

Mathematical Analysis of Plasmodium Falciparum Malaria Transmission Dynamics with Assessment the Effectiveness of Drug and Insecticide Resistance

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التحليل الرياضي لديناميكيات انتقال الملاريا بواسطة بلازموديوم فالسيباروم مع تقييم فعالية مقاومة الأدوية والمبيدات الحشرية

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Abstract:

This study presents a deterministic compartmental model to investigate Plasmodium falciparum malaria transmission dynamics under the combined effects of drug and insecticide resistance, explicitly incorporating asymptomatic infections to better capture silent transmission pathways. The population is divided into five classes: susceptible (S), exposed (E), asymptomatic (I_1), symptomatic (I_2), and recovered (R), alongside vector two classes, susceptible (U) and infectious (W). The model is proven to be mathematically and biologically well-posed, the basic reproduction number (R_0) is derived via the next-generation matrix method (NGM), and a sensitivity analysis is conducted to identify the parameters that significantly influence transmission. Numerical simulations demonstrate that escalating resistance drastically intensifies disease propagation, whereas integrated multi-pronged interventions successfully suppress transmission and ensure disease containment.

Keywords: Plasmodium Falciparum Malaria; Drug and Insecticide Resistance; Asymptomatic Infections; Basic Reproduction Number; Sensitivity Analysis.

المخلص

تقدم هذه الدراسة نموذجاً رياضياً حتمياً لديناميكيات انتقال ملاريا المتصورة المنجلية (Plasmodium falciparum) تحت التأثير المشترك لمقاومة الأدوية والمبيدات الحشرية، مع إدراج الإصابات غير الظاهرة (اللا أعراضية) بشكل صريح لانتقاط مسارات الانتقال الصامتة بشكل أفضل. يُقسّم المجتمع إلى خمس فئات: المعرضون للإصابة (S)، والحاضنون للمرض (E)، والمصابون غير الظاهري الاعراض (I_1)، والمصابون المصحوبون بأعراض (I_2)، والمتعافون (R)، إلى جانب فئتين للنقل (البعوض): المعرضون للإصابة (U) والمعديون (W). وقد أثبت أن النموذج محدد جيداً من الناحيتين الرياضية والبيولوجية، وأُشتق عدد التكاثر الأساسي (R_0) باستخدام طريقة مصفوفة الجيل التالي (NGM)، كما أُجري تحليل حساسية لتحديد المعلمات التي تؤثر بشكل ملحوظ على الانتقال. وتُظهر المحاكاة العددية أن تصاعد المقاومة يُكثف بشكل كبير من تفشي المرض، في حين أن التدخلات المتكاملة متعددة الجوانب تنجح في قمع الانتقال وضمان احتواء المرض.

الكلمات المفتاحية: ملاريا المتصورة المنجلية (*Plasmodium falciparum*)؛ مقاومة الأدوية والمبيدات الحشرية؛ الإصابات غير الظاهرة (اللاأعراضية)؛ عدد التكاثر الأساسي؛ تحليل الحساسية.

Introduction

Malaria is one of the oldest and most devastating vector-borne diseases known to humanity, with historical roots extending to antiquity [1, 2]. Despite remarkable advances in prevention, diagnosis, and treatment, the disease continues to impose a significant burden on public health, particularly in tropical and subtropical regions, where it remains a leading cause of morbidity and mortality [3]. According to the World malaria report 2025, the global estimate of malaria reached approximately 282 million clinical cases and 610,000 deaths in 2024, representing a 3% increase in cases and a 2% increase in mortality compared to 2023 [4]. This disease is caused by protozoan parasites belonging to the genus *Plasmodium*, which are transmitted to humans through the bites of infected female *Anopheles* mosquitoes [5]. While the genus *Plasmodium* encompasses over 200 species that infect a broad spectrum of vertebrates, only five primary species are recognized as pathogenic to humans: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*, and *Plasmodium knowlesi* [6]. Among these, *P. falciparum* is the most virulent species and is responsible for the majority of severe malaria cases and particularly, in sub-Saharan Africa [7]. Between 2000 and 2024, core vector control measures, specifically long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS), substantially mitigated global malaria transmission, averting an estimated 2.3 billion cases and 14 million deaths [4]. Nevertheless, resurgent malaria incidence underscores overlapping biological, systemic, environmental, and financial constraints. Central to this surge is the rapid dissemination of dual resistance, wherein reduced parasite susceptibility to artemisinin severely compromises therapeutic efficacy [8], while widespread pyrethroid resistance progressively undermines chemical vector control [9, 10]. The inception of this dual resistance arises from cumulative selection pressures, including non-compliant drug usage, indiscriminate insecticide application, and genetic mutations, alongside behavioral adaptations of *Anopheles* mosquitoes during feeding [11, 12]. Compounding these obstacles, asymptomatic carriers play a critical and strategic role by serving as a hidden reservoir that perpetuates the transmission cycle beyond the reach of routine diagnostic and clinical frameworks [13]. Malaria transmission modeling originated with Ronald Ross's seminal 1911 deterministic framework describing human-vector reciprocal dynamics, later expanded by George Macdonald in the 1950s to incorporate refined biological parameters [14]. Over subsequent decades, these structures evolved substantially to capture increasing epidemiological complexity. Specifically, recent investigations have incorporated dual resistance, combining parasite drug resistance and vector insecticide resistance, within a single framework [15, 16]. Conversely, other studies have focused on modeling asymptomatic infections to evaluate their role in sustained disease transmission [17, 18, 19]. Despite significant advancements in epidemiological modeling, frameworks investigating dual resistance, comprising both antimalarial drug and insecticide resistance, remain predominantly restricted to symptomatic clinical cases undergoing routine treatment. To establish a more realistic representation of malaria dynamics, this study proposes a deterministic model that integrates dual resistance with the explicit inclusion of asymptomatic individuals within a single dynamic structure. By explicitly distinguishing symptomatic individuals receiving therapy from asymptomatic carrier's silently perpetuating transmission, the framework provides a biologically realistic representation of endemic transmission cycles.

Model Formulation

To study the transmission dynamics of *Plasmodium falciparum* malaria under the combined effects of dual resistance, a deterministic compartmental model is formulated using a system of nonlinear ordinary differential equations that explicitly includes asymptomatic infections to better reflect the biological reality. The total human population, denoted by $N_h(t)$, is partitioned into five mutually exclusive compartments: susceptible individuals $S(t)$, exposed individuals $E(t)$, asymptomatic infected individuals $I_1(t)$, symptomatic infected individuals $I_2(t)$, and recovered individuals $R(t)$. Similarly, the total mosquito population, denoted by $N_v(t)$, is divided into two compartments: susceptible mosquitoes $U(t)$ and infected mosquitoes $W(t)$. Accordingly, the total human and mosquito populations are given, respectively, by:

$$N_h(t) = S(t) + E(t) + I_1(t) + I_2(t) + R(t), \quad N_v(t) = U(t) + W(t)$$

It is assumed that individuals enter the susceptible human class at a constant recruitment rate Λ through births or immigration. Malaria transmission occurs through effective contact between susceptible humans and infectious mosquitoes, with transmission rate b_1 . To account for the protective efficacy of insecticide-treated nets, the force of infection is formulated as $\frac{(1-c)b_1SW}{N_h}$ in this model; c represents the proportion of the population utilizing mosquito nets, which acts to reduce transmission intensity. Consequently, susceptible individuals transition to the exposed class. The total human population size is considered to influence the average number of mosquito bites experienced by individuals. Exposed individuals progress to the infectious stage at rate σ , where a proportion r develops asymptomatic infection $I_1(t)$, while the remaining proportion $(1 - r)$ develops symptomatic

infection $I_2(t)$. Asymptomatic individuals play a crucial role in sustaining malaria transmission, as they contribute to disease spread without exhibiting clinical symptoms. Recovery dynamics differ across infectious classes. Asymptomatic individuals recover naturally at rate τ_1 , whereas Symptomatic individuals receive treatment and recover at a rate $\alpha\tau_2$, where α denotes drug efficacy and τ_2 represents the treatment-induced recovery rate. To account for the emergence of drug resistance, the parameter $p \in [0, 1]$ is introduced to represent the proportion of individuals acquiring resistance to treatment. Recovered individuals increase through both natural and treatment-induced recovery from the infectious classes. In addition, individuals may transition directly from the susceptible class to the recovered class through vaccination at rate ζ . However, immunity is assumed to be temporary, and recovered individuals may lose immunity and return to the susceptible class at rate γ . With regard to the mosquito population, recruitment occurs into the susceptible class at a constant rate B . The force of infection from humans to mosquitoes is given by $(1 - c) \left[\frac{b_2 U I_2}{N_h} + \frac{b_3 U I_1}{N_h} \right]$ where b_2 and b_3 denote the transmission rates from symptomatic and asymptomatic humans, respectively. Mosquito mortality is governed by both natural death at rate μ_v and additional mortality induced by insecticide application at rate $\lambda\theta$. Where θ represents the insecticide-induced mortality rate and λ denotes the efficacy of the insecticide. To account for the emergence of insecticide resistance, the parameter $q \in [0, 1]$ is introduced to represent the proportion of mosquitoes acquiring resistance to the insecticide. All human compartments are subject to natural mortality at rate μ_h , while disease-induced mortality may occur in the symptomatic class at rate d . Based on these considerations and the interactions between human and mosquito populations, the transmission dynamics of malaria are governed by the following system of nonlinear ordinary differential equations:

$$\begin{aligned}
 \frac{dS}{dt} &= \Lambda + \gamma R - \frac{(1-c)b_1 S W}{N_h} - (\mu_h + \zeta) S, \\
 \frac{dE}{dt} &= \frac{(1-c)b_1 S W}{N_h} - (\mu_h + \sigma) E, \\
 \frac{dI_1}{dt} &= r\sigma E - (\mu_h + \tau_1) I_1, \\
 \frac{dI_2}{dt} &= (1-r)\sigma E - (\mu_h + d + \alpha\tau_2(1-p)) I_2, \\
 \frac{dR}{dt} &= \zeta S + \tau_1 I_1 + \alpha\tau_2(1-p) I_2 - (\gamma + \mu_h) R, \\
 \frac{dU}{dt} &= B - (1-c) \left[\frac{b_2 U I_2}{N_h} + \frac{b_3 U I_1}{N_h} \right] - (\mu_v + \lambda\theta(1-q)) U, \\
 \frac{dW}{dt} &= (1-c) \left[\frac{b_2 U I_2}{N_h} + \frac{b_3 U I_1}{N_h} \right] - (\mu_v + \lambda\theta(1-q)) W.
 \end{aligned}
 \tag{1}$$

With the initial conditions

$S(0), E(0), I_1(0), I_2(0), R(0), U(0), W(0) > 0$

The baseline parameter values used to characterize the system dynamics are summarized in Table 1

Table 1: Descriptions of the model parameters

Parameters	Description
Λ	Recruitment rate of susceptible humans either by birth or immigration
B	Recruitment of susceptible mosquitoes
μ_h	Natural mortality rate of humans
μ_v	Natural mortality rate of mosquitoes
γ	Rate of waning of immunity
σ	The transfer rate of exposed individuals to other infected individuals
r	The probability of asymptomatic infected individuals
τ_1	The recovery rate of asymptomatic infected individuals
b_1	The transmission rate of infected mosquitoes to susceptible individuals
b_2	The transmission rate of asymptomatic infected individuals to susceptible mosquitoes
b_3	The transmission rate of symptomatic infected individuals to susceptible mosquitoes
τ_2	Recovery rate due to the drug (ACTs)
α	Drug efficacy

p	Resistance acquisition ratio to the draug
ζ	recovery rate of susceptible humans with the use of malaria vaccines
d	disease induced mortality rate of human
λ	Insecticide efficacy
θ	mmortality rate due to the insecticides
q	Resistance acquisition ratio to the insecticides whether those used in long-lasting insecticide nets (LLINs) or in indoor residual spraying (IRS).
c	Reduction of infection rate due to use of mosquitoes nets

To help clarify the proposed mathematical model, Figure 1 provides a flowchart of its overall structure

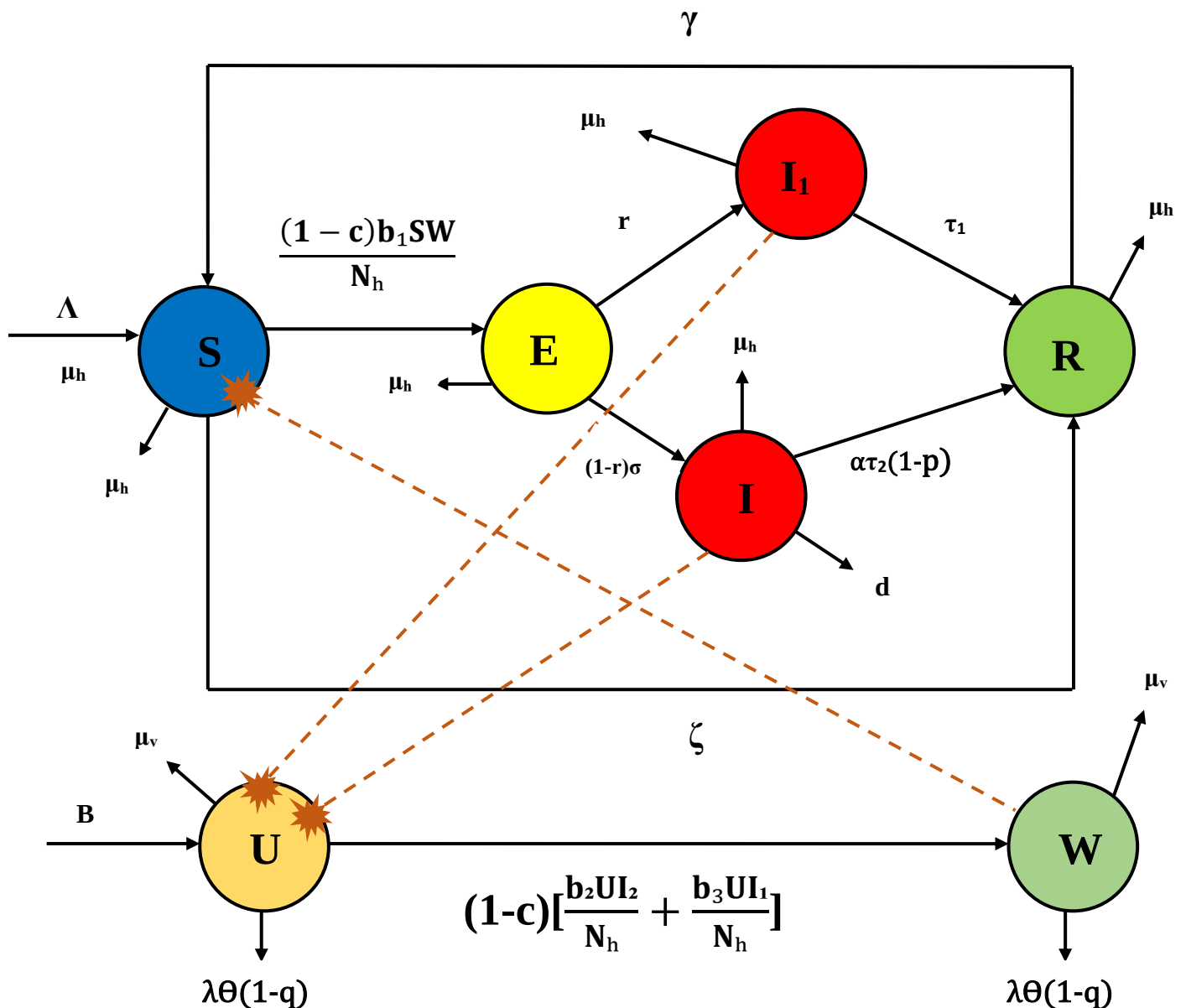


Figure 1: Flowchart of the proposed malaria model

Model analysis

To systematically analyze the malaria model (1), this section first confirms its fundamental well-posedness via positivity, boundedness, and existence and uniqueness of its solutions. It then determines the equilibrium points, derives the basic reproduction number (R_0), and performs sensitivity analysis.

Positivity of solutions

Theorem 1. Every solution of model (1) with initial conditions

$\{S(0), E(0), I_1(0), I_2(0), R(0), U(0), W(0) > 0\} \in \mathbb{R}_+^7$ are positive for all $t > 0$.

Proof: Let $t^* = \sup \{t > 0: S(t) > 0, E(t) > 0, I_1(t) > 0, I_2(t) > 0, R(t) > 0, U(t) > 0, W(t) > 0\}$

Hence

$t^* > 0$. If $t^* < \infty$, then $S(t), E(t), I_1(t), I_2(t), R(t), U(t)$ and $W(t)$, vanish at t^* .

Therefore, from the first equation of model (1) we have

$$\frac{dS}{dt} = \Lambda + \gamma R - \frac{(1-c)b_1SW}{N_h} - (\mu_h + \zeta)S$$

That is,

$$\frac{dS}{dt} + \left[\frac{(1-c)b_1W}{N_h} + (\mu_h + \zeta) \right] S = \Lambda + \gamma R$$

Applying the integrating factor, this can be written as:

$$\frac{d}{dt} \left[S(t) e^{\int_0^t \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} \right] = e^{\int_0^t \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} (\Lambda + \gamma R)$$

Hence

$$S(t^*) e^{\int_0^{t^*} \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} - S(0) = \int_0^{t^*} \left[(\Lambda + \gamma R(T)) e^{\int_0^T \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} \right] dT$$

So that

$$S(t^*) = S(0) e^{-\int_0^{t^*} \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} + e^{-\int_0^{t^*} \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} \times \int_0^{t^*} \left[(\Lambda + \gamma R(T)) e^{\int_0^T \left[\frac{(1-c)b_1W(x)}{N_h(x)} + (\mu_h + \zeta) \right] dx} \right] dT > 0$$

Similarly

It can be show that $E(t), I_1(t), I_2(t), R(t), U(t)$, and $W(t) > 0$ for all $t \geq 0$.

Boundedness of solutions

Theorem 2. The feasible region for the model (1) is defined by the Following set:

$$\pi = \{(S, E, I, I_2, R, U, W) \in \mathbb{R}_+^7: 0 \leq N_h \leq \frac{\Lambda}{\mu_h}, 0 \leq N_v \leq \frac{B}{\mu_v}\}.$$

Proof: Adding the first five equations of model (1) we derive the total population of the human, represented by:

$$N_h(t) = S(t) + E(t) + I_1(t) + I_2(t) + R(t)$$

Hence, the derivative of $N_h(t)$ with respect to t can be written as:

$$\frac{dN_h(t)}{dt} = \frac{dS(t)}{dt} + \frac{dE(t)}{dt} + \frac{dI_1(t)}{dt} + \frac{dI_2(t)}{dt} + \frac{dR(t)}{dt}$$

Then

$$\frac{dN}{dt} = \Lambda - \mu_h N_h - dI_2 \longrightarrow \quad (2)$$

Assuming there is no death rate due to malaria i.e $d = 0$

Then equation (2) by comes

$$\frac{dN}{dt} \leq \Lambda - \mu_h N_h$$

Applying the integrating factor, we get

$$N_h(t) \leq \frac{\Lambda}{\mu_h} + ce^{-\mu_h t}$$

Using the initial conditions at $t = 0$, $N_h(t) = N_h(0)$, we obtain

$$N_h(t) \leq \frac{\Lambda}{\mu_h} + (N_h(0) - \frac{\Lambda}{\mu_h}) e^{-\mu_h t}$$

So that

$$\limsup_{t \rightarrow \infty} N_h(t) \leq \frac{\Lambda}{\mu_h}$$

Now at $t = 0$, we have

$$N_h(0) \leq \frac{\Lambda}{\mu_h} \geq 0$$

That means

$$0 \leq N_h(t) \leq \frac{\Lambda}{\mu_h} \longrightarrow (3)$$

Similarly, by adding the last two equations of model (1) we obtain the total population for mosquito (vector), represented by

$$\frac{dN_v}{dt} = B - (\mu_v + \lambda \theta (1 - q))N_v$$

Then

$$\frac{dN_v}{dt} \leq B - \mu_v N_v \longrightarrow (4)$$

Solving differential inequality (4) we have

$$0 \leq N_v \leq \frac{B}{\mu_v} \longrightarrow (5)$$

From (3) and (5) the set π is positively invariant. Consequently, any solution from model (1) with initial conditions in π remains in π for all $t \geq 0$.

Existence and uniqueness of model

Let

$$F_1 = \Lambda + \gamma R - \frac{(1 - c)b_1 SW}{N_h} - (\mu_h + \zeta)S$$

$$F_2 = \frac{(1 - c)b_1 SW}{N_h} - (\mu_h + \sigma)E$$

$$F_3 = r\sigma E - (\mu_h + \tau_1)I_1$$

$$F_4 = (1 - r)\sigma E - (\mu_h + d + \alpha\tau_2(1 - p))I_2$$

$$F_5 = \zeta S + \tau_1 I_1 + \alpha\tau_2(1 - p)I_2 - (\gamma + \mu_h)R$$

$$F_6 = B - (1 - c) \left[\frac{b_2 UI_2}{N_h} + \frac{b_3 UI_1}{N_h} \right] - (\mu_v + \lambda \theta (1 - q))U$$

$$F_7 = (1 - c) \left[\frac{b_2 UI_2}{N_h} + \frac{b_3 UI_1}{N_h} \right] - (\mu_v + \lambda \theta (1 - q))W$$

Form the first equation F_1

$$\begin{aligned} \left| \frac{\partial F_1}{\partial S} \right| &= \left| - \left[\frac{(1 - c)b_1 W}{N_h} + (\mu_h + \zeta) \right] \right| < \infty, \left| \frac{\partial F_1}{\partial E} \right| = 0 < \infty, \left| \frac{\partial F_1}{\partial I_1} \right| = 0 < \infty, \left| \frac{\partial F_1}{\partial I_2} \right| = 0 < \infty, \left| \frac{\partial F_1}{\partial R} \right| = |\gamma| \\ &< \infty, \left| \frac{\partial F_1}{\partial U} \right| = 0 < \infty, \left| \frac{\partial F_1}{\partial W} \right| = 0 < \infty. \end{aligned}$$

Form the second equation F_2

$$\begin{aligned} \left| \frac{\partial F_2}{\partial S} \right| &= \left| \frac{(1 - c)b_1 W}{N_h} \right| < \infty, \left| \frac{\partial F_2}{\partial E} \right| = |-(\mu_h + \sigma)| < \infty, \left| \frac{\partial F_2}{\partial I_1} \right| = 0 < \infty, \left| \frac{\partial F_2}{\partial I_2} \right| = 0 < \infty, \left| \frac{\partial F_2}{\partial R} \right| = 0 \\ &< \infty, \left| \frac{\partial F_2}{\partial U} \right| = 0 < \infty, \left| \frac{\partial F_2}{\partial W} \right| = 0 < \infty. \end{aligned}$$

Form the third equation F_3

$$\begin{aligned} \left| \frac{\partial F_3}{\partial S} \right| &= 0 < \infty, \left| \frac{\partial F_3}{\partial E} \right| = |r\sigma| < \infty, \left| \frac{\partial F_3}{\partial I_1} \right| = |-(\mu_h + \tau_1)| < \infty, \left| \frac{\partial F_3}{\partial I_2} \right| = 0 < \infty, \left| \frac{\partial F_3}{\partial R} \right| = 0 < \infty, \left| \frac{\partial F_3}{\partial U} \right| = 0 \\ &< \infty, \left| \frac{\partial F_3}{\partial W} \right| = 0 < \infty. \end{aligned}$$

Form the fourth equation F_4

$$\left| \frac{\partial F_4}{\partial S} \right| = 0 < \infty, \left| \frac{\partial F_4}{\partial E} \right| = |(1-r)\sigma| < \infty, \left| \frac{\partial F_4}{\partial I_1} \right| = 0 < \infty, \left| \frac{\partial F_4}{\partial I_2} \right| = |-(\mu_h + d + \alpha\tau_2(1-p))| < \infty, \left| \frac{\partial F_4}{\partial R} \right| = 0 < \infty, \left| \frac{\partial F_4}{\partial U} \right| = 0 < \infty, \left| \frac{\partial F_4}{\partial W} \right| = 0 < \infty.$$

Form the fifth equation F_5

$$\left| \frac{\partial F_5}{\partial S} \right| = |\zeta| < \infty, \left| \frac{\partial F_5}{\partial E} \right| = 0 < \infty, \left| \frac{\partial F_5}{\partial I_1} \right| = |\tau_1| < \infty, \left| \frac{\partial F_5}{\partial I_2} \right| = |\alpha\tau^{2(1-p)}| < \infty, \left| \frac{\partial F_5}{\partial R} \right| = |-(\gamma + \mu_h)| < \infty, \left| \frac{\partial F_5}{\partial U} \right| = 0 < \infty, \left| \frac{\partial F_5}{\partial W} \right| = 0 < \infty.$$

Form the sixth equation F_6

$$\left| \frac{\partial F_6}{\partial S} \right| = 0 < \infty, \left| \frac{\partial F_6}{\partial E} \right| = 0 < \infty, \left| \frac{\partial F_6}{\partial I_1} \right| = \left| - \left[(1-c) \frac{b_3 U}{N_h} \right] \right| < \infty, \left| \frac{\partial F_6}{\partial I_2} \right| = \left| - \left[(1-c) \frac{b_2 U}{N_h} \right] \right| < \infty, \left| \frac{\partial F_6}{\partial R} \right| = 0 < \infty, \left| \frac{\partial F_6}{\partial U} \right| = \left| - \left((1-c) \left[\frac{b_2 I_2}{N_h} + \frac{b_3 I_1}{N_h} \right] + [\mu_v + \lambda \theta (1-q)] \right) \right| < \infty, \left| \frac{\partial F_6}{\partial W} \right| = 0 < \infty.$$

Form the seventh equation F_7

$$\left| \frac{\partial F_7}{\partial S} \right| = 0 < \infty, \left| \frac{\partial F_7}{\partial E} \right| = 0 < \infty, \left| \frac{\partial F_7}{\partial I_1} \right| = \left| (1-c) \frac{b_3 U}{N_h} \right| < \infty, \left| \frac{\partial F_7}{\partial I_2} \right| = \left| (1-c) \frac{b_2 U}{N_h} \right| < \infty, \left| \frac{\partial F_7}{\partial R} \right| = 0 < \infty, \left| \frac{\partial F_7}{\partial U} \right| = \left| (1-c) \left[\frac{b_2 I_2}{N_h} + \frac{b_3 I_1}{N_h} \right] \right| < \infty, \left| \frac{\partial F_7}{\partial W} \right| = |-(\mu_v + \lambda \theta (1-q))| < \infty.$$

The boundedness of the solutions ensures that the proposed model is mathematically well-posed, satisfying the conditions of existence, uniqueness, and continuous dependence on the initial data.

Model Equilibria:

Malaria-free equilibrium point (MFEP)

The malaria-free equilibrium point is obtained by setting the right-hand sides of the equations in the Model (1) to zero.

That is,

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI_1}{dt} = \frac{dI_2}{dt} = \frac{dR}{dt} = \frac{dU}{dt} = \frac{dW}{dt} = 0.$$

Assuming that there is no malaria infection in both the human and mosquito populations.

Hence,

$$E = I_1 = I_2 = W = 0.$$

Then the (MFEP) point is given by

$$\text{MFEP} = (S^0, E^0, I_1^0, I_2^0, R^0, U^0, W^0) = \left(\frac{\Lambda(\gamma + \mu_h)}{\mu_h(\mu_h + \gamma + \zeta)}, 0, 0, 0, \frac{\zeta\Lambda}{\mu_h(\mu_h + \gamma + \zeta)}, \frac{\beta}{\mu_v + \lambda \theta (1-q)}, 0 \right)$$

Malaria-endemic equilibrium point (MEEP)

Let

MFEP = $(S^*, E^*, I_1^*, I_2^*, R^*, U^*, W^*)$ as Malaria-endemic equilibrium where, $I_1, I_2, w \neq 0$. The equilibrium point MEEP is

$$S^* = \frac{N_h^*(\Lambda + \gamma R^*)}{(1-c)b_1 W^* + (\mu_h + \zeta)N_h^*}$$

$$E^* = \frac{(1-c)b_1 S^* W^*}{(\mu_h + \sigma)N_h^*}$$

$$I_1^* = \frac{r\sigma E^*}{\mu_h + \tau_1}$$

$$I_2^* = \frac{(1-r)\sigma E^*}{\mu_h + d + \alpha\tau_2(1-p)}$$

$$R^* = \frac{\zeta S^* + \tau_1 I_1^* + \alpha \tau_2 (1-p) I_2^*}{\gamma + \mu_h}$$

$$U^* = \frac{B N_h^*}{(1-c)[b_2 I_2^* + b_3 I_1^*] + [\mu_v + \lambda \theta (1-q)] N_h^*}$$

$$W^* = \frac{[(1-c)(b_2 I_2^* + b_3 I_1^*)] U^*}{[\mu_v + \lambda \theta (1-q)] N_h^*}$$

Hence

The total human population N_h at the endemic equilibrium is given by

$$N_h^* = S^* + E^* + I_1^* + I_2^* + R^*.$$

Basic Reproduction Number R_0

The basic reproduction number (R_0) is arguably the most important quantity in infectious disease epidemiology [20]. It determines whether the disease will decline or spread in the population [21]. Biologically, it is defined as the expected number of secondary infections caused by a single infected individual in an otherwise disease-free population. R_0 is calculated using the next-generation matrix (NGM) as: $R_0 = \rho(\mathcal{FV}^{-1})$ where $\rho(\mathcal{FV}^{-1})$ denotes the spectral radius of the next-generation operator [20].

The infection sub-model is deduced from the model (1) as follows

$$\frac{dE}{dt} = \frac{(1-c)b_1 SW}{N_h} - (\mu_h + \sigma)E$$

$$\frac{dI_1}{dt} = r\sigma E - (\mu_h + \tau_1)I_1$$

$$\frac{dI_2}{dt} = (1-r)\sigma E - (\mu_h + d + \alpha \tau_2(1-p))I_2$$

$$\frac{dW}{dt} = (1-c) \left[\frac{b_2 UI_2}{N_h} + \frac{b_3 UI_1}{N_h} \right] - (\mu_v + \lambda \theta (1-q)) W$$

The new infection vectors $\mathbf{F}$ and the transition vectors $\mathbf{V}$ are defined as

$$\mathbf{F} = \begin{bmatrix} \frac{(1-c)b_1 SW}{N_h} \\ 0 \\ 0 \\ (1-c) \left[\frac{b_2 UI_2}{N_h} + \frac{b_3 UI_1}{N_h} \right] \end{bmatrix}$$

$$\mathbf{V} = \begin{bmatrix} (\mu_h + \sigma)E \\ (\mu_h + \tau_1)I_1 - r\sigma E \\ (\mu_h + d + \alpha \tau_2(1-p))I_2 - (1-r)\sigma E \\ (\mu_v + \lambda \theta (1-q)) W \end{bmatrix}$$

The Jacobin matrices of $\mathcal{F}$ and $\mathcal{V}$ at MFEP is given by

$$\mathcal{F} = \begin{bmatrix} 0 & 0 & 0 & \frac{(1-c)b_1(\gamma + \mu_h)}{\mu_h + \gamma + \zeta} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & \frac{(1-c)b_3 B \mu_h}{\lambda(\mu_v + \lambda \theta (1-q))} & \frac{(1-c)b_2 B \mu_h}{\lambda(\mu_v + \lambda \theta (1-q))} & 0 \end{bmatrix}$$

$$\mathbf{V} = \begin{bmatrix} (\mu_h + \sigma) & 0 & 0 & 0 \\ -r\sigma & (\mu_h + \tau_1) & 0 & 0 \\ -(1-r)\sigma & 0 & (\mu_h + d + \alpha\tau_2(1-p)) & 0 \\ 0 & 0 & 0 & (\mu_v + \lambda\theta(1-q)) \end{bmatrix}$$

Then,

$$\mathbf{V}^{-1} = \begin{bmatrix} \frac{1}{\mu_h + \sigma} & 0 & 0 & 0 \\ \frac{r\sigma}{(\mu_h + \sigma)(\mu_h + \tau_1)} & \frac{1}{\mu_h + \tau_1} & 0 & 0 \\ \frac{(1-r)\sigma}{(\mu_h + \sigma)(\mu_h + d + \alpha\tau_2(1-p))} & 0 & \frac{1}{\mu_h + d + \alpha\tau_2(1-p)} & 0 \\ 0 & 0 & 0 & \frac{1}{\mu_v + \lambda\theta(1-q)} \end{bmatrix}$$

Now the next- generation matrix $\mathcal{FV}^{-1}$ is

$$\mathcal{FV}^{-1} = \begin{bmatrix} 0 & 0 & 0 & A \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ B & C & D & 0 \end{bmatrix}$$

Where,

$$A = \frac{(1-c)b_1(\gamma + \mu_h)}{(\mu_h + \gamma + \zeta)(\mu_v + \lambda\theta(1-q))}$$

$$B = \frac{\sigma\mu_h B}{\Lambda(\mu_v + \lambda\theta(1-q))(\mu_h + \sigma)} \left[\frac{(1-c)rb_3}{(\mu_h + \tau_1)} + \frac{(1-c)(1-r)b_2}{\mu_h + d + \alpha\tau_2(1-p)} \right]$$

$$C = \frac{(1-c)b_3B\mu_h}{\Lambda(\mu_v + \lambda\theta(1-q))(\mu_h + \tau_1)}$$

$$D = \frac{(1-c)b_2B\mu_h}{\Lambda(\mu_v + \lambda\theta(1-q))(\mu_h + d + \alpha\tau_2(1-p))}$$

Then the eigenvalues of matrix $\mathcal{FV}^{-1}$ are

$$\lambda_{1,2} = 0$$

$$\lambda_{3,4} = \pm \sqrt{\frac{\frac{B\mu_h}{\Lambda(\mu_v + \lambda\theta(1-q))} \times \frac{\gamma + \mu_h}{\mu_h + \gamma + \zeta} \times \frac{(1-c)b_1\sigma}{(\mu_h + \sigma)(\mu_v + \lambda\theta(1-q))} \times \left[\frac{(1-c)rb_3}{\mu_h + \tau_1} + \frac{(1-c)(1-r)b_2}{\mu_h + d + \alpha\tau_2(1-p)} \right]}$$

Since $\mathbf{R}_0$ is the dominant eigenvalue of the matrix $\mathcal{FV}^{-1}$, then

$$R_0 = \sqrt{\left[\frac{B\mu_h}{\Lambda(\mu_v + \lambda \theta (1 - q))} \times \frac{\gamma + \mu_h}{\mu_h + \gamma + \zeta} \times \frac{(1 - c)b_1\sigma}{(\mu_h + \sigma)(\mu_v + \lambda \theta (1 - q))} \times \left[\frac{(1 - c)rb_3}{\mu_h + \tau_1} + \frac{(1 - c)(1 - r)b_2}{\mu_h + d + \alpha\tau_2(1 - p)} \right] \right]}$$

Therefore, when $R_0 < 1$, the disease-free equilibrium (DFE) is stable, leading to the eventual elimination of the disease. In contrast, when $R_0 > 1$, the endemic equilibrium (EE) becomes stable, allowing the disease to persist within the population. However, recent studies have demonstrated that disease persistence may still occur even when $R_0 < 1$, indicating the presence of more complex underlying dynamics than traditionally assumed. This highlights the critical importance of conducting a comprehensive sensitivity analysis of all model parameters in order to identify the most influential factors driving disease transmission.

Sensitivity analysis of the reproduction number

Sensitivity analysis is performed to evaluate how parameters positively or negatively affect R_0 . The normalized forward sensitivity index of R_0 with respect to a parameter y is defined as follows [22]:

$$Y_y^{R_0} = \frac{\partial R_0}{\partial y} \times \frac{y}{R_0}$$

Where

$$R_0 = \sqrt{\left[\frac{B\mu_h}{\Lambda(\mu_v + \lambda \theta (1 - q))} \times \frac{\gamma + \mu_h}{\mu_h + \gamma + \zeta} \times \frac{(1 - c)b_1\sigma}{(\mu_h + \sigma)(\mu_v + \lambda \theta (1 - q))} \times \left[\frac{(1 - c)rb_3}{\mu_h + \tau_1} + \frac{(1 - c)(1 - r)b_2}{\mu_h + d + \alpha\tau_2(1 - p)} \right] \right]}$$

Then we have

$$Y_B^{R_0} = \frac{1}{2R_0} \times \frac{\mu_h}{\Lambda(\mu_v + \lambda \theta (1 - q))} \times \frac{\gamma + \mu_h}{\mu_h + \gamma + \zeta} \times \frac{(1 - c)b_1\sigma}{(\mu_h + \sigma)(\mu_v + \lambda \theta (1 - q))} \times \left[\frac{(1 - c)rb_3}{\mu_h + \tau_1} + \frac{(1 - c)(1 - r)b_2}{\mu_h + d + \alpha\tau_2(1 - p)} \right] \times \frac{B}{R_0}$$

$$\begin{aligned} Y_B^{R_0} &= \frac{1}{2} \\ &\times \frac{B \frac{\mu_h}{\Lambda(\mu_v + \lambda \theta (1 - q))} \times \frac{\gamma + \mu_h}{\mu_h + \gamma + \zeta} \times \frac{(1 - c)b_1\sigma}{(\mu_h + \sigma)(\mu_v + \lambda \theta (1 - q))} \times \left[\frac{(1 - c)rb_3}{\mu_h + \tau_1} + \frac{(1 - c)(1 - r)b_2}{\mu_h + d + \alpha\tau_2(1 - p)} \right]}{\frac{B\mu_h}{\Lambda(\mu_v + \lambda \theta (1 - q))} \times \frac{\gamma + \mu_h}{\mu_h + \gamma + \zeta} \times \frac{(1 - c)b_1\sigma}{(\mu_h + \sigma)(\mu_v + \lambda \theta (1 - q))} \times \left[\frac{(1 - c)rb_3}{\mu_h + \tau_1} + \frac{(1 - c)(1 - r)b_2}{\mu_h + d + \alpha\tau_2(1 - p)} \right]} \end{aligned}$$

And hence

$$Y_B^{R_0} = \frac{1}{2} > 0$$

Similarly, thus we have

$$Y_\Lambda^{R_0} = -\frac{1}{2} < 0$$

$$Y_c^{R_0} = -\left(\frac{c}{1 - c}\right) < 0$$

$$\gamma_{b_1}^{R_0} = \frac{1}{2} > 0$$

$$\gamma_{\mu_v}^{R_0} = -\left(\frac{\mu_v}{\mu_v + \lambda \theta (1 - q)}\right) < 0$$

$$\gamma_{\lambda}^{R_0} = -\left(\frac{\lambda \theta (1 - q)}{\mu_v + \lambda \theta (1 - q)}\right) < 0$$

$$\gamma_{\sigma}^{R_0} = \frac{\mu_h}{2(\mu_h + \sigma)} > 0$$

$$\gamma_{b_3}^{R_0} = \frac{1}{2} \left[\frac{rb_3(\mu_h + d + \alpha\tau_2(1 - p))}{rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)} \right] > 0$$

$$\gamma_{\tau_1}^{R_0} = -\frac{1}{2} \left[\frac{\tau_1 rb_3(\mu_h + d + \alpha\tau_2(1 - p))}{(\mu_h + \tau_1)(rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1))} \right] < 0$$

$$\gamma_{\gamma}^{R_0} = \frac{\gamma\zeta}{2(\gamma + \mu_h)(\mu_h + \gamma + \zeta)} > 0$$

$$\gamma_{\theta}^{R_0} = -\left(\frac{\lambda \theta (1 - q)}{\mu_v + \lambda \theta (1 - q)}\right) < 0$$

$$\gamma_q^{R_0} = \frac{\lambda \theta q}{\mu_v + \lambda \theta (1 - q)} > 0$$

$$\gamma_{\zeta}^{R_0} = -\frac{\zeta}{2(\mu_h + \gamma + \zeta)} < 0$$

$$\gamma_{b_2}^{R_0} = \frac{1}{2} \left[\frac{(1 - r)b_2(\mu_h + \tau_1)}{rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)} \right] > 0$$

$$\gamma_d^{R_0} = -\frac{1}{2} \left[\frac{(1 - r)b_2(\mu_h + \tau_1)d}{(\mu_h + d + \alpha\tau_2(1 - p))[rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)]} \right] < 0$$

$$\gamma_{\alpha}^{R_0} = -\frac{1}{2} \left[\frac{\alpha\tau_2(1 - p)(\mu_h + \tau_1)(1 - r)b_2}{(\mu_h + d + \alpha\tau_2(1 - p))[rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)]} \right] < 0$$

$$\gamma_{\tau_2}^{R_0} = -\frac{1}{2} \left[\frac{\alpha\tau_2(1 - p)(\mu_h + \tau_1)(1 - r)b_2}{(\mu_h + d + \alpha\tau_2(1 - p))[rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)]} \right] < 0$$

$$\gamma_p^{R_0} = \frac{1}{2} \left[\frac{(1 - r)b_2(\mu_h + \tau_1)\alpha\tau_2 p}{(\mu_h + d + \alpha\tau_2(1 - p))[rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)]} \right] > 0$$

$$\gamma_r^{R_0} = \frac{1}{2} r \left[\frac{b_3(\mu_h + d + \alpha\tau_2(1 - p)) - b_2(\mu_h + \tau_1)}{rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)} \right] > 0$$

if $b_3(\mu_h + d + \alpha\tau_2(1 - p)) > b_2(\mu_h + \tau_1)$

$$\gamma_{\mu_h}^{R_0} = \frac{1}{2} \left[\frac{1 + \frac{\zeta\mu_h}{(\gamma + \mu_h)(\mu_h + \gamma + \zeta)} - \frac{\mu_h}{\mu_h + \sigma}}{-\mu_h \frac{rb_3(\mu_h + d + \alpha\tau_2(1 - p))^2 + (\mu_h + \tau_1)^2(1 - r)b_2}{(\mu_h + \tau_1)(\mu_h + d + \alpha\tau_2(1 - p))[rb_3(\mu_h + d + \alpha\tau_2(1 - p)) + b_2(1 - r)(\mu_h + \tau_1)]}} \right] > 0$$

The normalized forward sensitivity indices of the basic reproduction number (R_0) with respect to the model parameters are presented in Table 2. The table summarizes the baseline parameter values and their corresponding sensitivity indices, providing a quantitative evaluation of the relative impact of each parameter on malaria transmission dynamics.

Table 2: Baseline values of the model parameters and their sensitivity indices with respect to R_0

Parameters	value	units	source	Sensitivity indices
Λ	$1000 / 65 \times 365$	Human / Day	23	- 0.5
B	$1000 / 21$	Mosq / Day	23	0.5
μ_h	$1 / 65 \times 365$	Day ⁻¹	23	0.4975
μ_v	$1 / 21$	Day ⁻¹	23	- 0.2841
d	2.19×10^{-4}	Day ⁻¹	17	- 2×10^{-5}
b_2	0.05	1 / Human $\times$ Day	Estimated	0.0151
b_3	0.03	1 / Human $\times$ Day	Estimated	0.4849
α	0.7	-	24	- 0.0151
τ_1	0.0035	Day ⁻¹	19	- 0.4791
λ	0.5	-	Estimated	- 0.7159
θ	0.3	Day ⁻¹	24	- 0.7159
σ	0.1	Day ⁻¹	25	2×10^{-4}
γ	0.0027	Day ⁻¹	25	0.1316
r	0.5	-	19	0.4697
p	0.1	-	Estimated	0.0017
b_1	0.022	1 / Mosq $\times$ Day	23	0.5
ζ	0.001	Day ⁻¹	Estimated	- 0.1336
τ_2	0.6	Day ⁻¹	Estimated	- 0.0151
c	0.1742	-	26	- 0.2109
q	0.2	-	Estimated	0.1790

Discussion of Sensitivity Analysis Results

The sensitivity analysis results presented in Tables (1) and (2) indicate that several parameters exhibit strong positive effects on the basic reproduction number R_0 . These parameters include the mosquito recruitment rate B, the transmission rate from infectious mosquitoes to susceptible humans b_1 , the transmission rate from asymptomatic individuals to susceptible mosquitoes b_3 , and the Natural Human Mortality Rate μ_h . These findings suggest that an increase in mosquito population density or an enhancement in transmission efficiency between humans and mosquitoes leads to a significant rise in R_0 , thereby promoting the spread of malaria within the population. Furthermore, the proportion of individuals progressing to the asymptomatic infection class r, was found to have a notable positive impact on R_0 . This highlights the critical role of asymptomatic carriers in sustaining disease transmission, as they are capable of transmitting the parasite without exhibiting clinical symptoms that would prompt medical intervention. In contrast, the results show that insecticide effectiveness λ , and the insecticide-induced mosquito mortality rate θ , possess strong negative sensitivity indices. This indicates that strengthening vector control interventions effectively reduces mosquito density and, consequently, limits malaria transmission. Additionally, both the human recruitment rate Λ , and the natural recovery rate τ_1 , exhibit significant negative effects on R_0 . Moreover, the natural death rate of mosquitoes μ_v , the usage rate of insecticide-treated bed nets c, and the Vaccination rate ζ , demonstrate moderate negative effects, confirming the importance of these interventions in mitigating disease spread. On the other hand, the rate of immunity loss γ , and insecticide resistance in mosquitoes q, show moderate positive effects, suggesting that waning immunity or increased resistance may contribute to sustained transmission. Additionally, Drug efficacy α , and the recovery rate due to treatment τ_2 , exhibit relatively weak negative effects on R_0 , while parasite resistance to treatment p, shows a weak positive effect. These results do not imply that treatment is clinically ineffective; rather, they reflect the model's structure, which assumes that treatment is primarily administered to symptomatic individuals, while asymptomatic carriers continue to transmit the infection without receiving medical care. Lastly, certain parameters specifically the progression rate from the exposed to the infectious class σ , the disease-induced death rate d, and the transmission rate from symptomatic individuals to susceptible mosquitoes b_2 , yielded sensitivity indices near zero. This suggests that their influence on R_0 is statistically marginal within the current model framework compared to other governing parameters.

Figure 2 provides a graphical representation of the normalized forward sensitivity indices of the model parameters with respect to R_0 . The plot highlights the relative importance of each parameter in influencing malaria transmission dynamics.

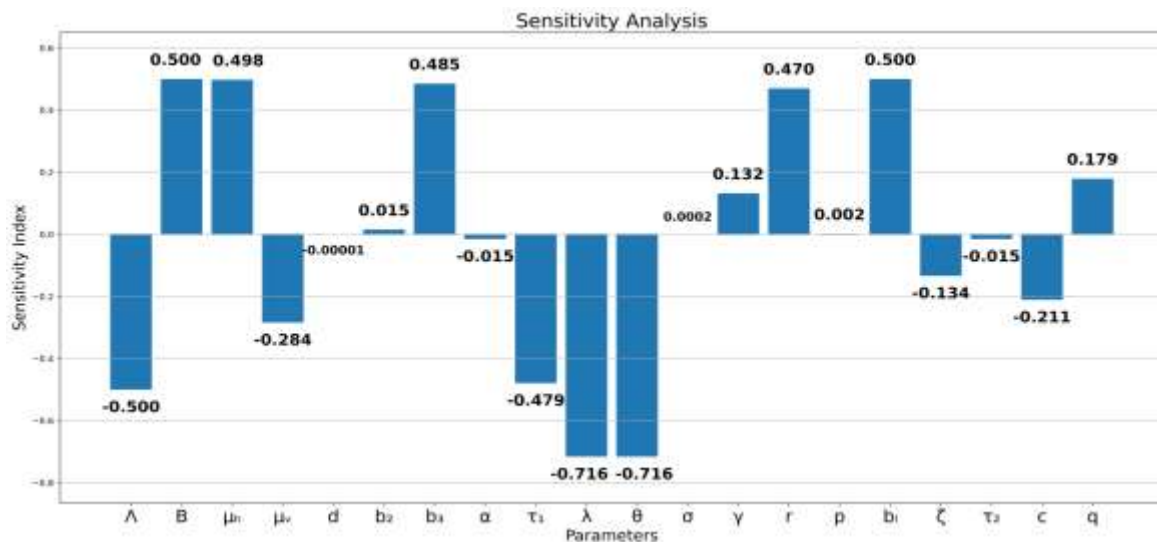


Figure 2: Sensitivity indices for R_0

Numerical Simulations

To illustrate the dynamical behavior of *Plasmodium falciparum* malaria transmission, numerical simulations were executed using MATLAB software, based on the parameter values listed in Table 2. The model was simulated under an initial condition: $S(0) = 650$, $E(0) = 110$, $I_1(0) = 80$, $I_2(0) = 110$, $R(0) = 50$, $U(0) = 900$, $W(0) = 100$, to examine the temporal evolution of human and mosquito population compartments. To assess the combined effects of antimalarial drug resistance and insecticide resistance on disease transmission, two different epidemiological scenarios were analyzed: a Low-Resistance Scenario and a High-Resistance Scenario. The simulation outcomes for both scenarios are presented and discussed in the following figures.

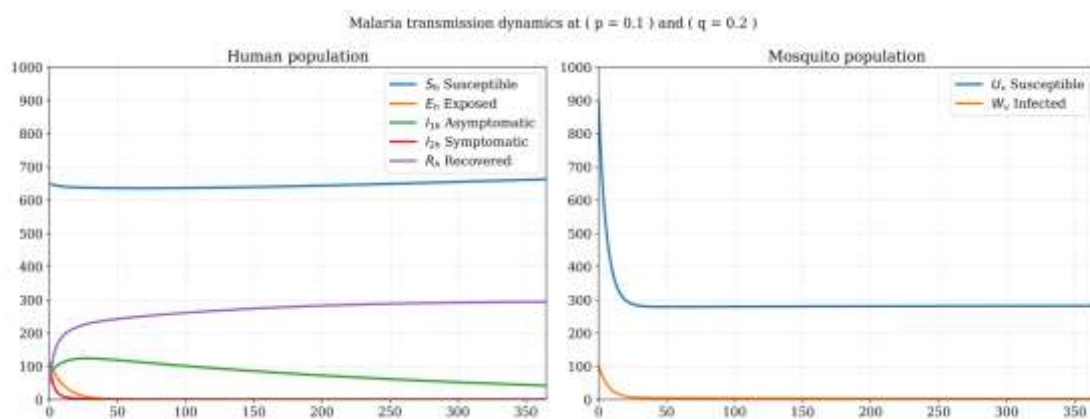


Figure 3: Human and mosquito population dynamics under low levels of drug and insecticide resistance conditions

Figure 3 shows the behavior of human and mosquito populations under low levels of both drug resistance ($p = 0.2$) and insecticide resistance ($q = 0.1$). In the human population, the susceptible class (S) exhibits transient decline under primary infection pressure, before steadily recovering and stabilizing as transmission intensity recedes. Driven by this waning force of infection, the exposed compartment (E) steadily drops toward zero, as entry into the incubation phase ceases while existing cases continuously progress out of this class. The symptomatic infected (I_2) exhibits a steady and rapid decline toward zero, driven by effective antimalarial treatment. In contrast, the asymptomatic infected compartment (I_1) demonstrates a slow and gradual reduction; this lingering behavior is attributed to the absence of direct clinical intervention, relying solely on the low natural recovery ($\tau_1 = 0.0035$). Consequently, the recovered population (R) steadily increases as infected individuals clear the parasite through treatment and natural immunity. In the mosquito population, the density of infectious mosquitoes (W) decreases continuously toward zero as a result of effective insecticide control, allowing the susceptible vector population (U) to stabilize at its natural carrying capacity. Overall, these

numerical results demonstrate that low levels of drug and insecticide resistance substantially reduce malaria transmission. The decline of exposed, symptomatic infected, and infectious mosquito populations indicates effective interruption of transmission pathways, while the slower reduction of asymptomatic infections highlights their potential persistence as a silent reservoir during the considered simulation period.

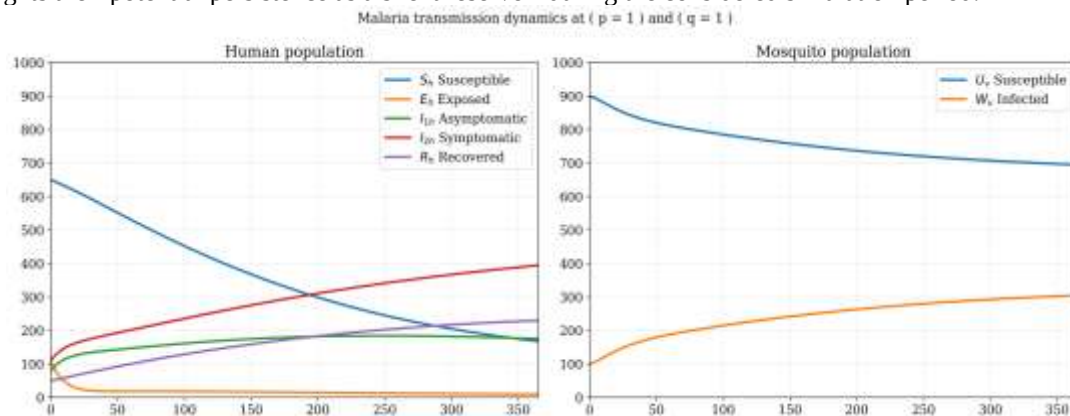


Figure 4: Human and mosquito population dynamics under high levels of drug and insecticide resistance

Figure 4 displays the temporal dynamics of human and mosquito population compartments under elevated levels of drug and insecticide resistance ($p = 1$, $q = 1$). In the human population, the susceptible (S) experiences a steady, steep decline under high primary infection pressure, before stabilizing at a significantly reduced level. Owing to compromised therapeutic efficacy and persistent vector transmission, the symptomatic infected compartment (I_2) constantly accumulates, reaching a high burden throughout the simulation period. The asymptomatic group (I_1) shows an initial transient increase before gradually declining to a lower stationary state, while the exposed population (E) drops rapidly to a very low level. Consequently, the recovered population (R) settles at a lower plateau, reflecting limited curative clearance under drug-resistant conditions. In the mosquito population, the density of infectious vectors (W) increases significantly and remains sustained at a high level owing to insecticide failure, while the susceptible vector population (U) stabilizes at a lower capacity. Taken together, these numerical trajectories confirm that high resistance levels severely undermine control interventions, resulting in persistent malaria transmission and a sustained disease burden across both host and vector populations.

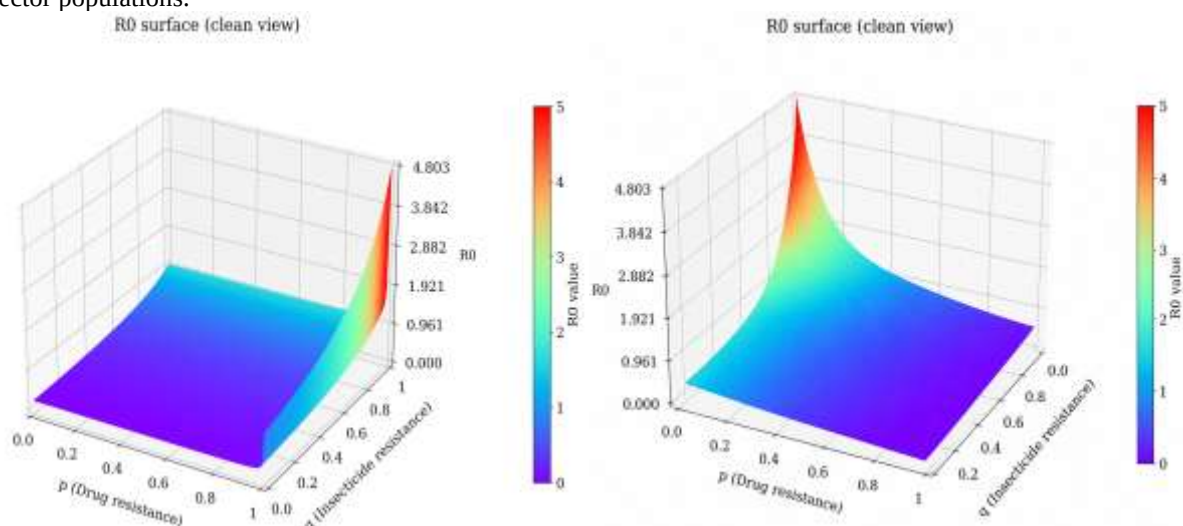


Figure 5: Three-dimensional surface plot of the malaria basic reproduction number (R_0) as a function of drug resistance (p) and insecticide resistance (q)

Figure 5 illustrates the relationship between the basic reproduction number (R_0) of malaria and two key resistance parameters: 1_ Drug resistance (p), 2_ Insecticide resistance (q). The response surface clearly delineates two distinct epidemiological regimes based on the critical epidemic threshold. Across a broad domain of low-to-moderate resistance levels, the surface remains relatively flat within the lower basin, where $R_0 < 1$. This highlights that when dual resistance is effectively constrained, current control interventions remain sufficient to suppress malaria transmission below the threshold, supporting disease elimination. Conversely, as drug and insecticide resistance co-escalate toward their upper bounds ($p, q \rightarrow 1$); the surface exhibits a sharp surge, driving R_0 to a peak value of approximately 4.803. This dramatic elevation demonstrates that high dual

resistance substantially heightens transmission potential, rendering vector control and treatment strategies ineffective and guaranteeing sustained disease endemicity.

Conclusion

In this study, a deterministic mathematical model was developed to study malaria transmission and evaluate the combined effects of drug resistance in humans and insecticide resistance in mosquitoes, with the incorporation of asymptomatic infections to achieve a more realistic biological representation. Sensitivity analysis was performed to identify the most influential parameters governing disease dynamics, and its results showed that transmission rates b_1 , b_3 , mosquito recruitment rate B , and the proportion of asymptomatic individuals r are among the primary drivers of malaria transmission. Meanwhile, both insecticide effectiveness and the associated mosquito mortality rate contribute significantly to reducing the value of R_0 . In addition, drug resistance p and insecticide resistance q reduce the effectiveness of intervention strategies and promote disease persistence. Numerical simulations supported the analytical findings and showed that increasing resistance levels leads to continued transmission, while reducing resistance enhances the effectiveness of control strategies. Overall, these findings highlight that malaria control cannot rely on a single intervention strategy; rather, it requires an integrated and comprehensive approach of interventions.

Regarding future work, the proposed model can be expanded through three main axes: dividing treated human cases according to their carriage of drug-sensitive or drug-resistant parasite strains, separating infected mosquito populations according to their susceptibility or resistance to the insecticide, incorporating climate change as a time-varying factor affecting transmission dynamics, and integrating population migration flows from endemic regions.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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