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Analysis of a Mathematical Model for Malaria Transmission with Vaccination Parameter

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Abstract

Malaria remains a significant global health challenge, particularly in tropical regions. In this study, we extended the existing compartmental model of S. O. Adewale et al, (2017) by incorporating a vaccination parameter. We established the positivity of solutions, existence and uniqueness of solutions, and analyze the disease-free equilibrium (DFE). The basic reproduction number is derived using the next-generation matrix method, and local/global stability conditions were established. Numerical simulations were carried out to determine the impact of vaccination on the transmission dynamics of the disease. Our findings provide insights into effective malaria control strategies. Also, the result shows that effective vaccination can drastically eradicate the scourge of malaria within the shortest period of time.

Keywords: Basic Reproduction Number, Next generation matrix, Stability, Linearization, Equlibrium points

Introduction

Malaria is one of the deadliest diseases caused by parasite that lives part of its life in humans and the remaining in vectors. Malaria is a major killer of humans worldwide, claiming the lives of millions of people around the world. Malaria is widely spreads in the tropical areas of Asia, Africa, and Central and South America, where it affects millions of people. Each year, about 350 to 500 million cases of malaria recorded globally. However, more than one million of its victims, mostly young children, die yearly, though, malaria has been virtually eradicated in the United States and other regions with temperate climates (Samwel Oseko Nyachae, et al 2014).

Malaria is caused by a single-celled parasite from the genus plasmodium, different species of plasmodium exist. They produce malaria in various types of animals and birds, as well in humans. Four of these species of plasmodium commonly infect humans. Each one has a different appearance under the microscope, and each one produces a somewhat different pattern of symptoms. More than two species can live in the same area and infect a single person at the same time. Plasmodium falciparum is responsible for most malaria deaths, especially in Africa. Suddenly, the infection can develop and produce several life-threatening complications. With prompt and effective treatment, however, it is almost always curable.

Malaria parasite is transmitted to people through genus Anopheles mosquitoes. In rare cases, a person may become infected through contaminated blood, or a fetus may become infected by its mother during pregnancy, or after delivery. Also, because the malaria parasite is found in RBCs, malaria can also be transmitted through the unscreened, blood transfusion, organ transplant, or the shared use of needles or syringes contaminated with blood. Many biological and environmental factors shape the character of malaria in a given location, nearly all the people who live in endemic areas are exposed to infection repeatedly. Those who survive malaria in childhood gradually build up some immunity. They may carry the infection, serving as a mode of transmission by vectors without developing severe disease (U.S. department of health and human service, national institute of allergy and diseases 2007).

Vaccination represents a promising tool in the fight against malaria. The development of malaria vaccines has been challenging due to the complexity of the parasite's lifecycle and the immune system's difficulty in targeting it. However, recent breakthroughs, such as the

RTS,S/AS01 vaccine (RTS,S), have shown that vaccines can reduce malaria incidence and mortality, especially in high-risk populations. As vaccination campaigns gain momentum, understanding the broader implications of vaccination on malaria transmission is crucial to optimizing control strategies.

Overview of Malaria Epidemiology

Malaria, caused by a protozoan parasite Plasmodium falciparum, is transmitted to humans by the bite of an infected and infectious female mosquito of the genus Anophe-les. It remains one of the major causes of morbidity and mortality (Molineaux, et al. 2001). Malaria is most common in the tropical regions especially Africa (Menach, et al. 2005). There are estimated 300-500 million clinical cases and there are between 1-1.5 million malaria related deaths annually. Though preventable and curable, controlling malaria has become more and more challenging as the malaria parasite becomes resistant to prophylactic drugs (Greenwood, et al. 2002) and as the mosquito that transmits the parasite develops resistance to insecticides (Hemingway, et al. 2002). Although child mortality in Africa has declined in recent years, malaria's share of that mortality has increased because of the spread of drug resistance of the parasite, the breakdown of health services in many affected areas, the interaction of the disease with human immunodeficiency virus (HIV) infection, and possibly the effects of climate change (Greenwood, et al. 2005). Traditional means of controlling malaria may save many lives, but they alone cannot adequately prevent the misery and deaths this devastating disease causes. Nor can they alone erase the enormous impact of malaria on local and national economic development (Gallup, et al. 2001).

Malaria control efforts include attempts to develop effective vaccines, eradicate mosquito vectors and develop new drugs (Olliaro, et al. 1996). Historically, vaccines have been one of the most cost effective and easily administered means of controlling infectious diseases, yet no licensed vaccines exist for malaria. The first report of human protection from malaria by vaccination was made in 1973 (Clyde, et al. 1973). History on malaria vaccination attempts is documented (Moorthy, et al. 2004). Accumulating basic and clinical research suggests that effective vaccines for malaria can be developed and could significantly reduce morbidity and mortality and potentially reduce spread of infection (Brown, 1991). The progress is slowed down by the parasite's intricate life cycle which has

distinct developmental stages in both the host and the vector. A vaccine effective in killing one stage may not inhibit the growth of the other (Dunavan, 2005). The stages involved in the movement of the parasite between host and vector are well documented (Bailey, 1982). The human immune response to Plasmodium falciparum is also well documented (Good, et al. 2005).

Malaria vaccines should be designed to protect people from disease and death, boosting the immune system to combat parasites. But unless a malaria vaccine leads to the death of every single parasite, the ones that survive could continue to circulate in a vaccinated population. An optimum vaccine should then have the ability to elicit protective immunity that blocks infection as well as prevent pathology and interrupt transmission of parasites. The most effective vaccine should be comprised of subunits from different parasite stages. These subunits are as follows:

a. Pre-erythrocytic vaccine protects against the infectious form injected by the anopheles mosquito (sporozoite) by inhibiting invasion of liver cells and /or inhibit parasite development in the liver. This is done by first targeting the parasite during the short time span that the sporozoites are in the bloodstream. Production of protective antibodies that will block and neutralize sporozoites from invading liver cells should be induced by the sporozoite vaccine. Secondly, sporozoites can be targeted once they are inside the liver cells, through induction of cytotoxic T-lymphocytes (CTLs) that will destroy sporozoite infected liver cells.

b. Erythrocytic (blood stage) vaccine prevents merozoites from infecting red blood cells and when inside the red blood cells antibodies can be directed towards malaria antigens that are expressed on the surface of red blood cells to inhibit parasite multiplication in the red blood cells or destroying infected cells, thus preventing (or diminishing) severe disease during blood infection (Holder, et al. 1999).

c. Transmission blocking (sexual stage) vaccine interrupts the cycle of transmission by inhibiting further development of parasites once they-along with anti-bodies produced in response are ingested by the mosquito. This vaccine does not prevent the disease in an infected host but is important in reducing the spread of malaria to new hosts.

Although modelling vaccination in other epidemic diseases has been done (Arino, et al. 2003) for malaria vaccination, a few analytic studies of stage-specific malaria vaccines have been done mathematically. (Anderson, et al. 1989) They assumed that the pre-erythrocytic

vaccine completely blocks infection so none of the vaccinated humans become infected as long as the vaccine does not wear off. They also considered the transmission blocking vaccine to block transmission to mosquitoes. They assumed a vaccination strategy that immunizes a fraction of infants before the age of infection. Struchiner et al. (Struchiner, et al. 1989) built upon the model of Dietz et al. (Dietz, et al. 1974) and considered natural immunity that can wane with time but its duration and effectiveness is prolonged by boosting from natural infection. On this model they considered the effects of stage specific vaccines independently (Halloran, et al. 1989). They considered a constant population and did not include disease induced death rate. de Zoysa (de Zoysa, 1990) also basing his model on that of Dietz et al. (Dietz, et al. 1974) developed it to account for transmission blocking immunity in an endemic area. Vaccine-induced immunity is assumed to be lost if not boosted within four months. These models have also been reviewed. The following aspects considered in our model differentiate it from those that have been done: we considered a variable population, vaccination is done throughout the susceptible population, the three subunits of malaria vaccine have been combined to determine their overall effect, we considered disease induced death rate and have been able to get critical vaccination rates for the different vaccines if considered singly and/or combined. We did not consider acquired natural immunity. This makes our model more suitable for describing the situation in non-endemic populations (Anderson, et al. 1991). In formulating our model we consider the dynamics of malaria infection including both human and mosquito populations. The uninfected class of humans is divided into two groups which are susceptibles which are not vaccinated and vaccinated groups. We assume that if the pre-erythrocytic vaccine is less than completely effective, then even a few sporozoites that emerge from the liver cause the host to suffer clinical malaria (Richie, and A. Saul, 2002). In all, only few studies have incorporated vaccination as a control strategy for malaria. And this will become the area concern of our studies.

Malaria Vaccine

Malaria vaccines are vaccines that prevent malaria, a mosquito-borne infectious disease which affected an estimated 249 million people globally in 85 malaria endemic countries and areas and caused 608,000 deaths in 2022. The first approved vaccine for malaria is RTS,S, known by the brand name Mosquirix. As of April 2023, the vaccine has been given

to 1.5 million children living in areas with moderate-to-high malaria transmission. It requires at least three doses in infants by age 2, and a fourth dose extends the protection for another 1–2 years.The vaccine reduces hospital admissions from severe malaria by around 30%. Research continues with other malaria vaccines. The most effective malaria vaccine is the R21/Matrix-M, with a 77% efficacy rate shown in initial trials and significantly higher antibody levels than with the RTS,S vaccine. It is the first vaccine that meets the World Health Organization's (WHO) goal of a malaria vaccine with at least 75% efficacy, and only the second malaria vaccine to be recommended by the WHO. In April 2023, Ghana's Food and Drugs Authority approved the use of the R21 vaccine for use in children aged between five months and three years old. Following Ghana's decision, Nigeria provisionally approved the RTS vaccine.

Malaria vaccine was developed by assessing many new vaccine technologies including novel adjuvants, vectored prime-boost regimes, and the concept of community vaccination to block malaria transmission. Of all these, RTS,S is the first and, to date, the only vaccine to show a protective effect against malaria and provide meaningful public health benefit by reducing the burden of malaria when used alongside currently available interventions such as bed nets and insecticides among young. RTS,S is a recombinant protein-based malaria vaccine. Phase III results showed that three doses of RTS,S reduced clinical malaria by approximately half in children 5–17 months of age at first vaccination. In a subsequent analysis after 18 months of follow-up, children vaccinated with RTS,S experienced 46% fewer cases of clinical malaria, compared to children immunized with a comparator vaccine. Hence, The WHO Regional Office for Africa announced on April 24, 2017, that Ghana, Kenya, and Malawi will partner with WHO in the Malaria Vaccine Implementation Programme that will make the RTS,S vaccine available in selected areas of the three countries, beginning in 2018.

Model Formulation

In this section, we will focus on the construction of a mathematical model that incorporates vaccination as an intervention to assess its impact on malaria transmission dynamics. Specifically, we will build on an existing model equation with modifications to account for malaria-specific factors like vector dynamics, immunity, and vaccination coverage.

Existing Model Equation

Existing model equation by S. O. Adewale *et al,* (2017)

$$\frac{dS_h}{dt} = \pi_h + \psi R_h + \alpha_h S_h - \mu_h S_h$$

$$\frac{dE_h}{dt} = \alpha_h S_h - \kappa_h E_h - \mu_h E_h$$

$$\frac{dI_h}{dt} = \kappa_h E_h - rI_h - (\mu_h + \delta)I_h - \tau I_h$$

$$\frac{dT_h}{dt} = \tau I_h - \varepsilon T_h - \mu_h T_h$$

$$\frac{dR_h}{dt} = rI_h + \varepsilon T_h - \psi R_h - \mu_h R_h$$

$$\frac{dS_v}{dt} = \pi_v - \alpha_v S_v - \mu_v S_v$$

$$\frac{dE_v}{dt} = \alpha_v S_v - \kappa_v E_v - \mu_v E_v$$

$$\frac{dI_v}{dt} = \kappa_v E_v - \mu_v I_v \qquad (1)$$

With initial condition $S_h(0) = S_{h0}$, $E_h(0) = E_{h0}$, $I_h(0) = I_{h0}$, $T_h(0) = T_{h0}(0)$, $R_h(0) = R_{h0}(0)$, $S_v(0) = S_{v0}(0)$, $E_v(0) = E_{v0}(0)$, $I_v(0) = I_{v0}(0)$

Where $\alpha_h = \frac{\beta_{vh}\emptyset I_v}{N_v}$ and $\alpha_v = \frac{\beta_{hv}\emptyset(E_h + \eta I_h)}{N_h}$ in the model. The term $\frac{\beta_{vh}\emptyset I_v}{N_v}$ denotes the rate at which the susceptible humans S_h becomes infected by infectious female vectors I_v, and $\frac{\beta_{hv}\emptyset(E_h + \eta I_h)}{N_h}$ refers to the rate at which the susceptible vector S_v becomes infected by infectious humans I_h.

A system of differential equations are introduced to model the impact of vaccination on the dynamics of malaria in two interacting population of humans and vector. We divide the total human population N_h(t), into susceptible humans S_h(t), Exposed humans E_h(t), Infectious humans I_h(t), Treated humans T_h(t), and Recovered humans R_h(t)

i.e. $N_h(t) = S_h(t) + E_h(t) + I_h(t) + T_h(t) + R_h(t)$.

Unlike human's population, we divide the vector population into three subclasses: Susceptible vector S_v(t), Exposed vector E_v(t), and Infectious vector I_v(t). The vector

remain infectious for life and have no recovered class. Thus, the total size of the vector population at any time (t) is denoted by $N_v(t) = S_v(t) + E_v(t) + I_v(t)$.

The population of susceptible human is increased through recruitment of humans (by birth or immigration) into the society at rate π_h, and by recovered humans at rate ψ due to waning of immunity acquired after successful treatment. It is decreased by infection acquired through bite with infected vector at rate α_h, and natural death at rate μ_h. This gives $\frac{dS_h}{dt} = \pi_h + \psi R_h - \alpha_h S_h - \mu_h S_h$

An exposed human is generated through infection of susceptible at rate α_h. It reduces due to progression of human from exposed to infectious at rate κ_h, and natural death at rate μ_h. Thus,

$$\frac{dE_h}{dt} = \alpha_h S_h - \kappa_h E_h - \mu_h E_h$$

Infected human is generated through progression of humans exposed to vectors at rate κ_h. It diminishes due to recovery at rate r, natural death at rate μ_h, vector induced death rate δ and treatment of infected human at rate τ. Therefore, $\frac{dI_h}{dt} = \kappa_h E_h - rI_h - (\mu_h + \delta)I_h - \tau I_h$

The treated human is generated by the treatment of human from infection at rate τ. It reduces through progression from treatment to recovery at rate ε, and natural death at rate μ. Thus,

$$\frac{dT_h}{dt} = \tau I_h - \varepsilon T_h - \mu_h T_h$$

The recovered humans are generated by the recovery of infected human and the progression from treatment to recovery at rate ε. It decreases by loss of immunity at rate ψ, and natural death at rate ψ_h. Thus, $\frac{dR_h}{dt} = rI_h + \varepsilon T_h - \psi R_h - \mu_h R_h$

The susceptible vector is generated through recruitment of vector (by birth or immigration) at rate π_v. It is reduced by infection, acquired when susceptible vector bite infected humans at rate α_v, and by natural death at rate μ_v. This yield $\frac{dS_v}{dt} = \pi_v - \alpha_v S_v - \mu_v S_v$

The population of exposed vector is generated through infection of susceptible at rate α_v. It is decreased progression of vector from exposed to infectious at rate κ_v, and also by natural death at rate μ_v. Thus, $\frac{dE_v}{dt} = \alpha_v S_v - \kappa_v E_v - \mu_v E_v$

The infected vector is generated through progression of vector from exposed to infectious class at rate κ_v. It is reduced by natural death at rate μ_v. Hence, $\frac{dI_v}{dt} = \kappa_v E_v - \mu_v I_v$

Modified Model Equation

$$\frac{dS_h}{dt} = \pi_h + \psi R_h - \alpha_h S_h - \mu_h S_h - \upsilon S_h$$

$$\frac{dE_h}{dt} = \alpha_h S_h - \kappa_h E_h - \mu_h E_h$$

$$\frac{dI_h}{dt} = \kappa_h E_h - rI_h - (\mu_h + \delta) I_h - \tau I_h$$

$$\frac{dT_h}{dt} = \tau I_h - \varepsilon T_h - \mu_h T_h$$

$$\frac{dR_h}{dt} = rI_h + \varepsilon T_h + \upsilon S_h - \psi R_h - \mu_h R_h$$

$$\frac{dS_v}{dt} = \pi_v - \alpha_v S_v - \mu_v S_v$$

$$\frac{dE_v}{dt} = \alpha_v S_v - \kappa_v E_v - \mu_v E_v$$

$$\frac{dI_v}{dt} = \kappa_v E_v - \mu_v I_v \qquad (2)$$

Table 1. **Variables and parameters description**

Variables/parameters	Description
S_h(t)	Number of susceptible humans at time t.
E_h(t)	Number of exposed humans at time t.
I_h(t)	Number of infected humans at time t.
T_h(t)	Number of treated humans at time t.
R_h(t)	Number of recovered humans at time t.
S_v(t)	Number of susceptible vectors at time t.
E_v(t)	Number of exposed vectors at time t.
I_v(t)	Number of infected vectors at time t.
N_h(t)	Total number of human population at time t.
N_v(t)	Total number of vector population at time t.
π_h	Recruitment rate of humans.

ψ	Rate of loss of immunity.
α_h	Force of infection of humans from susceptible state to exposed state.
μ_h	Natural death rate for humans.
κ_h	Rate of progression of humans from the exposed state to the infectious state.
τ	Treatment of humans from the infectious state to recovered state.
r	Recovery rate of infected humans.
ε	Progression rate from treated to recovered class.
π_v	Recruitment rate for vector.
α_v	Force of infection of vector from susceptible state to exposed state.
μ_v	Natural death rate for vector.
δ	Disease-induced death rate for humans
κ_v	Rate of progression of vector from the exposed state to the infectious state.
β_{vh}	Probability of transmission of infection from an infectious vector to a susceptible human provided there is a bite.
β_{hv}	The probability of transmission of infection from an infected human to a susceptible vector provided there is bite.
$\emptyset$	Biting rate of vector.
v	Vaccination rate for humans

The total population sizes are $N_h = S_h + E_h + I_h + T_h + R_h$ and $N_v = S_v + E_v + I_v$ with their differential equations

$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dE_h}{dt} + \frac{dI_h}{dt} + \frac{dT_h}{dt} + \frac{dR_h}{dt} = \pi_h - \mu_h N_h - \delta I_h$ and $\frac{dN_v}{dt} = \frac{dS_v}{dt} + \frac{dE_v}{dt} + \frac{dI_v}{dt} = \pi_v - \mu_v N_v$

Model Analysis

The modified malaria transmission dynamics with vaccination parameter are governed by the following system of differential equations:

$$\frac{dS_h}{dt} = \pi_h + \psi R_h - \alpha_h S_h - \mu_h S_h - v S_h$$

$$\frac{dE_h}{dt} = \alpha_h S_h - \kappa_h E_h - \mu_h E_h$$

$$\frac{dI_h}{dt} = \kappa_h E_h - r I_h - (\mu_h + \delta) I_h - \tau I_h$$

$$\frac{dT_h}{dt} = \tau I_h - \varepsilon T_h - \mu_h T_h$$

$$\frac{dR_h}{dt} = rI_h + \varepsilon T_h + vS_h - \psi R_h - \mu_h R_h$$

$$\frac{dS_v}{dt} = \pi_v - \alpha_v S_v - \mu_v S_v$$

$$\frac{dE_v}{dt} = \alpha_v S_v - \kappa_v E_v - \mu_v E_v$$

$$\frac{dI_v}{dt} = \kappa_v E_v - \mu_v I_v$$

where S_h, E_h, I_h, T_h, R_h are human compartments and S_v, E_v, I_v are vector compartments.

Existence and Uniqueness of Solutions

Theorem 1: **(Existence and Uniqueness)** If the function $F(X)$ satisfies the Lipschitz condition, then the system has a unique solution.

Proof: By the Picard-Lindelöf theorem, if $F(X)$ is continuously differentiable, then the system has a unique global solution.

Positivity and Boundedness of Solutions

To ensure that the model is well-posed, we must prove that all solutions remain positive for all time $t \geq 0$ and that the total population remains bounded.

Positivity of Solutions

Theorem 2: If the initial conditions satisfy:

$$S_h(0) \geq 0, E_h(0) \geq 0, I_h(0) \geq 0, T_h(0) \geq 0, R_h(0) \geq 0,$$

$$S_v(0) \geq 0, E_v(0) \geq 0, I_v(0) \geq 0,$$

then the solutions $S_h(t), E_h(t), I_h(t), T_h(t), R_h(t), S_v(t), E_v(t), I_v(t)$ remain non-negative for all $t \geq 0$.

Proof: Consider the first equation:

$$\frac{dS_h}{dt} = \pi_h + \psi R_h - a_h S_h - \mu_h S_h - V_h S_h.$$

Since all terms on the right-hand side are non-negative or involve a negative coefficient of S_h, it follows that if $S_h(0) \geq 0$, then $S_h(t)$ remains non-negative for all $t \geq 0$.

Similarly, the other equations can be analyzed:

- The equation for E_h has a non-negative term $a_h S_h$ and negative terms involvingE_h, ensuring E_h remains non-negative.
- The equations for I_h, T_h, R_h, and the vector population variables S_v, E_v, I_v follow the same reasoning.

Thus, all state variables remain positive for all $t \geq 0$.

Boundedness of Solutions

Theorem 3: The total human population N_h and the total vector population N_v are bounded.

Proof: Summing all human-related equations:

$$\frac{dN_h}{dt} = \frac{d}{dt}(S_h + E_h + I_h + T_h + R_h)$$

$$= \pi_h - \mu_h S_h - \mu_h E_h - (\mu_h + \delta) I_h - \mu_h T_h - \mu_h R_h.$$

Since all terms on the right-hand side are negative except for recruitment π_h, it follows that there exists an upper bound $N_h \leq \frac{\pi_h}{\mu_h}$. Similarly, for the vector population $\frac{dN_v}{dt} = \pi_v - \mu_v N_v$.

Solving for N_v, we get $N_v \leq \frac{\pi_v}{\mu_v}$, proving boundedness.

Disease-Free Equilibrium (DFE)

To find the DFE, we set all infected compartments to zero: $E_h = I_h = T_h = R_h = E_v = I_v = 0$.

Solving the system at equilibrium: $\pi_h - \mu_h S_h - V_h S_h = 0 \Rightarrow S_h^0 = \frac{\pi_h}{\mu_h + V_h}$.

$$\pi_v - \mu_v S_v = 0 \Rightarrow S_v^0 = \frac{\pi_v}{\mu_v}.$$

Thus, the disease-free equilibrium is $E_0 = \left(\frac{\pi_h}{\mu_h + V_h}, 0,0,0,0, \frac{\pi_v}{\mu_v}, 0,0\right)$.

The Basic Reproduction Number R_o

The basic reproduction number R_o measures the average number of new infections generated by a single infected person during his or her infectious period in a population that is fully susceptible Diekmann *et al.* (1990). One can easily predict if an infection will spread in exponential progression, die off after some time or remain constant with no further spread judging from the value of the reproduction number. When $R_o < 1$, the disease will die off because every infected person will transmit the disease to less than one person in the transmittable period. When $R_o = 1$, the disease will become endemic and will stay with each infected person transmitting to one new person. When $R_o > 1$, a disease will spread and the infected people will grow exponentially which will in the end lead to a pandemic. Using next generation method, the basic reproduction number (R_o) is given as $R_0 = \rho(FV^{-1})$ where ρ is the spectral radius.

Given the matrices F and V below,

The new infection rate matrix F is: $F = \begin{bmatrix} 0 & 0 & a_h & 0 \\ 0 & 0 & 0 & 0 \\ a_v & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$

Thus, the transition and recovery matrix V is:

$$V = \begin{bmatrix} \kappa_h + \mu_h & 0 & 0 & 0 \\ -\kappa_h & r + \mu_h + \delta + \tau & 0 & 0 \\ 0 & 0 & \kappa_v + \mu_v & 0 \\ 0 & 0 & -\kappa_v & \mu_v \end{bmatrix}$$

The matrices F and V help analyze the stability and dynamics of the disease model. These matrices are used in the Next Generation Matrix Method to determine the basic reproduction number R_0 which is crucial for understanding disease spread.

The next-generation matrix is given by $FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{a_h}{\kappa_v + \mu_v} & 0 \\ 0 & 0 & 0 & 0 \\ \frac{a_v}{\kappa_h + \mu_h} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$

Evaluating the determinant and simplifying gives

$$\begin{vmatrix} -\lambda & 0 & \frac{a_h}{\kappa_v+\mu_v} & 0 \\ 0 & -\lambda & 0 & 0 \\ \frac{a_v}{\kappa_h+\mu_h} & 0 & -\lambda & 0 \\ 0 & 0 & 0 & -\lambda \end{vmatrix} = 0$$

$$\lambda = \pm\sqrt{\frac{a_h a_v}{(\kappa_h+\mu_h)(\kappa_v+\mu_v)}}$$

Since the basic reproduction number R_0 is the largest eigenvalue, hence

$$R_0 = \sqrt{\frac{a_h a_v}{(\kappa_h+\mu_h)(\kappa_v+\mu_v)}}$$

Where $\alpha_h = \frac{\beta_{vh}\emptyset I_v}{N_v}$ and $\alpha_v = \frac{\beta_{hv}\emptyset(E_h+\eta I_h)}{N_h}$

Local Stability Analysis of Disease-Free Equilibrium

Theorem 4:

The disease-free equilibrium (DFE) E_0 is locally asymptotically stable if the basic reproduction number satisfies $R_0 < 1$. If $R_0 > 1$, the DFE is unstable.

The Jacobian matrix J corresponding to the modified model equation (2) is defined as:

J

$$= \begin{bmatrix} -a_h-\mu_h-V_h & 0 & 0 & 0 & \psi & 0 & 0 & 0 \\ a_h & -\kappa_h-\mu_h & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \kappa_h & -r-(\mu_h+\delta)-\tau & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau & -\varepsilon-\mu_h & 0 & 0 & 0 & 0 \\ \mathrm{v} & 0 & r & \varepsilon & -\psi-\mu_h & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -a_v-\mu_v & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & a_v & -\kappa_v-\mu_v & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \kappa_v & -\mu_v \end{bmatrix}$$

Solving for the eigenvalues, we have

$J-\lambda I$

$$= \begin{bmatrix} -a_h-\mu_h-V_h-\lambda & 0 & 0 & 0 & \psi & 0 & 0 & 0 \\ a_h & -\kappa_h-\mu_h-\lambda & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \kappa_h & -r-(\mu_h+\delta)-\tau-\lambda & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau & -\varepsilon-\mu_h-\lambda & 0 & 0 & 0 & 0 \\ \mathrm{v} & 0 & r & \varepsilon & -\psi-\mu_h-\lambda & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -a_v-\mu_v-\lambda & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & a_v & -\kappa_v-\mu_v-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \kappa_v & -\mu_v- \end{bmatrix}$$

The determinant simplifies into:

$$\det(J - \lambda I) = \det(J_h - \lambda I) \cdot \det(J_v - \lambda I) = 0$$

where:

$$J_h = \begin{bmatrix} -a_h - \mu_h - V_h & 0 & 0 & 0 & \psi \\ a_h & -\kappa_h - \mu_h & 0 & 0 & 0 \\ 0 & \kappa_h & -r - (\mu_h + \delta) - \tau & 0 & 0 \\ 0 & 0 & \tau & -\varepsilon - \mu_h & 0 \\ \mathrm{v} & 0 & r & \varepsilon & -\psi - \mu_h \end{bmatrix}$$

$$J_v = \begin{bmatrix} -a_v - \mu_v & 0 & 0 \\ a_v & -\kappa_v - \mu_v & 0 \\ 0 & \kappa_v & -\mu_v \end{bmatrix}$$

With Vector-related block reducing to

$$\begin{vmatrix} -a_v - \mu_v - \lambda & 0 & 0 \\ a_v & -\kappa_v - \mu_v - \lambda & 0 \\ 0 & \kappa_v & -\mu_v - \lambda \end{vmatrix} = 0$$

gives the three eigenvalues $\lambda_6 = -a_v - \mu_v, \lambda_7 = -\kappa_v - \mu_v, \lambda_8 = -\mu_v$

Similarly with the Human-related block, the characteristic equation for J_h is $\det(J_h - \lambda I) = 0$

which results in a quadratic equation $in\ \lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ These eigenvalues depend on $a_h, \mu_h, V_h, \kappa_h, r, \delta, \tau, \varepsilon, \psi$. The full set of eigenvalues is $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ from solving $\det(J_h - \lambda I) = 0$, and $\lambda_6 = -a_v - \mu_v,\ \lambda_7 = -\kappa_v - \mu_v,\ \lambda_8 = -\mu_v$ from J_v.

Since all eigenvalues have negative real parts, the system is Locally and Asymptotically Stable

Global Stability Analysis of Disease-Free Equilibrium

Theorem 5: The disease-free equilibrium (DFE) E_0 is globally asymptotically stable if the basic reproduction number satisfies $R_0 < 1$. That is,

$$\lim_{t \to \infty} (E_h, I_h, T_h, E_v, I_v) = (0,0,0,0,0).$$

Proof: We define the Lyapunov function $V = E_h + I_h + T_h + E_v + I_v$.

Differentiating along system trajectories $\frac{dV}{dt} = \frac{dE_h}{dt} + \frac{dI_h}{dt} + \frac{dT_h}{dt} + \frac{dE_v}{dt} + \frac{dI_v}{dt}$.

Substituting from the system equations $\frac{dV}{dt} = (\alpha_h S_h - \kappa_h E_h - \mu_h E_h) + (\kappa_h E_h - rI_h - (\mu_h + \delta)I_h - \tau I_h) + (\tau I_h - \varepsilon T_h - \mu_h T_h) + (\alpha_v S_v - \kappa_v E_v - \mu_v E_v) + (\kappa_v E_v - \mu_v I_v)$.

Rearranging $\frac{dV}{dt} = \alpha_h S_h + \alpha_v S_v - (\kappa_h + \mu_h)E_h - (r + \mu_h + \delta + \tau)I_h - (\varepsilon + \mu_h)T_h - (\kappa_v + \mu_v)E_v - \mu_v I_v$, since $R_0 < 1$, we get $\frac{dV}{dt} \leq 0$.

By LaSalle's Invariance Principle, the system approaches the largest invariant set where $\frac{dV}{dt} = 0$, which is $E_h = I_h = T_h = E_v = I_v = 0$, corresponding to the disease-free equilibrium.

Hence, The disease-free equilibrium is globally asymptotically stable whenever $R_0 < 1$.

Sensitivity Analysis of R_0

The sensitivity index of R_0 with respect to a parameter p is given by $\Upsilon_{R_0}^{p} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0}$.

From the previous derivation, we have $R_0 = \sqrt{\frac{a_h a_v}{(\kappa_h+\mu_h)(\kappa_v+\mu_v)}}$.

Sensitivity of R_0 to Key Parameters

a. Sensitivity of R_0 to a_h (Human Infection Rate)

$$\frac{\partial R_0}{\partial a_h} = \frac{1}{2}\left(\frac{1}{a_h}\right)R_0 = \frac{1}{2}\frac{R_0}{a_h}.$$

Thus, the sensitivity index is $\Upsilon_{R_0}^{a_h} = \frac{1}{2}$.

b. Sensitivity of R_0 to a_v (Vector Infection Rate), similarly, $\Upsilon_{R_0}^{a_v} = \frac{1}{2}$.

c. Sensitivity of R_0 to κ_h (Progression Rate in Humans)

$$\frac{\partial R_0}{\partial \kappa_h} = -\frac{1}{2}\left(\frac{1}{\kappa_h + \mu_h}\right)R_0$$

$$\Upsilon_{R_0}^{\kappa_h} = -\frac{1}{2}\frac{\kappa_h}{\kappa_h + \mu_h}.$$

d. *Sensitivity of* R_0 *to* μ_h *(Human Death/Exit Rate)*

$$\Upsilon_{R_0}^{\mu_h} = -\frac{1}{2}\frac{\mu_h}{\kappa_h + \mu_h}.$$

e. *Sensitivity of* R_0 *to* κ_v *(Progression Rate in Vectors)*

$$\Upsilon_{R_0}^{\kappa_v} = -\frac{1}{2}\frac{\kappa_v}{\kappa_v + \mu_v}.$$

Sensitivity Summary

Parameter	Sensitivity Index $\Upsilon_{R_0}^{p}$	Effect on R_0
Human infection rate (a_h)	$\frac{1}{2}$	Increase ⇒ Increases R_0
Vector infection rate (a_v)	$\frac{1}{2}$	Increase ⇒ Increases R_0
Human progression rate (κ_h)	$-\frac{1}{2}\frac{\kappa_h}{\kappa_h + \mu_h}$	Increase ⇒ Decreases R_0
Vector progression rate (κ_v)	$-\frac{1}{2}\frac{\kappa_v}{\kappa_v + \mu_v}$	Increase ⇒ Decreases R_0
Human mortality (μ_h)	$-\frac{1}{2}\frac{\mu_h}{\kappa_h + \mu_h}$	Increase ⇒ Decreases R_0

Model Parameterization

The following table provides the parameter values used in the numerical simulations.

Table 2: Parameter values used in the simulations.

Parameter	Description	Value
β_{vh}	Transmission rate (vector to human)	0.3
β_{hv}	Transmission rate (human to vector)	0.25
μ_h	Human natural death rate	0.0005
μ_v	Vector natural death rate	0.02
κ_h	Incubation rate (human)	0.1
κ_v	Incubation rate (vector)	0.1
π_h	Human recruitment rate	100
π_v	Vector recruitment rate	200
v	Vaccination rate	Variable

Numerical Simulations

Numerical simulations were carried out to show the effects of vaccination on the modified model. The graphical illustration are presented below

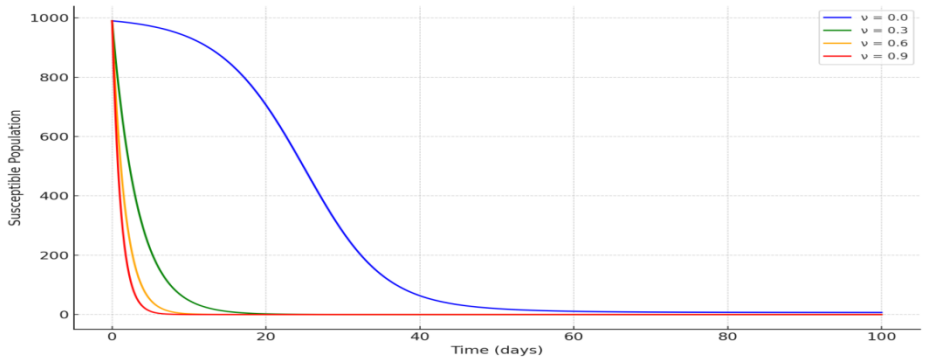

Fig 1: Graph showing the effect of different vaccination rates on the Susceptible Population

The illustration in fig 1 shows how different vaccination rates affect the susceptible population over time. We observed that with no vaccination ($\nu = 0.0$), the susceptible population declines due to infection alone. As the vaccination rate increases, fewer people remain susceptible, and the drop in the susceptible population is sharper and more pronounced early on. However, at $\nu = 0.9$, vaccination quickly removes people from the susceptible group, flattening the disease spread.

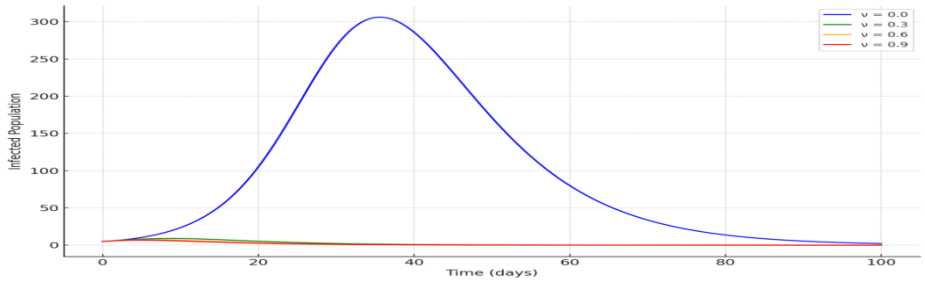

Fig 2: Graph showing the effect of different vaccination rates on the Infected Population

The illustration in fig 2 shows the Infected population under different vaccination rates. We observed that with no vaccination, the infection peaks higher and lasts longer. As the vaccination rate increases, the peak infection is significantly reduced and occurs earlier. However, At $\nu = 0.9$, the infection is quickly suppressed.

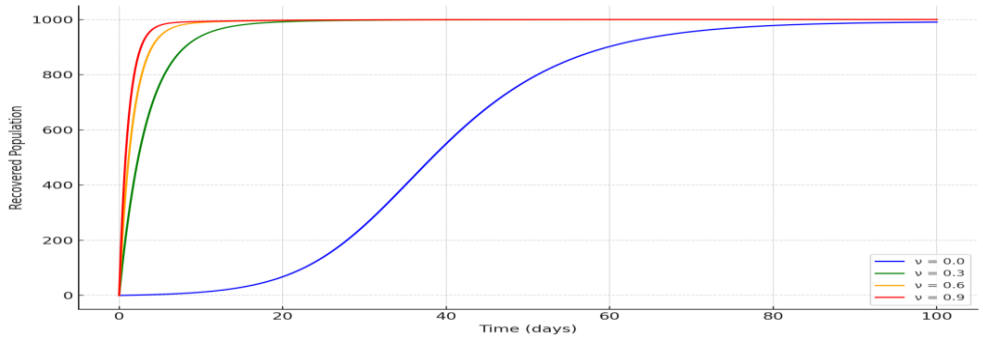

Fig 3: Graph showing the effect of different vaccination rates on the Recovered Population

The illustration in fig 3 shows the plot for the Recovered population over time across different vaccination rates. Higher vaccination rates lead to a faster and larger accumulation in the recovered group. Since vaccinated individuals move directly to the recovered class in this model, the curves rise more sharply with higher v. With no vaccination, recovery comes only from infection, so the rise is slower and less pronounced.

Conclusion

The numerical simulations presented in this chapter validate the theoretical results and demonstrate the significant impact of vaccination on malaria transmission. The results confirm that vaccination plays a crucial role in reducing the number of infected individuals and increasing the number of recovered individuals over time. When vaccination is introduced, the infected human population declines at a much faster rate compared to the scenario without vaccination. This aligns with the theoretical findings that when the basic reproduction number R_o is reduced below 1, the disease-free equilibrium is globally stable, leading to malaria elimination. Additionally, the increase in recovered individuals highlights the long-term benefits of vaccination in building population immunity.

Furthermore, the sensitivity analysis suggests that increasing vaccination coverage, alongside vector control measures and effective treatment strategies, can significantly reduce malaria prevalence. These findings emphasize the importance of a multi-faceted approach to malaria control, incorporating vaccination, treatment, vector management, and public health interventions.

In conclusion, this study confirms that vaccination is an effective tool for malaria control and eradication. For optimal results, policymakers should focus on scaling up vaccination

programs, improving access to treatment, and implementing integrated vector management strategies to achieve long-term disease control.

The numerical simulations validate the theoretical findings:

a. Vaccination significantly reduces the number of infections.
b. Recovery rates increase, leading to faster disease elimination.
c. The disease-free equilibrium is achieved when R0 <1, confirming the stability results.

Recommendations

a. Increase Vaccination Coverage: Higher vaccination rates lead to faster malaria elimination.
b. Improve Vector Control Strategies: Reducing mosquito populations decreases transmission.
c. Combine Vaccination with Treatment: Treating infected individuals while vaccinating the susceptible population is the most effective strategy.
d. Public Awareness and Health Campaigns: Educating the population on the benefits of vaccination can enhance compliance.

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