteria (g), α is the average contribution of each Cholera infected individuals to the aquatic population. The bacteria population is decreased by bacteria mortality rate (μ_b). Thus,

$$\frac{dB_C}{dt} = gB_C + \alpha(I_C + \eta_5 I_{MC}) - \mu_b B_C \quad (2.19)$$

Also, the Population Size $N_V(t)$ of Vectors (Mosquitoes) is sub-divided into Susceptible Mosquitoes $S_V(t)$, Exposed Mosquitoes $E_V(t)$ and Infectious Mosquitoes $I_V(t)$. So that,

$$N_V(t) = S_V(t) + E_V(t) + I_V(t) \quad (2.20)$$

Susceptible mosquitoes (S_V) are generated at a constant rate π_V (recruitment rate) and acquire Malaria infection following effective contact with human infected with Malaria (at a rate λ_v). Where the force of infection is given by

$$\lambda_V = \frac{\beta_V b(E_m + \eta_1 I_m)}{N_h} \quad (2.21)$$

Where β_V is the transmission probability of infection from human to mosquito, b is the number of human bites one mosquito has per unit time, N_h is the total human population, η_1 is the modification parameter comparing the transmissibility of infectious individuals in relationship to exposed individual. Newly infected mosquitoes move to exposed class and they are assumed to suffer natural death rate (μ_V). Thus,

$$\frac{dS_V}{dt} = \pi_V - \lambda_V S_V - \mu_V S_V \quad (2.22)$$

The exposed mosquito consists of newly infected mosquitoes and their population decreased by progressing to infectious class at the rate (σ_V) and the natural death rate (μ_V). Thus,

$$\frac{dE_V}{dt} = \lambda_V S_V - (\sigma_V + \mu_V) E_V \quad (2.23)$$

The infectious mosquito has those that progress from exposed class and decrease by natural death rate (μ_v). Thus,

$$\frac{dI_V}{dt} = \sigma_V E_V - \mu_V I_V \quad (2.24)$$

Positivity of Solutions

Lemma: The closed Set

$D_1 = \{(S_h, E_M, I_M, R_M, E_{MC}, I_{MC}, R_{MC}, E_C, I_C, R_C) \in R_+^{10} : N \le \frac{\pi_h}{\mu_h}\}$ and

$D_2 = \{(S_V, E_V, I_V) \in R_+^3 : N \le \frac{\pi_V}{\mu_V}\}$ are positively-invariant and attracting with respect to model (2.3).

Proof: Consider the biologically-feasible region D_1 and D_2, we shall show that D_1 and D_2 are positive invariance (i.e all solutions remain in D_1 and D_2 for all time t>0). The rate of change of the total population obtained by adding all the equations in the model above is given by

$$\frac{dN}{dt} = \pi_h - \mu_h N - \delta_M I_M - \delta_{MC} I_{MC} - \delta_C I_C \qquad (2.25)$$

And

$$\frac{dN}{dt} = \pi_V - \mu_V N - \delta_V I_V \qquad (2.26)$$

Therefore $\frac{dN}{dt} < 0$, whenever the subtotal population $N > \frac{\pi_h}{\mu_h}$ and $N > \frac{\pi_V}{\mu_V}$. Note that $\frac{dN}{dt}$ is bounded by $\pi - \mu N$ and a standard comparison theorem can be used to show that $N(t) \le N(0)e^{-\mu t} + \frac{\pi}{\mu_h}(1 - e^{-\mu t})$. In particular, $N(t) \le \frac{\pi}{\mu_h}$ if $N(0) \le \frac{\pi}{\mu_h}$. Therefore, all solutions of the model with initial conditions in D_1 and D_2 are positively-invariant and attracting. In this region model can be considered as been epidemiologically and mathematically well-posed.

Analysis of Sub-Model: Before the full model it is of important to gain insight into dynamics of the models of Malaria only model and cholera only model.

Malaria Only Model: The model is given by

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \pi_h - \lambda_m S_h - \mu_h S_h + \phi R_m \\
\frac{dE_m}{dt} &= \varepsilon_1 \lambda_m S_h - (\kappa_M + \mu_h) E_m - \tau_1 E_m \\
\frac{dI_m}{dt} &= (1-\varepsilon_1)\lambda_m S_h + \tau_1 E_m + \kappa_M I_m - (\tau_2 + r + \delta_M + \mu_h) I_m \\
\frac{dR_m}{dt} &= \tau_1 E_m + \tau_2 I_m + r I_m - (\phi + \mu_h) R_m \\
\frac{dS_V}{dt} &= \pi_V - \lambda_V S_V - \mu_V S_V \\
\frac{dE_V}{dt} &= \lambda_V S_V - (\sigma_V + \mu_V) E_V \\
\frac{dI_V}{dt} &= \sigma_V E_V - \mu_V I_V
\end{aligned}\right\} \quad (2.27)$$

Where

$$\lambda_m = \frac{\beta_M a I_V}{N_V} \quad (2.28)$$

And

$$\lambda_V = \frac{\beta_V b(E_m + \eta_1 I_m)}{N_m} \quad (2.29)$$

For this model, it can be shown that the region

$$D_3 = \{(S_h + E_m + I_m + R_m) \in R_+^4 : N \le \frac{\pi_h}{\mu_h}\} \text{ and } D_4 = \{(S_V + E_V + I_V) \in R_+^3 : N \le \frac{\pi_V}{\mu_V}\}$$

Stability of the Disease Free Equilibrium (DFE)

Disease free equilibrium

For critical points, we set

$$\frac{dS_h}{dt} = \frac{dE_m}{dt} = \frac{dI_m}{dt} = \frac{dR_m}{dt} = 0$$

$$\frac{dS_h}{dt} = \frac{dE_m}{dt} = \frac{dI_m}{dt} = \frac{dR_m}{dt} = 0 \text{ and } \frac{dS_V}{dt} = \frac{dE_V}{dt} = \frac{dI_V}{dt} = 0$$

At this point we assume there is no infection,

So $E_m = 0, I_m = 0, R_m = 0, E_V = 0, I_V = 0$

$\lambda_m = 0$ and $\lambda_V = 0$

Therefore,

$$E_O = \{S_h, .E_m, I_m, R_m, S_V, E_V, I_V\} = \{\frac{\pi_h}{\mu_h}, 0.0.0, \frac{\pi_V}{\mu_V}, 0, 0\}$$

(2.30)

Derivation of Basic Reproduction Number (R_0) For Malaria Model Only

The basic reproduction number of the model (2.27) R_M is calculated by using next generation matrix (Adeniran *et al.*, 2022; Adewale *et al*, 2017a; 2017b; 2016; 2015; 2017c; Adesola *et al*, 2024a; 2024b; Ajao *et al*, 2023; Akinwumi *et al*, 2021), we have,

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & \frac{\varepsilon_1 \beta_M a \pi_h \mu_V}{\pi_V \mu_h} \\ 0 & 0 & 0 & 0 & \frac{(1-\varepsilon_1)\beta_M a \pi_h \mu_V}{\pi_V \mu_h} \\ 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_V b \mu_V \mu_h}{\pi_h \mu_V} & \frac{\beta_V b \pi_V \mu_h \eta_1}{\pi_h \mu_V} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} k_1 & 0 & 0 & 0 & 0 \\ -\kappa_M & k_2 & 0 & 0 & 0 \\ -\tau_1 & k_3 & k_4 & 0 & 0 \\ 0 & 0 & 0 & k_5 & 0 \\ 0 & 0 & 0 & -\delta_V & \mu_V \end{pmatrix}$$

The reproduction number is the dominant eigen values of $F \times V^{-1}$. Thus,

$$R_M = \frac{\sqrt{\mu_V k_1 k_2 k_5 \beta_V b \beta_M a \sigma_V (\kappa_m \eta_1 \varepsilon_1 - \eta_1 k_1 \varepsilon_1 + \eta_1 k_1 + k_2 \varepsilon_1)}}{\mu_V k_1 k_2 k_5}$$

(2.31)

Where $k_1 = \kappa_M + \mu_h + \tau_1$, $k_2 = \tau_2 + r + \delta_M + \mu_h$ and $k_5 = \sigma_V + \mu_V$

Local Stability of Disease Free Equilibrium for Malaria Model Only

Theorem 1: The disease free equilibrium of malaria model is locally asymptotically stable (LAS) if $R_M < 1$ and unstable if $R_M > 1$.

Proof: Thus, the theorem implies the disease can be eliminated from the community. Now to determine the local stability of E_O, the following Jacobian matrix is computed corresponding to equilibrium point E_O. Considering the stability of the disease free equilibrium at the critical point (0, 0, 0, 0, 0, 0, 0). Equation (2.27), we have

$$J_M = \begin{pmatrix} -\mu_h & 0 & 0 & \phi & 0 & 0 & 0 \\ 0 & -(\kappa_M + \mu_h + \tau_1) & 0 & 0 & 0 & 0 & 0 \\ 0 & \kappa_M & -(\tau_2 + r + \delta_M + \mu_h) & 0 & 0 & 0 & 0 \\ 0 & \tau_1 & (\tau_2 + r) & -(\phi + \mu_h) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\mu_V & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -(\sigma_V + \mu_V) & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma_V & -\mu_V \end{pmatrix} \quad (2.32)$$

Hence $|J - \lambda I| = 0$ implies that

$$\begin{pmatrix} -\mu_h - \lambda_1 & 0 & 0 & \phi & 0 & 0 & 0 \\ 0 & -C_2 - \lambda_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & \kappa_M & -C_3 - \lambda_3 & 0 & 0 & 0 & 0 \\ 0 & \tau_1 & C_4 & -C_5 - \lambda_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -C_6 - \lambda_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -C_7 - \lambda_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma_V & -C_8 - \lambda_7 \end{pmatrix} = 0 \quad (2.33)$$

From (3.4.2) clearly,

$\lambda_1 = -\mu_h,\ \lambda_2 = -C_2,\ \lambda_3 = -C_3,\ \lambda_4 = -C_5,\ \lambda_5 = -C_6,\ \lambda_6 = -C_7,\ \lambda_7 = -C_8$

Where, $C_1 = \mu_h,\ C_2 = \kappa_M + \mu_h + \tau_1,\ C_3 = \tau_2 + r + \delta_M + \mu_h,\ C_4 = \tau_2 + r,\ C_5 = \phi + \mu_h,$ $C_6 = \mu_V,\ C_7 = \sigma_V + \mu_V$ and $C_8 = \mu_V$. Since all the roots are real, negative and distinct, hence the disease free equilibrium points of Malaria only model is Locally Asymptotically Stable (LAS).

Global Stability of Disease Free Equilibrium (Malaria)

Here, the global asymptotic stability (GAS) property of the DFE of the MALARIA model will be explored.

Theorem 2: The disease free-equilibrium of malaria modelis globally asymptotically stable whenever $R_M < 1$ and unstable if $R_M > 1$.

Proof: It follows that $S = N^* - E_m - I_m - E_V - I_V$ at steady state. The proof is based on using comparism theorem (Castillo-Chavez, 2002) to prove the global stability. The rate of change of the variables representing the infected component of the system can be written as follows.

$$\begin{aligned}
\frac{dE_m}{dt} &= \varepsilon_1\lambda_m(N^* - E_m - I_m - E_V - I_V) - k_1E_m \\
\frac{dI_m}{dt} &= (1-\varepsilon_1)\lambda_m(N^* - E_m - I_m - E_V - I_V) + \kappa_M - k_2I_m \\
\frac{dE_V}{dt} &= \lambda_V S_V - k_5E_V \\
\frac{dI_V}{dt} &= \sigma_V E_V - \mu_V I_V
\end{aligned} \tag{2.34}$$

$$D^* = \{(E_m, I_{m,}, E_V, I_V) \in R_+^4 : E_m + I_{m,} + E_V + I_V \le N^*\}$$

For the model (2.27), the associated reproduction number, R_M where

$$R_M = \frac{\sqrt{\mu_V k_1 k_2 k_5 \beta_V b \beta_m a \sigma_V (\kappa_M \eta_1 \varepsilon_1 - \eta_1 k_1 \varepsilon_1 + \eta_1 k_1 + k_2 \varepsilon_1)}}{\mu_V k_1 k_2 k_5}.$$

The DFE of the malaria model given by disease free is globally asymptotically stable in D^* if $R_M < 1$.Using comparism method, we have

$$\begin{pmatrix} \frac{dE_m}{dt} \\ \frac{dI_m}{dt} \\ \frac{dE_V}{dt} \\ \frac{dI_V}{dt} \end{pmatrix} = (F - V)\begin{pmatrix} E_m \\ I_m \\ E_V \\ I_V \end{pmatrix} - F_i\begin{pmatrix} E_m \\ I_m \\ E_V \\ I_V \end{pmatrix}$$

According to (Adesola *et al.*, 2024b), all eigen values of the matrix (F-V) have negatives real parts.

$$\begin{pmatrix} -k_1-\lambda & 0 & 0 & \frac{\varepsilon_1\beta_m a\pi_h\mu_V}{\pi_V\mu_h} \\ \kappa_M & -k_2-\lambda & 0 & \frac{(1-\varepsilon_1)\beta_m a\pi_h\mu_V}{\pi_V\mu_h} \\ \frac{\beta_V b\pi_V\mu_h}{\pi_h\mu_V} & \frac{\beta_V b\eta_1\pi_V\mu_h}{\pi_h\mu_V} & -k_3-\lambda & 0 \\ 0 & 0 & \sigma_V & -\mu_V-\lambda \end{pmatrix} = 0 \qquad (2.35)$$

From equation (2.33), the characteristic equation is given by

$$\lambda^4+(\mu_V+k_3+k_2+k_1)\lambda^3+(k_1k_2+k_1k_3+k_1\mu_V+k_2k_3+k_2\mu_V+k_3\mu_V)\lambda^2+(ab\eta_1\varepsilon_1\beta_M\beta_V\sigma_V - ab\eta_1\beta_M\beta_V\sigma_V-ab\varepsilon_1\beta_M\beta_V\sigma_V+k_1k_2\mu_V+k_1k_3\mu_V+k_2k_3\mu_V+k_3k_2k_1)\lambda-\sigma_V ab\beta_M\beta_V\kappa_M\eta_1\varepsilon_1 + \sigma_V ab\beta_M\beta_V\eta_1\varepsilon_1k_1-\sigma_V ab\beta_M\beta_V\eta_1k_1-\sigma_V ab\beta_M\beta_V\kappa_2\varepsilon_1+\mu_V k_3k_2k_1$$

We let $\lambda^3=a_4$, $\lambda^2=a_3$, $\lambda=a_2$ and constant by a_1.

Applying Routh-Hurwitz criteria of order 4; Where $n=4$

$$a_4=\mu_V+k_3+k_2+k_1$$

$$a_3=k_1k_2+k_1k_3+k_1\mu_V+k_2k_3+k_2\mu_V+k_3\mu_V$$

$$a_2=ab\eta_1\varepsilon_1\beta_M\beta_V\sigma_V-ab\eta_1\beta_M\beta_V\sigma_V-ab\varepsilon_1\beta_M\beta_V\sigma_V+k_1k_2\mu_V+k_1k_3\mu_V+k_2k_5\mu_V+k_3k_2k_1$$

$$a_1=-\sigma_V ab\beta_M\beta_V\kappa_M\eta_1\varepsilon_1+\sigma_V ab\beta_M\beta_V\eta_1\varepsilon_1k_1-\sigma_V ab\beta_M\beta_V\eta_1k_1-\sigma_V ab\beta_M\beta_V\kappa_2\varepsilon_1+\mu_V k_3k_2k_1$$

$$n=4: a_1>0, a_2>0, a_3>0, a_4>0$$

Then for $a_1>0$ we have

$$-\sigma_V ab\beta_M\beta_V\kappa_M\eta_1\varepsilon_1+\sigma_V ab\beta_M\beta_V\eta_1\varepsilon_1k_1-\sigma_V ab\beta_M\beta_V\eta_1k_1-\sigma_V ab\beta_M\beta_V\kappa_2\varepsilon_1+\mu_V k_3k_2k_1>0$$

Implying that $R_M<1$. According to (Castillo-Chavez, 2002; Driessche, and Watmough, 2002), all eigen values of the matrix F-V have negative real parts. It follows that the linearized differential inequality above is stable whenever $R_M<1$. Consequently $S=(E_m=I_m=E_V=I_V=0)\to(0,0,0,0)$ as time $t\to\infty$. Substituting $E_m=I_m=E_V=I_V=0$ in (R_M) gives $S(t)\to S(0)$ as $t\to\infty$. Hence, we have established

that the disease free equilibrium is globally asymptotically stable whenever $R_M < 1$ and unstable $R_M > 1$.

Cholera Only Model: The cholera model is given by

$$\begin{aligned}
\frac{dS_h}{dt} &= \pi_h - \lambda_c S_h - \mu_h S_h + \omega R_c \\
\frac{dE_c}{dt} &= \varepsilon_2 \lambda_c S_h - (\kappa_C + \mu_h) E_c \\
\frac{dI_c}{dt} &= (1-\varepsilon_2)\lambda_c S_h - (\tau_3 + \mu_h + \delta_c) I_c + \kappa_c E \\
\frac{dR_c}{dt} &= \tau_3 I_c - (\omega + \mu_h) R_c \\
\frac{dB_c}{dt} &= g B_c + \alpha I_c - \mu_b B_c
\end{aligned} \tag{2.36}$$

$$\lambda_C = \frac{\beta_C (E_C + \eta_2 I_C + \eta_3 B_C)}{N} \tag{2.37}$$

For this model, it can be shown that the region

$$D_2 = \{(S_h, +E_C + I_C + R_C + B_C) \in R_+^5 : N \le \frac{\pi_h}{\mu_h}\} \tag{2.38}$$

Stability of the Disease Free Equilibrium (DFE)

Disease Free Equilibrium (DFE)

For critical points, we set

$$\frac{dS_h}{dt} = \frac{dE_C}{dt} = \frac{dI_C}{dt} = \frac{dR_C}{dt} = \frac{dB_C}{dt} = 0$$

At disease free equilibrium, it is assumed that there is no infection, then we set $\lambda_C = 0$

So, $S_h = E_C = I_C = R_C = B_C = 0$

Disease free equilibrium of cholera model is given by

$$E_O = (S_h, E_C, I_C, R_C, B_C) = (\frac{\pi_h}{\mu_h}, 0, 0, 0, 0)$$

Derivation of Basic Reproduction Number (R_0) for Cholera Model

The Next Generation Matrix ($F.V^{-1}$) Method

The basic reproduction number of the model (2.36) R_0 is calculated by using next generation matrix (Akinwumi, *et al.,* 2021; Olopade *et al.,* 2017, 2021a, 2021b) Using their approach, we have

$$F_i = \begin{pmatrix} F_1 \\ F_2 \\ F_3 \\ F_4 \end{pmatrix} = \begin{pmatrix} \varepsilon_2 \lambda_C S_h \\ (1-\varepsilon_2)\lambda_C S_h \\ 0 \\ 0 \end{pmatrix}$$

$$V_i = \begin{pmatrix} V_1 \\ V_2 \\ V_3 \\ V_4 \end{pmatrix} = \begin{pmatrix} (\kappa_C + \mu_h)E_C \\ -\kappa_C E_C + (\tau_3 + \mu_h + \delta_C)I_C \\ -\tau_3 I_C + (\omega + \mu_h)R_C \\ -\alpha I_C - (g - \mu_b)B_C \end{pmatrix}$$

$$F = \begin{pmatrix} \varepsilon_2\beta_C & \varepsilon_2\eta_2\beta_C & 0 & \varepsilon_2\eta_3\beta_C \\ (1-\varepsilon_2)\beta_C & (1-\varepsilon_2)\eta_2\beta_C & 0 & (1-\varepsilon_2)\eta_3\beta_C \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} k_1 & 0 & 0 & 0 \\ -\kappa_C & k_2 & 0 & 0 \\ 0 & -\tau_3 & k_3 & 0 \\ 0 & -\alpha & 0 & k_4 \end{pmatrix}$$

The reproduction number is the dominant eigen values of $F.V^{-1}$.Thus,

$$R_{0C} = \frac{\beta_C(\alpha\eta_3 k_1\varepsilon_2 - \alpha\eta_3\varepsilon_2\kappa_C - \eta_2 k_1 k_4\varepsilon_2 + \eta_2\varepsilon_2 k_4\kappa_C - \alpha\eta_3 k_1 + \eta_2 k_1 k_4 + k_2 k_4\varepsilon_2)}{k_1 k_2 k_4}$$

(2.39)

Where $k_1 = \kappa_C + \mu_h, k_2 = \kappa_C + \mu_h,\ k_3 = \tau_3 + \mu_h + \delta_C$ and $k_4 = g - \mu_b$

Local Stability of Disease Free Equilibrium (DFE) of Cholera Model

Theorem 3: The disease free equilibrium of the system (2.36) is locally asymptotically stable (LAS) if $R_{0C} < 1$ and unstable if $R_{0C} > 1$.

Proof: To determine the local stability of E_O, the following Jacobian matrix is computed corresponding to the equilibrium point E_O. Considering the stability of the disease free equilibrium at the critical point (0, 0, 0, 0, 0). We have

$$J_C = \begin{pmatrix} -\mu_h & 0 & 0 & \omega & 0 \\ 0 & -k_1 & 0 & 0 & 0 \\ 0 & \kappa_C & -k_2 & 0 & 0 \\ 0 & \tau & \tau_3 & -k_3 & 0 \\ 0 & 0 & \alpha & 0 & -k_4 \end{pmatrix} \tag{2.4}$$

Hence $|J_C - \lambda I| = 0$ implies that

$$\begin{pmatrix} -\mu_h - \lambda_1 & 0 & 0 & \omega & 0 \\ 0 & -k_1 - \lambda_2 & 0 & 0 & 0 \\ 0 & \kappa_C & -k_2 - \lambda_3 & 0 & 0 \\ 0 & \tau & \tau_3 & -k_3 - \lambda_4 & 0 \\ 0 & 0 & \alpha & 0 & -k_4 - \lambda_5 \end{pmatrix} \tag{2.41}$$

From equation (3.9.2) clearly, $\lambda_1 = -\mu, \lambda_2 = -k_1,\ \lambda_3 = -k_2,\ \lambda_4 = -k_3,\ \lambda_5 = -k_5$

Hence, the corresponding eigen values of equation (3.9.2) are;

$$\lambda_1 = -\mu_h,\ \lambda_2 = -(\tau + \kappa_C + \mu_h),\ \lambda_3 = -(\tau_3 + \mu_h),\ \lambda_4 = -(\omega + \mu_h),\ \lambda_5 = -(g - \mu_b)$$

Since all the real roots are negative, real and distinct, hence the disease free equilibrium of (2.36) is locally asymptotically stable (LAS)

Global Stability of Disease Free Equilibrium (Cholera)

Here, the global asymptotic stability (GAS) property of the DFE of the Cholera model only will be explored.

Theorem 4: The disease free-equilibrium of the system (2.36) is globally asymptotically stable whenever $R_{OC} < 1$ and unstable if $R_{OC} > 1$.

Proof: It follows that $S = N^* - E_C - I_C - B_C$ at steady state. The proof is based on using the comparism theorem (Lakshmkanthan, *et al.*, 1989), to prove the global stability. The rate of change of the variables representing the infected component of the system can be written as follows.

$$\begin{aligned}
\frac{dE_C}{dt} &= \varepsilon_2 \lambda_C (N^* - E_C - I_C - B_C) - k_1 E_C \\
\frac{dI_C}{dt} &= (1-\varepsilon_2)\lambda_C (N^* - E_C - I_C - B_C) - k_2 I_C + \kappa_C E \\
\frac{dB_C}{dt} &= gB_C + \alpha I_C - \mu_b B_C
\end{aligned} \tag{2.42}$$

$$D^* = \{(E_C, I_{C,}, B_C) \in R_+^3 : E_C + I_{C,} + B_C \le N^*\}$$

For the model (37), the associated reproduction number, denoted by R_{oC} where

$$R_{OC} = \frac{\beta_C(\alpha\eta_2 k_1\varepsilon_2 - \alpha\eta_2\varepsilon_2\kappa_C - \eta_1 k_1 k_4\varepsilon_2 + \eta_1\varepsilon_2 k_4\kappa_C - \alpha\eta_2 k_1 + \eta_1 k_1 k_4 + k_2 k_4\varepsilon_2)}{k_1 k_2 k_4}$$

The DFE of the model (2.36) given by disease free, is GAS in D if $R_{OC} < 1$.

Using comparism method, we have

$$\begin{pmatrix} \frac{dE_C}{dt} \\ \frac{dI_C}{dt} \\ \frac{dB_C}{dt} \end{pmatrix} = (F - V)\begin{pmatrix} E_C \\ I_C \\ B_C \end{pmatrix} - F_i \begin{pmatrix} E_C \\ I_C \\ B_C \end{pmatrix}$$

According to (Castillo-Chavez, 2002; Driessche, and Watmough, 2002), all eigen values of the matrix (F-V) have negative real parts.

$$\begin{pmatrix} (\varepsilon_2\beta_C - k_1) - \lambda & \varepsilon_2\beta_C\eta_2 & \varepsilon_2\beta_C\eta_3 \\ (1-\varepsilon_2)\beta_C + k_C & ((1-\varepsilon_2)\beta_C\eta_2 - k_2 - \lambda) & (1-\varepsilon_2)\beta_C\eta_3 \\ 0 & \alpha & -k_4 - \lambda \end{pmatrix} = 0 \tag{2.41}$$

From equation (2.41) the characteristics equation is given by

$$A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 = 0$$

$$\lambda^3 - (-\eta_2\varepsilon_2\beta_C + \eta_2\beta_C + \varepsilon_2\beta_C - k_1 - k_2 - k_4)\lambda^2 - (-\alpha\eta_3\varepsilon_2\beta_C - k_1\eta_2\varepsilon_2\beta_C - k_4\eta_2\varepsilon_2\beta_C + \kappa_C\eta_2\varepsilon_2\beta_C + \alpha\eta_3\beta_C + k_1\eta_2\beta_C + k_2\varepsilon_2\beta_C + k_4\eta_2\beta_C + k_4\varepsilon_2\beta_C - k_1k_2 - k_1k_4 - k_2k_4)\lambda + \alpha k_1\eta_3\varepsilon_2\beta_C - \alpha\kappa_C\eta_3\varepsilon_2\beta_C + k_1k_4\eta_2\varepsilon_2\beta_C - k_4\kappa_C\eta_2\varepsilon_2\beta_C - \alpha k_1\eta_3\beta_C - k_2k_4\varepsilon_2\beta_C - k_1k_4\eta_2\beta_C + k_1k_2k_4$$

Where $A_3 = 1, A_2 = \eta_2\varepsilon_2\beta_C - \eta_2\beta_C - \varepsilon_2\beta_C + k_1 + k_2 + k_4)$,

$$A_1 = \alpha\eta_3\varepsilon_2\beta_C + k_1\eta_2\varepsilon_2\beta_C + k_4\eta_2\varepsilon_2\beta_C$$

$$-\kappa_C\eta_2\varepsilon_2\beta_C \quad -\alpha\eta_3\beta_C - k_1\eta_2\beta_C - k_2\varepsilon_2\beta_C - k_4\eta_2\beta_C - k_4\varepsilon_2\beta_C + k_1k_2 + k_1k_4 + k_2k_4)$$

$$A_0 = \alpha k_1\eta_3\varepsilon_2\beta_C - \alpha\kappa_C\eta_3\varepsilon_2\beta_C + k_1k_4\eta_2\varepsilon_2\beta_C - k_4\kappa_C\eta_2\varepsilon_2\beta_C - \alpha k_1\eta_3\beta_C - k_2k_4\varepsilon_2\beta_C - k_1k_4\eta_2\beta_C + k_1k_2k_4$$

According to Routh-Hurwitz Criteria of order three, all the roots of the equation will be negative if; $A_3 > 0, A_2 > 0, A_1 > 0,$ then for $A_0 > 0$ we have;

$$\frac{-\alpha\kappa_C\eta_3\varepsilon_2\beta_C - k_1k_4\eta_2\varepsilon_2\beta_C + k_4\kappa_C\eta_2\varepsilon_2\beta_C + \alpha k_1\eta_3\beta_C + k_2k_4\varepsilon_2\beta_C + k_1k_4\eta_2\beta_C}{k_1k_2k_4} < 1$$

Implying that $R_{OC} < 1$.

According to (Adewale et al, 2017b), all eigen values of the matrix F-V have negative real parts. It follows that the linearized differential inequality above is stable whenever $R_{OC} < 1$. Consequently, $S = (E_C = I_C = B_C = 0) \to (0,0,0,)$ as time $t \to \infty$. Substituting $E_C = I_C = B_C = 0$ in (R_C) gives $S(t) \to S(0)$ as $t \to \infty$. Hence, we have established that the disease free equilibrium is globally asymptotically stable whenever $R_{OC} < 1$ and unstable $R_{OC} > 1$.

Mathematical Analysis Of Optimality Of The Full Model

In this section, we analyze the mathematical analysis of the possible control strategy that will be useful to the public health practitioners achieve the best control strategy in the spread of Malaria with Cholera co-infection in the environment. In order to derive the necessary conditions for these optimal control variables, we introduce Malaria Prevention (Mosquitoes treated bed net (u_1)), Malaria Treatment (u_2), Malaria/Cholera Prevention (u_3),

Cholera Prevention (u_4), Cholera Treatment (u_5) and Boosting of Immune System (u_6) as the control strategy for the spread of Malaria-Cholera Co-infection. In order to obtain an optimal system, the controls $u_1, u_2, u_3, u_4, u_5, and\ u_6$ are introduced into the system to reduce the spread of Malaria-Cholera disease in the society. Let the function $0 \le u_1 \le 1$ represents the control on the use of mosquito nets to reduce the bite of mosquitoes, $0 \le u_3 \le 1$ represents the spray of insecticides so as to reduce mosquito population, $0 \le u_4 \le 1$ represents water treatment to reduce cholera bacteria, $0 \le u_6 \le 1$ represents the boosting of immune system. The control on the treatment of Malaria is denoted by u_2 which satisfies $0 \le u_2 \le g_1$ where g_1 represents drug efficacy for the treatment of malaria. The control functions on the treatment of cholera $0 \le u_5 \le g_2$ where g_2 represents drug efficacy on the treatment of cholera. Hence, these time dependent controls $u_1, u_2, u_3, u_4, u_5\ and\ u_6$ are incorporated into the system (2.3) to obtain the optimal control strategy for the spread of Malaria-cholera disease in the population. Therefore,

$$\frac{dS_h}{dt} = \pi_h - ((1-u_1)+(1-u_6))\lambda_m S_h - ((1-u_4)+(1-u_6))\lambda_C S_h - ((1-u_1)+(1-u_3)+(1-u_6))\lambda_{mc} S_h$$
$$- \mu_h S_h + \phi R_m + \omega R_C + \psi R_{mC}$$

$$\frac{dE_m}{dt} = ((1-u_1)+(1-u_6))\varepsilon_1 \lambda_m S_h - (\kappa_m + \mu)E_m - u_2\tau_1 E_m$$

$$\frac{dI_m}{dt} = ((1-u_1)+(1-u_6))(1-\varepsilon_1)\lambda_m S_h + \kappa_m E_m - (u_2\tau_2 + r + \delta_m + \mu)I_m$$

$$\frac{dR_m}{dt} = \tau_1 E_m + \tau_2 I_m + rI_m - (\phi + \mu)R_m + \gamma(1-\rho)u_3\theta I_{mc}$$

$$\frac{dE_{mc}}{dt} = ((1-u_1)+(1-u_3)+(1-u_6))\varepsilon_3 \lambda_{mc} S_h - (\kappa_{mc} + \mu + \delta_{mc})\, E_{mc}$$

$$\frac{dI_{mC}}{dt} = ((1-u_1)+(1-u_3)+(1-u_6))(1-\varepsilon_{\backslash 3})\lambda_{mC} S_h + \kappa_{mC} E_{mC} - (u_3\tau_4 + \mu + \delta_{mc} + \theta)I_{mc}$$

$$\frac{dR_{mc}}{dt} = \theta\rho I_{mc} + u_3\tau_4 I_{mc} - (\psi + \mu)R_{mc}$$

(2.42)

$$\frac{dE_C}{dt} = ((1-u_4)+(1-u_6))\varepsilon_2 \lambda_C S_h - (\kappa_C + \mu)E_C$$

$$\frac{dI_C}{dt} = ((1-u_4)+(1-u_6))(1-\varepsilon_2)\lambda_C S_h + \kappa_C E_C - (u_5\tau_3 + \mu + \delta_C)I_C$$

$$\frac{dR_C}{dt} = u_5\tau_3 I_C - (\omega + \mu_h)R_C + (1-\gamma)(1-\rho)\theta I_{mC}$$

$$\frac{dB_C}{dt} = gB_C + (1-u_4)\alpha(I_C + \eta_5 I_{MC}) - \mu_b B_C$$

$$\frac{dS_V}{dt} = \pi_V - (1-u_1)\lambda_V S_V - u_4\mu_V S_V$$

$$\frac{dE_V}{dt} = (1-u_1)\lambda_V S_V - (\sigma_V + \mu_V)E_V$$

$$\frac{dI_V}{dt} = \sigma_V E_V - \mu_V I_V$$

Analysis of Optimal Control

The objective functional J is constructed in order to minimize the number of people infected with malaria-cholera disease and the cost involved in applying the controls

$u_1, u_2, u_3, u_4, u_5, and\ u_6$. The objective functional J is given as:

$$J(u_1, u_2, u_3, u_4, u_5, u_6) = min \int_0^{t_f} \begin{matrix}(Z_1E_M + Z_2I_M + Z_3E_C + Z_4I_C + Z_5E_{MC} + Z_6I_{MC} + Z_7S_V \\ +Z_8E_V + Z_9I_V + A_1U_1^2 + A_2U_2^2 + A_3U_3^2 + A_4U_4^2 + A_5U_5^2 \\ +A_6U_6^2)dt\end{matrix}$$

(2.43)

Where t_f is the final time and the coefficients Z_1, Z_2, Z_3, Z_4, Z_5, Z_6 are the balancing cost factors of Malaria exposed, Malaria Infected, Malaria-Cholera exposed, Malaria-Cholera Infected and Mosquito Population respectively. While A_1, A_2, A_3, A_4, A_5 and A_6 are the positive weight constants for the use of treated bed net, treatment of malaria, spray of insecticide, water treatment, treatment of cholera and boosting of immune. The terms $Z_1E_M, Z_2I_M, Z_3E_C, Z_4I_C, Z_5E_{MC}, Z_6I_{MC}$ are the cost incurred by Exposed Malaria, Infected Malaria, exposed malaria-cholera, infected malaria-cholera individuals. While Z_7E_V, Z_8E_V and Z_9I_V are the cost on mosquito population. The term $A_1u_1^2 + A_2u_2^2 + A_3u_3^2 + A_4u_4^2 + A_5u_5^2 + A_6u_6^2$

represent the cost in making use of treated bed net, treatment of malaria, spray of insecticide, water treatment, treatment of cholera and boosting of immune. We seek to find an optimal control $u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*$

Such that

$$J(U_1^*, U_2^*, U_3^*, U_4^*, U_5^*, U_6^*) = Min\{J(u_1, u_2, u_3, u_4, u_5, u_6)/(u_1, u_2, u_3, u_4, u_5, u_6) \in U\} \quad (2.44)$$

where $U = \{(u_1, u_2, u_3, u_4, u_5, u_6)\}$ Such that $u_1, u_2, u_3, u_4, u_5, u_6$ are Lebesque measurable with

$0 \le u_1 \le 1, 0 \le u_3 \le 1, 0 \le u_4 \le 1, \ 0 \le u_6 \le 1, 0 \le u_2 \le g_1, 0 \le u_5 \le g_2,$

for $t \in [0, t_f] \to [0,1]$ is the control set.

The necessary conditions that an optimal control must satisfy come from Pontryagin`s Maximum Principle. The principle converts equations (2.43) and (2.44) into a

problem of minimizing point wise a Hamiltonian "H" with respect to $(u_1, u_2, u_3, u_4, u_5, u_6)$.

Hence;

$$\begin{aligned}
H &= Z_1E_M + Z_2I_M + Z_3E_{MC} + Z_4I_{MC} + Z_5E_C + Z_6I_C + Z_7E_V + Z_8I_V + A_1u_1^2 + A_2u_2^2 + A_3u_3^2 \\
&+ A_4u_4^2 + A_5u_5^2 + A_6u_6^2 + A_7u_7^2 + M_{Sh}[\pi_h - [((1-u_1) + (1-u_5))\lambda_M + ((1-u_4) + (1-u_6))\lambda_C + \\
&((1-u_1) + (1-u_3) + (1-u_6))\lambda_{MC}]S_h + \phi_1 R_M + \omega R_C + \psi R_{MC} - \mu S_h] + M_{E_M}[((1-u_1) + (1-u_5))\varepsilon_1\lambda_M S_h - \\
&(\kappa_M + \mu)E_M - u_2\tau_1 E_M] + M_{I_M}[((1-u_1) + (1-u_5))(1-\varepsilon_1)\lambda_M S_h + \kappa_M E_M - (u_2\tau_2 + r + \mu + \delta_M)I_M] \\
&+ M_{E_{MC}}[((1-u_1) + (1-u_3) + (1-u_6))\varepsilon_3\lambda_{MC}S_h] - (\kappa_{MC} + \mu + \delta_{MC})E_{MC} + M_{I_{MC}}[((1-u_1) + (1-u_3) + (1-u_6)) \\
&(1-\varepsilon_3)\lambda_{MC}S_h] + \kappa_{MC}E_{MC} - (u_3\tau_4 + \mu + \delta_{MC} + \theta)I_{MC} + M_{E_C}[((1-u_4) + (1-u_6))\varepsilon_2\lambda_C S_h - (\kappa_C + \mu)E_C] \\
&+ M_{I_C}[((1-u_4) + (1-u_6))(1-\varepsilon_2)\lambda_C S_h + \kappa_C E_C - (u_5\tau_3 + \mu + \delta_C)I_C] + M_{R_M}[u_2\tau_1 E_M + u_2\tau_2 I_M + rI_M \\
&- (\phi + \mu)R_M] + M_{R_C}[u_5\tau_3 I_C - (\omega + \mu)R_C + (1-\gamma)(1-\rho)\theta I_{MC}] + M_{R_{MC}}[u_3\tau_4 I_{MC} + \theta\rho I_{MC} - (\psi + \mu)R_{MC}] \\
&+ M_{B_C}[gB_C + (1-u_4)\alpha(I_C + \eta_5 I_{MC}) - \mu_b B_C] + M_{S_V}[\pi_V - (1-u_1)\lambda_V S_V - \mu_V S_V] \\
&+ M_{E_V}[(1-u_1)\lambda_V S_V - (\sigma_V + u_4\mu_V)E_V] + M_{I_V}[\sigma_V E_V - \mu_V I_V]
\end{aligned} \quad (3.281)$$

Where; $M_{S_h}, M_{E_M}, M_{I_M}, M_{E_{MC}}, M_{I_{MC}}, M_{E_C}, M_{I_C}, M_{R_M}, M_{R_{MC}}, M_{R_C}, M_{B_C}, M_{S_V}, M_{E_V}, M_{I_V}$

are the adjoint variables or co-state variables.

Existence of control Problem

The theorem 3.12 below will be used to prove the existence of optimal control pairs.

Theorem 3.12: There exists an optimal control

$$u^* = (u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*) \in U$$

Such that;

$$J(u_1^*, u_2^*, u^*, u_4^*, u_5^*, u_6^*) = Min\, J(u_1, u_2, u_3, u_4, u_5, u_6) \quad / (u_1, u_2, u_3, u_4, u_5, u_6) \in U$$

Subject to the control system

Proof: To prove the existence of an optimal control pairs, the result in (Lukes, 1982) will be used. The control and the state variables are non-negative values. The necessary convexity of the objectives functional in $u_1, u_2, u_3, u_4, u_5, u_6$ are satisfied. The set of all the control variables $(u_1, u_2, u_3, u_4, u_5, u_6) \in U$ is also convex and closed by definition. The optimal system is bounded which determines the compactness needed for the existence of the optimal control. Also, the integrand is convex on the control set U. Therefore, there exist positive numbers $D_1, D_2\ and$ a constant $r > 1$ such that;

$$J(u_1, u_2, u_3, u_4, u_5, u_6, u_7) \geq D_1 \left(|u_1|^2 + |u_2|^2 + |u_3|^2 + |u_4|^2 + |u_5|^2 + |u_6|^2 \right)^{p/2} - D_2$$

The Lipschitz property of the state system with respect to the state variables is satisfied since the state variables are bounded. This completes the existence of an optimal control.

Theorem 3.13: Given an optimal control $u_1^*, u_2^*, u^*, u_4^*, u_5^*, u_6^*$ and solutions

$S_h^*, E_M^*, I_M^*, R_M^*, E_{MC}^*, I_{MC}^*, R_{MC}^*, E_C^*, I_C^*, R_C^*, B_C^*, S_V^*, I_V^*, E_V^*,$

of the corresponding state system (2.43) that minimizes $J(u_1, u_2, u_3, u_4, u_5, u_6, u_7)$ over U. Then, there exists adjoint variables $M_{S_h}, M_{E_M}, M_{I_M}, M_{E_{MC}}, M_{I_{MC}}, M_{E_C}, M_{I_C}, M_{R_M}, M_{R_{MC}}, M_{R_C}, M_{B_C}, M_{S_V}, M_{E_V}, M_{I_V}$ satisfying;

$$-\frac{dM_{S_h}}{dt}=\frac{\partial H}{\partial S_h}=[((1-u_1)+(1-u_6))\frac{\beta_m a I_V}{N_V}-\frac{((1-u_4)+(1-u_6))\beta_C(E_C+\eta_2 I_C+\eta_3 B_C)(E_C+I_C+R_C)}{N_C^2}-$$
$$\frac{((1-u_1)+(1-u_3)+(1-u_6))\beta_{MC}(E_{MC}+\eta_4 I_{MC})(E_{MC}+I_{MC})}{N_C^2}-\mu_h]M_{S_h}+$$
$$[((1-u_1)+(1-u_6))\frac{\varepsilon_1\beta_m a I_V}{N_V}]M_{E_M}+((1-u_1)+(1-u_6))\frac{(1-\varepsilon_1)\beta_m a I_V}{N_V}]M_{I_M}+$$
$$[\frac{((1-u_4)+(1-u_6))\varepsilon_2\beta_C(E_C+\eta_2 I_C+\eta_3 B_C)(E_C+I_C+R_C)}{N_C^2}]M_{E_C}+$$
$$[\frac{((1-u_4)+(1-u_6))(1-\varepsilon_2)\beta_C(E_C+\eta_2 I_C+\eta_3 B_C)(E_C+I_C+R_C)}{N_C^2}]M_{I_C}+$$
$$[\frac{((1-u_1)+(1-u_3)+(1-u_6))\varepsilon_3\beta_{MC}(E_{MC}+\eta_4 I_{MC})(E_{MC}+I_{MC})}{N_{MC}^2}]M_{E_{MC}}+$$
$$[\frac{((1-u_1)+(1-u_3)+(1-u_6))(1-\varepsilon_3)\beta_{MC}(E_{MC}+\eta_4 I_{MC})(E_{MC}+I_{MC})}{N_{MC}^2}]M_{I_{MC}}$$

$$-\frac{dM_{E_M}}{dt}=\frac{\partial H}{\partial E_M}=Z_1-(\kappa_m+\mu+u_3\tau_1)M_{E_M}+\kappa_m M_{I_M}+u_3\tau_1 M_{R_M}$$

$$-\frac{dM_{I_M}}{dt}=\frac{\partial H}{\partial I_M}=Z_2-(u_3\tau_2+r+\delta_m+\mu)M_{I_M}+(u_3\tau_2+r)M_{R_M}$$

$$-\frac{dM_{R_M}}{dt}=\phi M_{S_h}+(u_3\tau_2+r+\delta_m+\mu)M_{I_M}+(u_3\tau_2+r)M_{R_M}+(\phi+\mu)M_{R_M}$$

$$-\frac{dM_{E_C}}{dt}=Z_3-\frac{[-((1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)])S_h\beta_C]M_{S_h}}{N_C^2}$$
$$+\frac{[-((1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)])\varepsilon_2 S_h\beta_C-(\kappa_C+\mu)]M_{E_C}}{N_C^2}$$
$$+\frac{[-((1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)])(1-\varepsilon_2)S_h\beta_C+\kappa_C]M_{I_C}}{N_C^2}$$

$$\frac{-dM_{I_C}}{dt}=Z_4-\frac{[-((1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)])S_h\beta_C]M_{S_h}}{N_C^2}$$
$$+\frac{[(1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)]\varepsilon_2 S_h\beta_C]M_{E_C}}{N_C^2}$$
$$+\frac{[(1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)](1-\varepsilon_2)S_h\beta_C]M_{I_C}}{N_C^2}-(u_5\tau_3+\delta_C+\mu_h)M_{I_C}$$
$$+u_5\tau_3 M_{R_C}$$

$$-\frac{dM_{R_C}}{dt} = \omega M_{S_h} - (\omega + \mu_h) M_{R_C}$$

$$\frac{-dM_{E_{MC}}}{dt} = Z_5 + \frac{[-(1-u_1)+(1-u_3)+(1-u_6))(S_h + I_{MC} + R_{MC}) - (E_{MC} + \eta_4 I_{MC})\beta_{MC}]}{N_{MC}^2} M_{S_h}$$
$$+ \frac{[(1-u_1)+(1-u_3)+(1-u_6)[(S_h + I_{MC} + R_{MC}) - (E_{MC} + \eta_4 I_{MC})\varepsilon_3 \beta_{MC} S_h - (\kappa_{MC} + \mu)] M_{E_{MC}}}{N_{MC}^2} + \kappa_{MC} I_{MC}$$
$$+ \frac{[(1-u_1)+(1-u_3)+(1-u_6)[(S_h + I_{MC} + R_{MC}) - (E_{MC} + \eta_4 I_{MC})(1-\varepsilon_3)\beta_{MC} S_h] M_{I_{MC}}}{N_{MC}^2} + \kappa_{MC} I_{MC}$$

$$\frac{-dM_{I_{MC}}}{dt} = Z_6 + \frac{[-((1-u_1)+(1-u_3)+(1-u_6))[(S_h + I_{MC} + R_{MC})\eta_4 - (E_{MC} + \eta_4 I_{MC})]\beta_{MC} S_h] M_{S_h}}{N_{MC}^2}$$
$$+ \frac{[((1-u_1)+(1-u_3)+(1-u_6))[(S_h + I_{MC} + R_{MC})\eta_4 - (E_{MC} + \eta_4 I_{MC})]\varepsilon_3 \beta_{MC} S_h] M_{E_{MC}}}{N_{MC}^2}$$
$$+ \frac{[-((1-u_1)+(1-u_3)+(1-u_6))[(S_h + I_{MC} + R_{MC})\eta_4 - (E_{MC} + \eta_4 I_{MC})](1-\varepsilon_3)\beta_{MC} S_h] M_{I_{MC}}}{N_{MC}^2} -$$
$$(u_3\tau_4 + \mu_h + \delta_{MC} + \theta) M_{I_{MC}} + (1-\gamma)(1-\rho)\theta M_{R_C}$$

$$\frac{-dM_{S_V}}{dt} = Z_7 + \frac{((1-u_1)+(1-u_6))\beta_m a I_V S_h}{N_V^2} M_{S_h} - \frac{((1-u_1)+(1-u_6))\varepsilon_1 \beta_m a I_V S_h}{N_V^2} M_{E_M} +$$
$$\frac{((1-u_1)+(1-u_6))(1-\varepsilon_1)\beta_m a I_V S_h}{N_V^2} M_{I_M} - [(1-u_1)\lambda_V + \mu_V] M_{S_V} + (1-u_1)\lambda_V M_{E_V}$$

$$-\frac{dM_{E_V}}{dt} = Z_8 + \frac{((1-u_1)+(1-u_6))\beta_m a I_V S_h}{N_V^2} M_{S_h} - \frac{((1-u_1)+(1-u_6))\varepsilon_1 \beta_m a I_V S_h}{N_V^2} M_{E_M} +$$
$$\frac{((1-u_1)+(1-u_6))(1-\varepsilon_1)\beta_m a I_V S_h}{N_V^2} M_{I_M} - (\sigma_V + \mu_V) M_{E_V} + \sigma_V M_{I_V}$$

$$-\frac{dM_{I_V}}{dt} = Z_9 - \frac{((1-u_1)+(1-u_6))(S_V + E_V)\beta_m a I_V S_h}{N_V^2} M_{S_h} - \frac{((1-u_1)+(1-u_6))(S_V + E_V)\varepsilon_1 \beta_m a I_V S_h}{N_V^2} M_{E_M}$$
$$+ \frac{((1-u_1)+(1-u_6))(S_V + E_V)(1-\varepsilon_1)\beta_m a I_V S_h}{N_V^2} M_{I_M} - \mu_V M_{I_V}$$

and with transversality conditions;

$$M_{S_h}(t_f)=M_{E_M}(t_f)=M_{I_M}(t_f)=M_{R_M}(t_f)=M_{E_C}(t_f)=M_{I_C}(t_f)=M_{R_C}(t_f)=M_{E_{MC}}(t_f)=M_{I_{MC}}(t_f)$$
$$M_{R_{MC}}(t_f)=M_{S_V}(t_f)=M_{E_V}(t_f)=M_{I_V}(t_f)=0$$

and with the controls $u_1^*,u_2^*,u_3^*,u_4^*,u_5^*$ *and* u_6^* satisfying the optimality condition;

$$u_1^*=max\left\{0,min\left[1,\frac{[(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M+(\varepsilon_3 M_{E_{MC}}+(1-\varepsilon_3)M_{E_{MC}})\lambda_{MC}-(\lambda_M+\lambda_{MC})M_{S_h}]S_h}{2A_1}\right]\right\}$$

$$u_2^*=max\left\{0,min\left[1,\frac{\tau_1 E_M M_{E_M}+\tau_2 I_M M_{I_M}-\tau_1 E_M M_{R_M}-\tau_2 I_M M_{R_M}}{2A_2}\right]\right\}$$

$$u_3^*=max\left\{0,min\left[1,\frac{\tau_4 I_{MC} M_{E_{MC}}-(\tau_4+\theta\rho)I_{MC}M_{R_{MC}}-(1-\gamma)(1-\rho)\theta M_{R_C}-\gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}$$

$$u_4^*=max\left\{0,min\left[1,\frac{[(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_C})\lambda_C-\alpha M_{I_C}-\alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\} \qquad (2.45)$$

$$u_5^*=max\left\{0,min\left[1,\frac{\tau_3 I_C M_{I_C}-\tau_3 I_C M_{R_C}}{2A_5}\right]\right\}$$

$$u_6^*=max\left\{0,min\left[1,\frac{[(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M-(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_c})\lambda_C+(\varepsilon_3 M_{E_{MC}}+(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC}}{2A_6}\right]\right\}$$
$$-(\lambda_M+\lambda_C+\lambda_{MC})M_{S_h}]$$

Proof: The Pontryagin's Maximum principle will be used. The differential equations governing the adjoint variables were obtained by differentiating the Hamiltonian function H with respect to the state variables, evaluated at the optimal control. Then, the adjoint becomes;

$$-\frac{dM_{S_h}}{dt}=\frac{\partial H}{\partial S_h}=[((1-u_1)+(1-u_6))\frac{\beta_m aI_V}{N_V}-\frac{((1-u_4)+(1-u_6))\beta_C(E_C+\eta_2 I_C+\eta_3 B_C)(E_C+I_C+R_C)}{N_C^2}-$$

$$\frac{((1-u_1)+(1-u_3)+(1-u_6))\beta_{MC}(E_{MC}+\eta_4 I_{MC})(E_{MC}+I_{MC})}{N_C^2}-\mu_h]M_{S_h}+$$

$$[((1-u_1)+(1-u_6))\frac{\varepsilon_1\beta_m aI_V}{N_V}]M_{E_M}+((1-u_1)+(1-u_6))\frac{(1-\varepsilon_1)\beta_m aI_V}{N_V}]M_{I_M}+$$

$$[\frac{((1-u_4)+(1-u_6))\varepsilon_2\beta_C(E_C+\eta_2 I_C+\eta_3 B_C)(E_C+I_C+R_C)}{N_C^2}]M_{E_C}+$$

$$[\frac{((1-u_4)+(1-u_6))(1-\varepsilon_2)\beta_C(E_C+\eta_2 I_C+\eta_3 B_C)(E_C+I_C+R_C)}{N_C^2}]M_{I_C}+$$

$$[\frac{((1-u_1)+(1-u_3)+(1-u_6))\varepsilon_3\beta_{MC}(E_{MC}+\eta_4 I_{MC})(E_{MC}+I_{MC})}{N_{MC}^2}]M_{E_{MC}}+$$

$$[\frac{((1-u_1)+(1-u_3)+(1-u_6))(1-\varepsilon_3)\beta_{MC}(E_{MC}+\eta_4 I_{MC})(E_{MC}+I_{MC})}{N_{MC}^2}]M_{I_{MC}}$$

$$-\frac{dM_{E_M}}{dt}=\frac{\partial H}{\partial E_M}=Z_1-(\kappa_m+\mu+u_3\tau_1)M_{E_M}+\kappa_m M_{I_M}+u_3\tau_1 M_{R_M}$$

$$-\frac{dM_{I_M}}{dt}=\frac{\partial H}{\partial I_M}=Z_2-(u_3\tau_2+r+\delta_m+\mu)M_{I_M}+(u_3\tau_2+r)M_{R_M}$$

$$-\frac{dM_{R_M}}{dt}=\frac{\partial H}{\partial R_M}=\phi M_{S_h}+(u_3\tau_2+r+\delta_m+\mu)M_{I_M}+(u_3\tau_2+r)M_{R_M}(\phi+\mu)M_{R_M}+\phi M_{S_h}$$

$$-\frac{dM_{E_C}}{dt}=\frac{\partial H}{\partial I_C}=Z_3-\frac{[-((1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)])S_h\beta_C]M_{S_h}}{N_C^2}$$

$$+\frac{[(1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)]\varepsilon_2 S_h\beta_C]M_{E_C}}{N_C^2}$$

$$+\frac{[(1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)](1-\varepsilon_2)S_h\beta_C]M_{I_C}}{N_C^2}-(u_5\tau_3+\delta_C+\mu_h)M_{I_C}$$

$$+u_5\tau_3 M_{R_C}$$

$$-\frac{dM_{I_C}}{dt}=\frac{\partial H}{\partial I_C}=Z_4-\frac{[-((1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)])S_h\beta_C]M_{S_h}}{N_C^2}$$
$$+\frac{[(1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)]\varepsilon_2 S_h\beta_C]M_{E_C}}{N_C^2}$$
$$+\frac{[(1-u_4)+(1-u_6)[(S_h+I_C+R_C)-(E_C+\eta_2 I_C+\eta_3 B_C)](1-\varepsilon_2)S_h\beta_C]M_{I_C}}{N_C^2}-(u_5\tau_3+\delta_C+\mu_h)M_{I_C}$$
$$+u_5\tau_3 M_{R_C}$$

$$-\frac{dM_{R_C}}{dt}=\frac{\partial H}{\partial R_C}=\omega M_{S_h}-(\omega+\mu_h)M_{R_C}$$
$$-\frac{dM_{E_{MC}}}{dt}=\frac{\partial H}{\partial E_{MC}}=Z_5+\frac{[-(1-u_1)+(1-u_3)+(1-u_6))(S_h+I_{MC}+R_{MC})-(E_{MC}+\eta_4 I_{MC})\beta_{MC}]}{N_{MC}^2}M_{S_h}$$
$$+\frac{[(1-u_1)+(1-u_3)+(1-u_6)[(S_h+I_{MC}+R_{MC})-(E_{MC}+\eta_4 I_{MC})\varepsilon_3\beta_{MC}S_h-(\kappa_{MC}+\mu)]M_{E_{MC}}}{N_{MC}^2}+\kappa_{MC}I_{MC}$$
$$+\frac{[(1-u_1)+(1-u_3)+(1-u_6)[(S_h+I_{MC}+R_{MC})-(E_{MC}+\eta_4 I_{MC})(1-\varepsilon_3)\beta_{MC}S_h]M_{I_{MC}}}{N_{MC}^2}+\kappa_{MC}I_{MC}$$

$$\frac{-dM_{I_{MC}}}{dt}=\frac{\partial H}{\partial I_{MC}}=Z_6+\frac{[-((1-u_1)+(1-u_3)+(1-u_6))[(S_h+I_{MC}+R_{MC})\eta_4-(E_{MC}+\eta_4 I_{MC})]\beta_{MC}S_h]M_{S_h}}{N_{MC}^2}$$
$$+\frac{[((1-u_1)+(1-u_3)+(1-u_6))[(S_h+I_{MC}+R_{MC})\eta_4-(E_{MC}+\eta_4 I_{MC})]\varepsilon_3\beta_{MC}S_h]M_{E_{MC}}}{N_{MC}^2}$$
$$+\frac{[-((1-u_1)+(1-u_3)+(1-u_6))[(S_h+I_{MC}+R_{MC})\eta_4-(E_{MC}+\eta_4 I_{MC})](1-\varepsilon_3)\beta_{MC}S_h]M_{I_{MC}}}{N_{MC}^2}-$$
$$(u_3\tau_4+\mu_h+\delta_{MC}+\theta)M_{I_{MC}}+(1-\gamma)(1-\rho)\theta M_{R_C}$$
$$-\frac{dM_{S_V}}{dt}=Z_7+\frac{((1-u_1)+(1-u_6))\beta_m a I_V S_h}{N_V^2}M_{S_h}-\frac{((1-u_1)+(1-u_6))\varepsilon_1\beta_m a I_V S_h}{N_V^2}M_{E_M}+$$
$$\frac{((1-u_1)+(1-u_6))(1-\varepsilon_1)\beta_m a I_V S_h}{N_V^2}M_{I_M}-[(1-u_1)\lambda_V+\mu_V]M_{S_V}+(1-u_1)\lambda_V M_{E_V}$$

$$-\frac{dM_{E_V}}{dt}=\frac{\partial H}{\partial E_V}=Z_8+\frac{((1-u_1)+(1-u_6))\beta_m a I_V S_h}{N_V^2}M_{S_h}-\frac{((1-u_1)+(1-u_6))\varepsilon_1\beta_m a I_V S_h}{N_V^2}M_{E_M}+$$
$$\frac{((1-u_1)+(1-u_6))(1-\varepsilon_1)\beta_m a I_V S_h}{N_V^2}M_{I_M}-(\sigma_V+\mu_V)M_{E_V}+\sigma_V M_{I_V}$$

$$-\frac{dM_{I_V}}{dt}=\frac{\partial H}{\partial I_V}=Z_9-\frac{((1-u_1)+(1-u_6))(S_V+E_V)\beta_m aI_V S_h}{N_V^2}M_{S_h}-$$
$$\frac{((1-u_1)+(1-u_6))(S_V+E_V)\varepsilon_1\beta_m aI_V S_h}{N_V^2}M_{E_M}$$
$$+\frac{((1-u_1)+(1-u_6))(S_V+E_V)(1-\varepsilon_1)\beta_m aI_V S_h}{N_V^2}M_{I_M}-\mu_V M_{I_V}$$

Thus differentiating with respect to u_1,u_2,u_3,u_4,u_5,u_6 and setting them to zero to obtain;

$$\frac{\partial H}{\partial u_1}=\frac{\partial H}{\partial u_2}=\frac{\partial H}{\partial u_3}=\frac{\partial H}{\partial u_4}=\frac{\partial H}{\partial u_5}=\frac{\partial H}{\partial u_6}=0$$

$$0=\frac{\partial H}{\partial u_1}=2A_1u_1+(\lambda_M+\lambda_{MC})M_{S_h}S_h-\varepsilon_1\lambda_M M_{E_M}-(1-\varepsilon_1)\lambda_M S_h M_{I_M}-\varepsilon_3\lambda_{MC}S_h M_{E_{MC}}-(1-\varepsilon_3)\lambda_{MC}S_h M_{E_{MC}}$$
$$+\lambda_V S_v M_{S_V}-\lambda_V S_v M_{E_V}$$

$$0=\frac{\partial H}{\partial u_2}=2A_2u_2-\tau_1 E_M M_{E_M}-\tau_2 I_M M_{I_M}+\tau_1 E_M M_{R_M}+\tau_2 I_M M_{R_M}$$

$$0=\frac{\partial H}{\partial u_3}=2A_3u_3-\tau_4 I_{MC}M_{E_{MC}}+(\tau_4+\theta\rho)I_{MC}M_{R_{MC}}+(1-\gamma)(1-\rho)\theta M_{R_C}+\gamma(1-\rho)\theta M_{R_M}$$

$$0=\frac{\partial H}{\partial u_4}=2A_4u_4-(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_C})\lambda_C+\alpha M_{I_C}+\alpha\eta_5 M_{I_{MC}}$$

$$0=\frac{\partial H}{\partial u_5}=2A_5u_5-\tau_3 I_C M_{I_C}+\tau_3 I_C M_{R_C}$$

$$0=\frac{\partial H}{\partial u_6}=2A_6u_6-(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M+(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_c})\lambda_C+(\varepsilon_3 M_{E_{MC}}$$
$$-(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC}+(\lambda_M+\lambda_C+\lambda_{MC})M_{S_h}$$

Hence, solving at $u_1=u_1^*$, $u_2=u_2^*$, $u_3=u_3^*$, $u_4=u_4^*$, $u_5=u_5^*$, $u_6=u_6^*$ to obtain;

$$u_1^* = max\left\{0, min\left[1, \frac{\begin{matrix}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} - (\lambda_M + \lambda_{MC})M_{S_h}]S_h \\ -(M_{S_V} + M_{E_V})\lambda_V\end{matrix}}{2A_1}\right]\right\}$$

$$u_2^* = max\left\{0, min\left[1, \frac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2}\right]\right\}$$

$$u_3^* = max\left\{0, min\left[1, \frac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho) I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}$$

$$u_4^* = max\left\{0, min\left[1, \frac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\}$$

$$u_5^* = max\left\{0, min\left[1, \frac{\tau_3 I_C M_{I_C} - \tau_3 I_C M_{R_C}}{2A_5}\right]\right\}$$

$$u_6^* = max\left\{0, min\left[1, \frac{\begin{matrix}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{matrix}}{2A_6}\right]\right\}$$

By standard control arguments involving the bounds on the control variables, we have

$$u_1^* = \begin{cases} \dfrac{\begin{matrix}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{matrix}}{2A_1}, & if \\ \\ 0 \qquad if \ \dfrac{\begin{matrix}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{matrix}}{2A_1} \le 0 \\ \\ 1 \qquad if \ \dfrac{\begin{matrix}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{matrix}}{2A_1} \ge 1 \end{cases}$$

$$u_2^* = \begin{cases} \dfrac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2}, if \\ 0 < \dfrac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2} < 1 \\ 0 \quad if \quad \dfrac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2} \le 0 \\ 1 \quad if \quad \dfrac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2} \ge 1 \end{cases}$$

$$u_3^* = \begin{cases} \dfrac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho) I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3}, if \\ 0 < \dfrac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho) I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3} < 1 \\ 0 \quad if \quad \dfrac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho) I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3} \le 0 \\ 1 \quad if \quad \dfrac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho) I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3} \ge 1 \end{cases} \tag{2.46}$$

$$u_4^* = \begin{cases} \dfrac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2) M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4}, if \\ 0 < \dfrac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2) M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4} < 1 \\ 0 \quad if \quad \dfrac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2) M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4} \le 0 \\ 1 \quad if \quad \dfrac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2) M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4} \ge 1 \end{cases}$$

$$u_5^* = \begin{cases} \dfrac{\tau_3 I_C M_{I_C} - \tau_3 I_C M_{R_C}}{2A_5}, if \quad 0 < \dfrac{\tau_3 I_C M_{I_C} - \tau_3 I_C M_{R_C}}{2A_5} < 1 \\ 0 \quad if \quad \dfrac{\tau_3 I_C M_{I_C} - \tau_3 I_C M_{R_C}}{2A_5} \le 0 \\ 1 \quad if \quad \dfrac{\tau_3 I_C M_{I_C} - \tau_3 I_C M_{R_C}}{2A_5} \end{cases}$$

$$u_6^* = \begin{cases} \dfrac{[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]}{2A_6}, & if \\ 0 < \dfrac{[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]}{2A_6} < 1 & \\ 0 \quad if \quad \dfrac{[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]}{2A_6} \le 0 & \\ 1 \quad if \quad \dfrac{[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]}{2A_6} \ge 1 & \end{cases}$$

This completes the proof.

The optimality system consists of the state system coupled with the adjoint system with the initial and tranversality conditions together with the characterization of the optimal control pair.

$$u_1^* = max\left\{0, min\left[1, \frac{[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} - (\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V}{2A_1}\right]\right\}$$

$$u_2^* = max\left\{0, min\left[1, \frac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2}\right]\right\}$$

$$u_3^* = max\left\{0, min\left[1, \frac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho) I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}$$

$$u_4^* = max\left\{0, min\left[1, \frac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\}$$

$$u_5^* = max\left\{0, min\left[1, \frac{\tau_3 I_C M_{I_C} - \tau_3 I_C M_{R_C}}{2A_5}\right]\right\}$$

$$u_6^* = max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}$$

Substituting (2.45) into (2.42) we obtained the following optimality system;

$$\frac{dS_h}{dt} = \pi_h - \left(\left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h\end{array}}{2A_1}\right]\right\}\right)$$

$$+\left(\left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} \\ +(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right)\lambda_M$$

$$+\left(\left(1 - max\left\{0, min\left[1, \frac{[(\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_C})\lambda_C - \alpha M_{I_C} - \alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\}\right) +$$

$$\left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} \\ +(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right)\lambda_C$$

$$+\left(\left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right) +$$

$$\left(1 - max\left\{0, min\left[1, \frac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho)I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}\right.$$

$$\left.+\left(\left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + (\varepsilon_3 M_{E_{MC}} \\ +(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right)\lambda_{MC}\right)S_h$$

$$+\phi R_M + \omega R_C + \psi R_{MC} - \mu S_h$$

$$\frac{dE_M}{dt} = \left[1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right] S_h +$$

$$\left[1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + \\ (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right] \varepsilon_1 \lambda_M S_h - (\kappa_M + \mu)E_M$$

$$-\left(max\left\{0, min\left[1, \frac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2}\right]\right\}\right)\tau_1 E_M$$

$$\frac{dI_M}{dt} = \left[1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right] S_h +$$

$$\left[1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + \\ (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right] (1-\varepsilon_1)\lambda_M S_h + \kappa_M E_M$$

$$-\left(max\left\{0, min\left[1, \frac{\tau_1 E_M M_{E_M} + \tau_2 I_M M_{I_M} - \tau_1 E_M M_{R_M} - \tau_2 I_M M_{R_M}}{2A_2}\right]\right\}\tau_2 + r + \delta_M + \mu\right) I_M$$

$$\frac{dE_{MC}}{dt} = \left[1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right] +$$

$$\left[1 - max\left\{0, min\left[1, \frac{\tau_4 I_{MC} M_{E_{MC}} - (\tau_4 + \theta\rho)I_{MC} M_{R_{MC}} - (1-\gamma)(1-\rho)\theta M_{R_C} - \gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}\right] +$$

$$\left[1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M - (\varepsilon_2 M_{E_C} + (1-\varepsilon_2)M_{I_c})\lambda_C + \\ (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{I_{MC}})\lambda_{MC} - (\lambda_M + \lambda_C + \lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right] \varepsilon_3 \lambda_{MC} S_h - (\kappa_{MC} + \mu + \delta_{MC})E_{MC}$$

$$\frac{dI_{MC}}{dt}=\left[1-max\left\{0,min\left[1,\frac{\begin{array}{l}[(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M+(\varepsilon_3 M_{E_{MC}}+(1-\varepsilon_3)M_{E_{MC}})\lambda_{MC}\\ -(\lambda_M+\lambda_{MC})M_{S_h}]S_h-(M_{S_V}+M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right]+$$

$$\left[1-max\left\{0,min\left[1,\frac{\tau_4 I_{MC}M_{E_{MC}}-(\tau_4+\theta\rho)I_{MC}M_{R_{MC}}-(1-\gamma)(1-\rho)\theta M_{R_C}-\gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}\right]+$$

$$\left[1-max\left\{0,min\left[1,\frac{\begin{array}{l}[(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M-(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_c})\lambda_C+\\ (\varepsilon_3 M_{E_{MC}}+(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC}-(\lambda_M+\lambda_C+\lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right](1-\varepsilon_3)\lambda_{MC}S_h+\kappa_{MC}E_{MC}-$$

$$\left(max\left\{0,min\left[1,\frac{\tau_4 I_{MC}M_{E_{MC}}-(\tau_4+\theta\rho)I_{MC}M_{R_{MC}}-(1-\gamma)(1-\rho)\theta M_{R_C}-\gamma(1-\rho)\theta M_{R_M}}{2A_3}\right]\right\}\tau_4+\mu+\delta_{MC}+\theta\right)I_{MC}$$

$$\frac{dE_C}{dt}=\left(1-max\left\{0,min\left[1,\frac{[(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_C})\lambda_C-\alpha M_{I_C}-\alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\}\right)+$$

$$\left(1-max\left\{0,min\left[1,\frac{\begin{array}{l}[(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M-(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_c})\lambda_C+(\varepsilon_3 M_{E_{MC}}\\ +(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC}-(\lambda_M+\lambda_C+\lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right)\varepsilon_2\lambda_C S_h+$$

$$(\kappa_C+\mu)E_C$$

$$\frac{dI_C}{dt}=\left(1-max\left\{0,min\left[1,\frac{[(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_C})\lambda_C-\alpha M_{I_C}-\alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\}\right)+$$

$$\left(1-max\left\{0,min\left[1,\frac{\begin{array}{l}[(\varepsilon_1 M_{E_M}+(1-\varepsilon_1)M_{I_M})\lambda_M-(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_c})\lambda_C+(\varepsilon_3 M_{E_{MC}}\\ +(1-\varepsilon_3)M_{I_{MC}})\lambda_{MC}-(\lambda_M+\lambda_C+\lambda_{MC})M_{S_h}]\end{array}}{2A_6}\right]\right\}\right)(1-\varepsilon_2)\lambda_C S_h+$$

$$\kappa_C E_C-\left(max\left\{0,min\left[1,\frac{\tau_3 I_C M_{I_C}-\tau_3 I_C M_{R_C}}{2A_5}\right]\right\}\tau_3+\mu+\delta_C\right)I_C$$

$$\frac{dB_C}{dt}=gB_C+\left(1-max\left\{0,min\left[1,\frac{[(\varepsilon_2 M_{E_C}+(1-\varepsilon_2)M_{I_C})\lambda_C-\alpha M_{I_C}-\alpha\eta_5 M_{I_{MC}}]}{2A_4}\right]\right\}\alpha\left(I_C+\eta_5 I_{MC}\right)\right)-\mu_b B_C$$

$$\frac{dS_V}{dt} = \pi_V - \left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right)\lambda_V S_V$$

$$- \mu_V S_V$$

$$\frac{dE_V}{dt} = \left(1 - max\left\{0, min\left[1, \frac{\begin{array}{l}[(\varepsilon_1 M_{E_M} + (1-\varepsilon_1)M_{I_M})\lambda_M + (\varepsilon_3 M_{E_{MC}} + (1-\varepsilon_3)M_{E_{MC}})\lambda_{MC} \\ -(\lambda_M + \lambda_{MC})M_{S_h}]S_h - (M_{S_V} + M_{E_V})\lambda_V\end{array}}{2A_1}\right]\right\}\right)\lambda_V S_V$$

$$-(\sigma_V + \mu_V)E_V$$

$$\frac{dI_V}{dt} = \sigma_V E_V - \mu_V I_V$$

Table of parameter Values used in Simulation

Parameters	Value	Sources
π_h	2000	Assumed
ε_1	0.4	Assumed
β_M	0.03	Assumed
a	0.282	Assumed
μ_h	0.290	Assumed
ϕ	0.01460	Adesola *et al.*, 2024a
τ_1	0.143	Assumed
τ_2	0.3	Assumed
r	0.005	Assumed
δ_M	0.05	Assumed
κ_m	0.0588	Assumed
β_C, β_{MC}, β_V	0.5, 0.9, 0.5	Assumed
η_1	0.01	Assumed
σ_V	0.1	Assumed
π_V	0.071	Assumed
μ_V	0.04	Assumed
b	0.6	Adesola *et al.*, 2024a
ε_2	1	Adeniran et al., 2022
η_2, η_3, η_4	0.001, 0.001, 0.002	Assumed
τ_3	0.3	Adeniran et al., 2022
ω	0.4	Assumed
κ_C	0.5	Adeniran et al., 2022
μ_C	0.02	Adeniran et al., 2022

δ_C δ_{MC}	0.3	Assumed
α	0.0001	Assumed
g	0.1	Adeniran et al., 2022
μ_b	0.01	Assumed
τ_4	0.1	Assumed
κ_{MC}	0.1	Assumed
	0.4	Assumed

Presentation of Results and Discussion

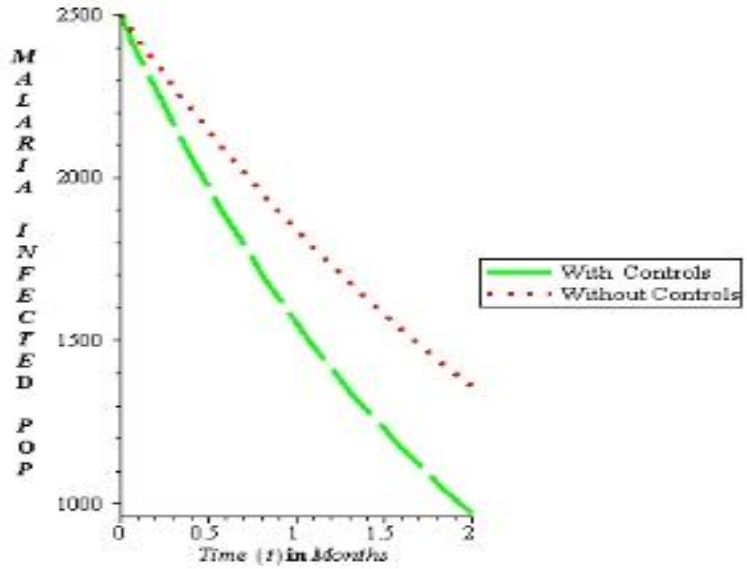


Figure 1: Optimal control graph of Malaria Infected Population with controls and without controls

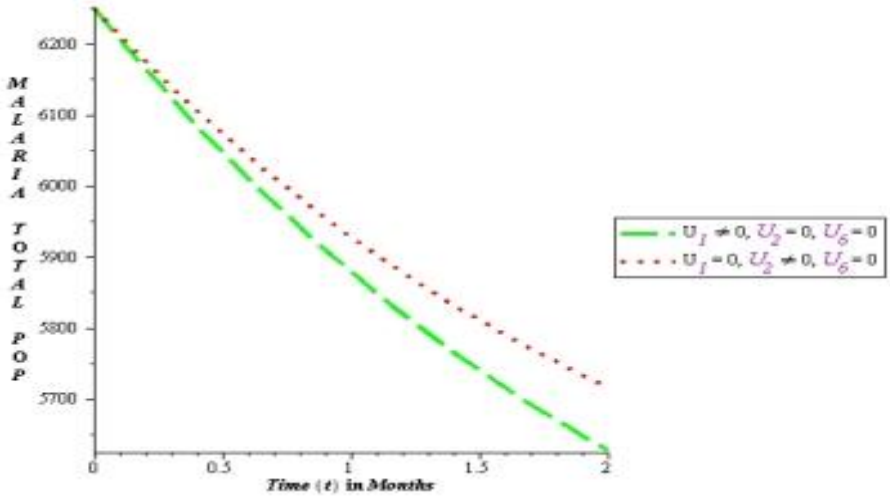


Figure 2: Optimal control graph of Malaria Total Population with prevention and treatment

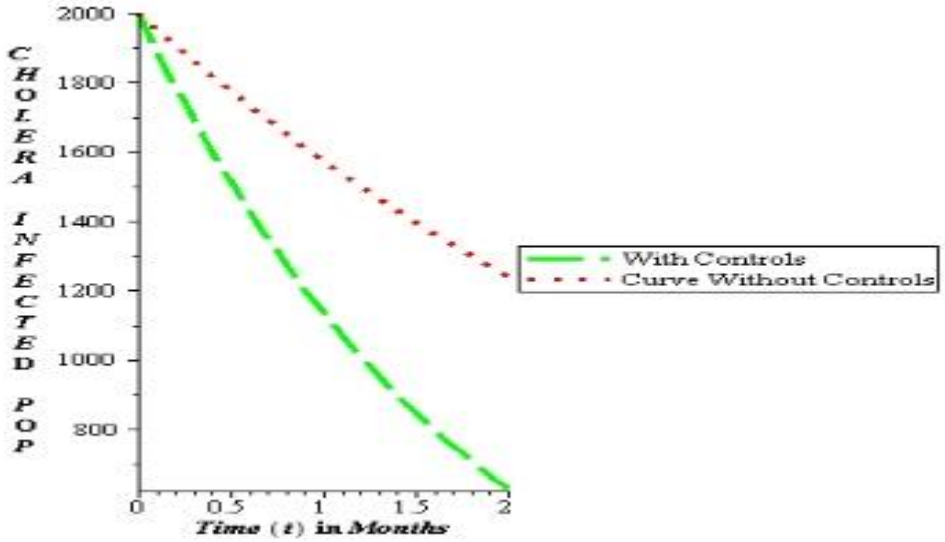


Figure 3: Optimal control graph of Cholera Infected Population with Controls and Without Controls

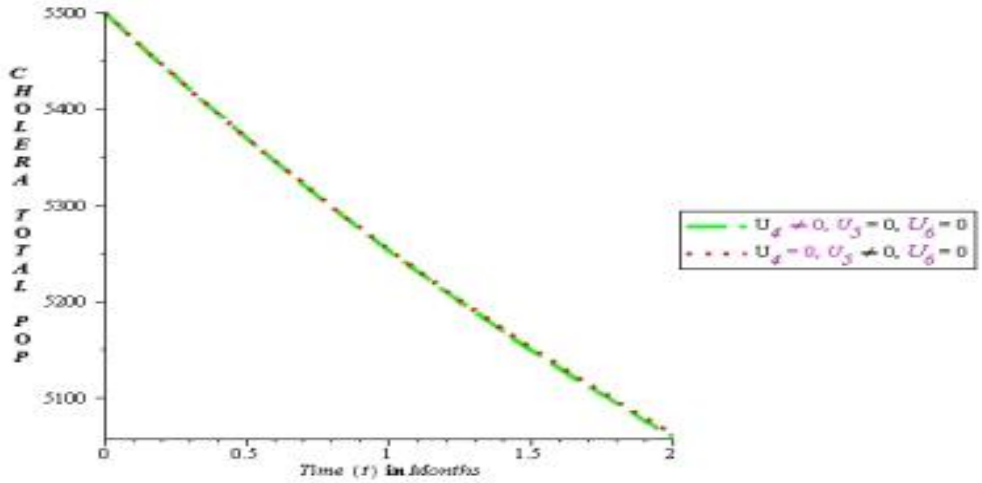


Figure 4: Optimal control graph of Total Cholera Population with Prevention and treatment

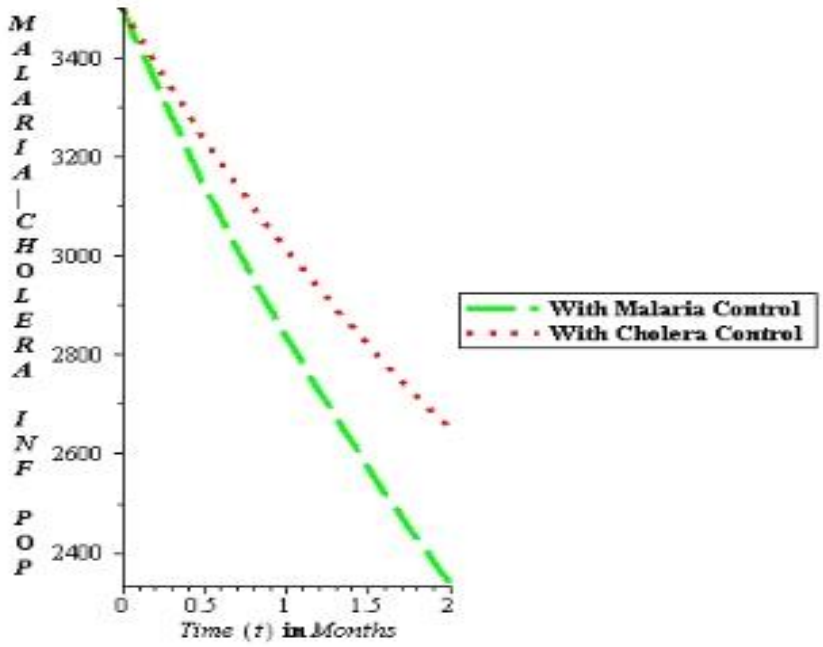


Figure 5: Optimal control graph of Malaria- Cholera Infected Population with malaria controls and cholera controls

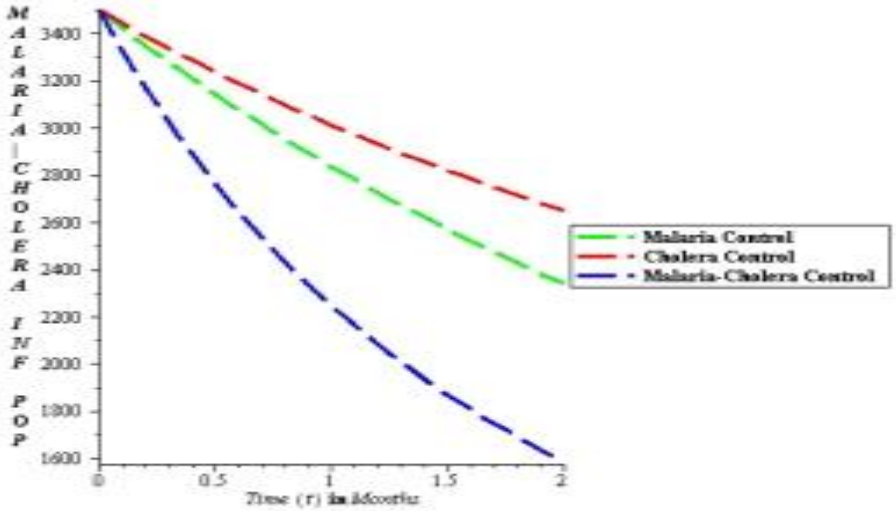


Figure 6: Optimal control graph of Malaria- Cholera Infected Population with different controls

Discussion of Results and Conclusion

In this paper, fourteen (14) non-linear compartmental models was presented and analyzed rigorously to gain insight on the impact of different controls implemented in curtailing the

spread of Malaria/Cholera Co-infection. Figure 1: shows the optimal control graph of Malaria Infected population with controls and without controls. It was discovered that all the controls implemented were efficient to curtail the spread of malaria in the population. Figure 2: Shows the optimal control graph of malaria total population with prevention and treatment. It was discovered that out of the two controls implemented, the use of treated bed nets played a crucial role in reducing the number of infected individual to zero level. Figure 3: shows the optimal control graph of cholera infected population with controls and without controls. It was discovered that all the control were efficient. Figure 4: shows the optimal control graph of cholera total population. It was discovered the prevention and treatment controls implemented were efficient to reduce the spread of cholera to zero level in the population. Figure 5: shows the optimal control graph of malaria/cholera co-infection infected population with malaria controls and cholera controls. It was discovered that the malaria controls implemented showed a great significant reduction to zero level compared to the cholera controls. Figure 6: shows the optimal control graph of malaria/cholera infected population with different controls. It was discovered that the prevention control is of great impact in order to reduce the spread of their co-infection. In conclusion, the work suggested that in order to curtail the spread of malaria/cholera diseases in the total population, efforts should be put in place to prevent every individuals against the spread of the two diseases. Also, adequate and prompt treatment should also be given to major priority in curtailing the spread of malaria/cholera co-infection in the entire population.

References

Adeniran, G. A., Olopade, I. A., Ajao S. O., Akinrinmade V. A., Aderele O. R. & Adewale, S. O. (2022). Sensitivity and Mathematical Analysis of Malaria and Cholera Co-Infection. *Asian Journal of Pure and Applied Mathematics*. https://globalpresshub.com/index.php /AJRMMS/article/view/1620

Adewale S.O., Adeniran G.A., Olopade I.A., Ajao S.O. and Mohammed I.T. (2017a) "Mathematical and Sensitivity Analysis of the Dynamical Spread of Cholera," *International Journal of Innovation and Applied Studies*, Vol. 19, No. 1, Pp. 46–54.

Adewale S.O., Omoloye M. A., Olopade I .A and Adeniran G.A (2017b): Mathematical Analysis for Dynamical Spread of Malaria in the Population with Controlling Measures. Innovative Space of Scientific Research Journals, Vol. 31 No. 2 Pp. 225-233.

Adewale, S.O., Adeniran, G.A., Olopade, I.A., and Mohammed, I.T. (2015). Mathematical analysis of the effect of growth rate of vibrio-cholera in the dynamical spread of cholera. Research journalli's Journal of Mathematics Vol. 2, No .3. March 2015. ISSN 2349-5375.

Adewale, S.O., Ajao, S.O., Olopade, I.A., Adeniran, G.A., and Oyewumi, A.A. (2016). Effect of Chemoprophylaxis Treatment on the Dynamical spread of Malaria. International Journal of Scientific and Engineering Research, Volume 7, Issue 1, January 2016. ISSN. 2229-5518.

Adewale, S.O., Olopade I. A., Adeniran G. A., Ajao S. O. and Mohammed I. T. (2017): Mathematical Analysis of Quarantine Individuals on the Dynamical Transmission of Diphtheria Disease. International Journal of Science and Engineering Investigations. (IJSEI), Vol. 6, Issue 64, Pp. 8-17.

Adesola, O.I., Oloruntoyin, S.S., Emmanuel, P.M., Temilade, M.I., Adeyemi, A.G., Oladele, A.S., Mamman, A.U., Kareem, A.A. (2024a): Mathematical Modelling and Analyzing the Dynamics of Condom Efficacy and Compliance in the Spread of HIV/AIDS. – Asian Research Journal of Current Science 6(1): 54-65.

Adesola, O.I., Temilade, M.I., Emmanuel, P.M., Oladele, A.S., Adeyemi, A.G., Sunday, S., Olumuyiwa, A.S. (2024b): Mathematical Analysis of Optimal Control of Human Immunodeficiency Virus (HIV) Co-infection with Tuberculosis (TB). – Asian Research Journal of Current Science 6(1): 23-53.

Ajao, S.O., Olopade, I.A., Akinwumi, T.O., Adewale, S.O and Adesanya, A.O.(2023). Understanding the transmission dynamics and control of HIV infection: A mathematical model approach.*Journal of the Nigerian Society of Physical Sciences***5**(2): 1389.

Akinwumi, T.O., Olopade, I.A., Adesanya, A.O and Alabi, M.O. (2021). A mathematical model for the transmission of hiv/aids with early treatment. *Journal of Advances in Mathematics and Computer Science***36**(5): 35–51.

Ali,M., Nelson,A.R.& SackD. (2015). Updated global burden of cholera in endemic countries. PLOS Negl Trop Dis 9(6),e0003832 https://doi:10.1371/journal.pntd.0003832.

Azman, A S., Rudolph, K.E.,Cummings, D.A.&Lesser, J. (2013). The incubation period of cholera: a-systematic review," Journal of Infection, 66(5), 432–438.

Castillo-Chavez, C., Feng, Z., and Huang, W. (2002). On the computation of R_0 and its role on global stability. Available at math.laasu.edu/chavez/2002/JB276.pdf

Chitnis, N., Cushing, J. M., and Hyman, J. M. (2006). Bifurcation analysis of mathematical model for malaria transmission. Society for Industrial and Applied Mathematics. (SIAM) Journal of Applied Mathematics. Vol. 67.No.1. pp. 24 – 45.

Colwell, R.R., and Huq, A. (1994). Environmental reservoir of vibro cholera, the causative agent of cholera. Ann. N.Y Acad. Sci., 740, 44-53.

Driessche, P., and Watmough, J. (2002). Reproduction numbers and sub-threshold endemic equilibrium for compartmental moels of disease transmission, Mathematical Biosciences 180, 29-48.

Hartley, D.M., MorrisJr, J.G., and Smith, D.L. (2006). Hyperinfectivity: a critical element in the ability of V.cholera to cause epidemic. PLos Med., 3(1), 63-69.

http://www.who. int/mediacentre/factsheets/fs107/en.

Lakshmkanthan, V., Leela, S., and Martynyuk, A.A. (1989). Stability Analysis of Non-Linear System. Marcel Dekker, Inc., New York and Basel.

Longini, I.M., Nizam, A., Ali, M., Yunus, M., Shenvi, N., and Clements, J.D. (2007). Controlling endemic cholera with oral vaccines. PLos Med., 4(11), 1776-1783.

Magambedze, G., Chiyaka, C., and Mukandavive. (2011). Optimal control of malaria chemotherapy, Nonlinear analysis: Modeling and Control. 16, No. 4(2011), 415-434.

Mahalanabis, A., Lopez, A.L., Sur, D., Deen, Jr, and Manna, B., (2008). A randomized, placebo controlled trial of the bivalent killed, whole-cell, oral cholera vaccine in adults and children in a cholera endemic area in Kolkata, Indian, PLos One, 3(6), 17.

Nelson, E.J., Chowdhuy, A., Flynn, J., Schild S., and Bourassa L. (2008). Transmission of vibrio Cholera antagonized by lytic phage and Entry into the Aquatic Environment. PLos Pathogens 4(10), 1-15.

Ochoche, J.M. (2013). A mathematical model for the transmission dynamics of cholera with control strategy. International Journal of science and technology Volume 2, No. 11, November 2013.

Olopade, I.A., Adesanya, A.O. and Akinwumi, T.O. (2021a). Mathematical Transmission of SEIR Epidemic Model with Natural Immunity.Asian Journal of Pure and Applied Mathematics. 3(1):19-29.

Olopade, I.A., Adewale, S.O., Mohammed, I.T., Adeniran, G.A., Ajao, S.O. and Ogunsola, A.W. (2021b). Effect of Effective Contact Tracing in Curtaining the Spread of Covid19. Asian Journal of Research in Biosciences. 3(2):118-134.

Olopade, I.A., Adesanya, A.O. and Mohammed, I.T. (2017). Mathematical Analysis of the Global Dynamics of an SVEIR Epidemic Model with Herd Immunity. International Journal of Science and Engineering Investigations. (IJSEI). 6(69):141-148.

Politzer, R. (1995). "Cholera studies" Bulletin of the world Health organization, Vol.13, No. 1, pp. 1-25.

Sarkar, B.L. (2002). "Cholera studies," Bulletin of the world Health Organization, Vol. 13. No 1, pp. 1-25.

Saymov, R.M. (1963). "Treatment and Prophylaxis of cholera with bacteriophage" Bulletin of the world Health Organization, Vol. 28,pp, 361-367. View at scopus.

Seidlein, L.V. (2007). Vaccines for Cholera Control: does herd immunity play a role? PLos med., 4(11), 1719-1721.

Shaima Al-Shanfari, Ibrahim M. Elmojtaba, Nasser Al-Salti and Fatima Al-Shandari (2024). Mathematical Analysis and Optimal control of Cholera-Malaria Co-infection model. Results in control and optimization 14(2024) 100393. ELSEVIER.

Sulyman Fatima, Isthrimayagy Krishnarajah, M.Z.A.M, Jaftar and Mohd Bakri Adam (2014). A Mathematical Model for the cpntrol of cholera in Nigeria. Research journal of Environmental and Earth Sciences 6(6): 321-325, 2014.

Summers, W.C. (2001). "Bacteriophage therapy", Annual Review of Microbiology, Vol. 55, pp.437-451. View at publisher. View at Google Scholar. View at Scopus.

Sur, D. (2009). Efficacy and Safety of a modified killed-whole-cell oral cholera vaccine in India; an interim analysis of a cluster-randomized, double-blind, Placebo-controlled trial. Lancet, 349, 1694-1702.

Tumwiine J., Hove-Musekwa S.D., Nyabadza F. International Scholarly Research Notices; 2014. A mathematical model for the transmission and spread of drug sensitive and resistant malaria strains within a human population. 2014.

WHO (World Health Organization), 2013a. Cholera 2012 wkly. Epidemiol. Rec., 88(31): 321-336

WHO (World Health Organization), 2013b. Media Center: Cholera. Retrieved from:

World Health Organisation. (2019, 17 January). Cholera fact sheets. https://www.who.int/newsroom/fact-sheets/detail/cholera

World Health Organization, World Malaria report, WHO press Switzerland (2012).

World Health Organization.10 facts on malaria, WHO online (2011).

Wurtz N., Pascual A., Marin-Jauffre A., Bouchiba H., Benoit N., Desbordes M., Briolant S. Early treatment failure during treatment of Plasmodium falciparum malaria with atovaquone-proguanil in the Republic of Ivory Coast. *Malaria Journal.* 2012;11(1):1–4. [PMC free article] [PubMed] [Google Scholar]

Yusuf O.B., Oladepo O., Odunbaku S.O., Alaba O., Osowole O.S. Factors associated with malaria treatment failures in Ibadan. *African Journal of Medicine & Medical Sciences.* 2005;34:251–258. [PubMed] [Google Scholar]

Zuckerman, J.N., Rombo, L., and Fish, A. (2007). The true burden risk of cholera: Implications for prevention and control. Lancet infect. Dis., 7(8), 521-53