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Vector-Borne Malaria Epidemic Model with Vaccination

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Abstract This paper presents the dynamic epidemic model of the direct transmission of the vector-host type. The malaria distribution model is determined by a system of ordinary differential equations. The host population is divided into four subpopulations: susceptible, exposed, infected, and recovered, and the vector population is divided into three subpopulations: susceptible, exposed, and infected. Using the theory of Lyapunov functions, certain sufficient conditions are achieved for the stability of the disease-free equilibrium and endemic equilibrium. The basic reproductive number R_0 has been found, it characterizes the epidemic development in the population. The part of the human population is vaccinated and we examine how this prevents the development of mosquitoes in the vector population. Finally, numerical modeling is carried out to study the influence of key parameters on the spread of vector-borne diseases.

Keywords: malaria, vector-host epidemic model, numerical modeling, host population, vector population, subpopulations, reproductive number, disease-free equilibrium, endemic equilibrium.

1. Introduction

Malaria is a vector-borne disease transmitted during blood meal by infectious anopheles mosquitoes as a result of sporozoites spreading into the blood of susceptible people (Niare et al., 2016). According to the latest global malaria report from the World Health Organization (WHO), in 2020, there were about 241 million cases of malaria worldwide and 627000 deaths from malaria. This is about 14 million more cases in 2020 compared to 2019 and 69000 more deaths. Approximately two thirds of these additional deaths (47000) have been associated with interruptions in the provision of malaria prevention, diagnosis, and treatment services during the pandemic (Labadin et al., 2009, WHO, 2021).

Mathematical modeling is an important tool for understanding the spread of infectious diseases. Modeling means describing the real situation in a mathematical form, most often in equations, so one cannot pretend to model the spread of the disease without knowing, at least in general terms, the mechanisms of its spread.

The mathematical model provides only part of the theory to determine the dynamics and possible measures to combat the transmission of pathogens by mosquitoes: it is also necessary to use epidemiological and entomological concepts to measure disease transmission (Smith et al., 2021). Mathematical modeling uses more or less computerized models to describe, explain, or predict behavior or phenomena in the real world. This approach is especially relevant for studying questions or testing ideas in complex systems. It makes an important contribution to decision-making in the fight against simulated disease, which involves a profound change in the complex network of interconnected biological systems. The evolutionary potential of parasites and vectors, the increase and decrease of human immunity, behavioral

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changes in human and vector populations, as well as interactions within numerous and heterogeneous subpopulations of the corresponding organisms complicate the development of optimal programs and policies (WHO, 2024).

The popularity of modeling the spread of malaria is partly explained by its virulence. It is indeed one of the causes of mortality among infectious diseases worldwide, such as respiratory infections, HIV/AIDS, diarrhea diseases, and tuberculosis (Jia, 2013). From one to three million people die from malaria every year, 75% of which are African children (Nakul et al., 2006). In sub-Saharan Africa, it is the second leading cause of death.

In the Millennium Development Goals, WHO has set itself the goal of eradicating this disease. The joint efforts of many stakeholders are needed to achieve this goal. Among these subjects, mathematicians have a role to play in developing mathematical models that will help public health authorities take consistent measures to reduce the spread of this disease and thus lead to a reduction in mortality rates.

Since the nineteenth century, the development of mathematical models has been crucial in providing a foundation and understanding of the dynamics of infectious diseases (Bernoulli, 1760, Kermack et al., 1927, Dietz et al., 2002). Several mathematical models of malaria dynamics have appeared in the literature, studying various aspects of this disease (Herdicho et al., 2021). While the mosquito population fluctuates depending on the climatic seasons, the seasonal factor usually affects the dynamics of infected mosquitoes and human populations in regions with a warm climate (Herdicho et al., 2021). Due to mathematical traceability and convenience, we will not take into account the seasonality of mosquito birth rates. For several decades, concerted and determined efforts have been made around the world to develop an effective and safe vaccine for usage in the human population against malaria (Forouzannia et al., 2014), with several candidate vaccines targeted at various stages of the malaria parasite life cycle (Forouzannia et al., 2015). In this mathematical model, the strategy of destroying the mosquito population is investigated. A review of integrated mathematical models for predicting the epidemiological and economic impact of malaria vaccines on clinical epidemiology and the natural history of malaria *Plasmodium falciparum* at both the individual and population levels were presented in Smith et al., 2006, Atcheson et al., 2019. It should be noted that these models provide a unique platform for predicting the short- and long-term effects of malaria vaccines on disease burden, as well as on mosquito eradication strategy, which allows to consider the temporal dynamics of effects on immunity and transmission. As mathematical models are increasingly used to make informed decisions throughout the product development process, from preclinical research to the introduction of new health interventions in countries, Galactionova et al., 2021 illustrate the usefulness of simulation approaches by considering research on the modeling of an antimalarial vaccine. A mathematical model of the vaccine association suitable for mouse malaria research based on simple probabilistic assumptions is developed in Atcheson et al., 2019.

Vaccines blocking malaria transmission have been investigated in Takashima et al., 2021, where it is shown, as expected, that vaccination has a positive effect on reducing disease burden, while malaria can be controlled if the duration of effectiveness is within the range of human life expectancy (Koella, 1991). The impact of the dynamic transmission blocking vaccine model on public health, along with existing interventions, suggests that school-age children are an attractive

population group to target when vaccinating (Challenger et al., 2021). That is, the benefits of vaccination, widespread among the population, make it possible to avoid the greatest number of cases of the disease in the population of young children. Even an imperfect malaria vaccine (with modest effectiveness and coverage) can lead to effective disease control (Teboh-Ewungkem et al., 2010).

This paper is a continuation of the work Ndiaye, 2022, where the epidemic model of malaria in the absence of vaccination is examined. It proposes a mathematical model of malaria spreading in a human population that is divided into susceptible, exposed, infected, and recovered while the mosquito population is divided into susceptible, exposed, and infected subpopulations. The system is modeled by differential equations. The stability of the equilibrium of the differential equation system is studied. The analysis shows that there are equilibria characterizing the state of the system without an epidemic, as well as stable states in the presence of an epidemic. Using the theory of Lyapunov functions and the Routh-Hurwitz criterion, we study the problem of asymptotic stability of equilibria (Ndiaye and Parilina, 2022). It is shown that the disease-free equilibrium is locally asymptotically stable when $R_0 \leq 1$. The endemic equilibrium is also locally asymptotically stable when $R_0 > 1$. In Ndiaye and Parilina, 2022, Aldila and Seno, 2019, Lipsitch et al., 2003, Britton, 2010, Diekmann et al., 2010, Van den Driessche, 2017, Jones, 2007, it is shown that the dynamics of the system is determined by the value of the basic reproductive number R_0. If $R_0 \leq 1$, the state of the system is stable in the absence of disease. If $R_0 \geq 1$, there is a single endemic equilibrium and it is asymptotically stable. Numerical modeling is carried out to study the effect of the level of vaccination of the population on the spread of the disease.

The rest of the paper has the following structure. In Section 2, the construction of a model is proposed. The equilibria are studied in Section 3. The definition of the basic reproductive number R_0 is provided in Section 4. The stability of the equilibria is investigated in Section 5. Numerical modeling results are presented in Section 6. We briefly conclude in Section 7.

2. Mathematical Model

Let there be two populations: a host (human population) and a vector (mosquito population) that have been vaccinated to reduce disease. Vaccination is expressed as a percentage. Note that dv is the percentage of vaccination performed in host population, and σ is a reduction rate of malaria infected mosquitoes by a set of methods used to eliminate or prevent mosquito development.

The model shown in Fig. 1 is based on the following hypotheses:

1. Absence of migration of individuals in the population;
2. Assumption that the sizes of both populations (human and mosquito) are not constant during a study interval;
3. Relatively short lifespan (an infected mosquito does not have time to recover);
4. Assumption that a susceptible person becomes contagious after an infected mosquito bite and becomes susceptible again after recovery; and a healthy mosquito becomes infected after it bites an infected person.

The total host population can be represented as $N(t) = S(t) + E(t) + I(t) + R(t)$ and the total vector population can be represented as $N_k(t) = S_k(t) + E_k(t) + I_k(t)$.

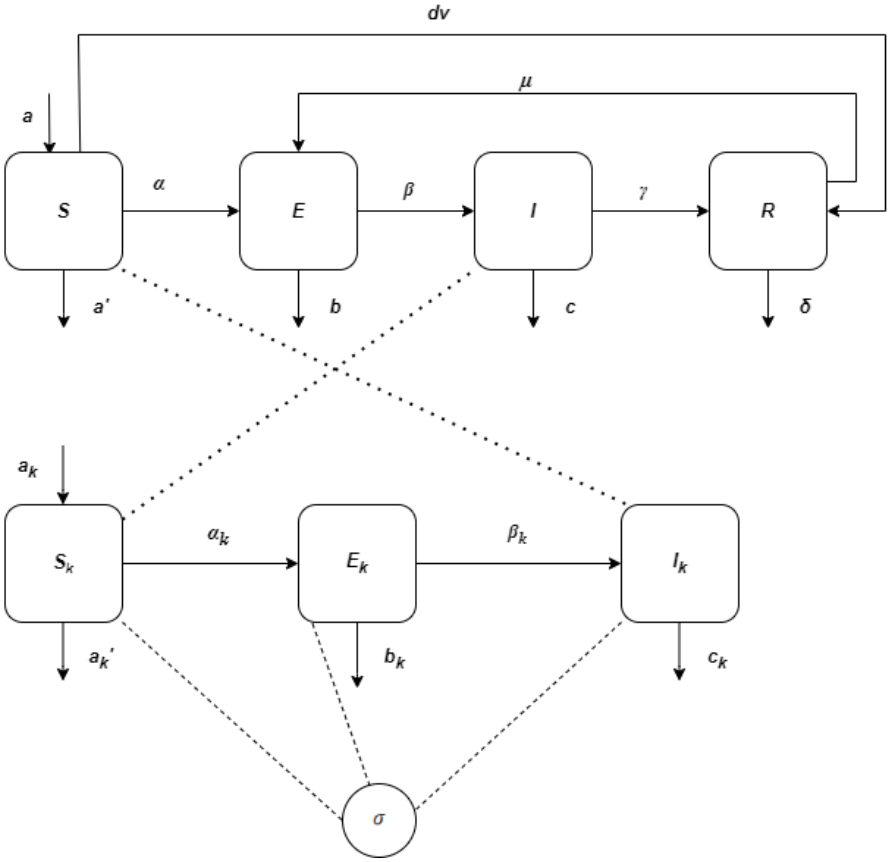

Fig. 1. Vector-borne model with vaccination

The mathematical model of population dynamics (human and mosquito) can be represented analytically by the following nonlinear system of seven ordinary differential equations:

$$\begin{cases} \dfrac{dS(t)}{dt} = -\alpha S(t)I_k(t) + aN_0(t) - a'S(t) - dvS(t), \\ \dfrac{dE(t)}{dt} = \alpha S(t)I_k(t) + \mu R(t) - bE(t) - \beta E(t), \\ \dfrac{dI(t)}{dt} = \beta E(t) - cI(t) - \gamma I(t), \\ \dfrac{dR(t)}{dt} = \gamma I(t) - \delta R(t) - \mu R(t) + dvS(t), \\ \dfrac{dS_k(t)}{dt} = -\alpha_k S_k(t)I(t) + a_k N_{k_0}(t) - a_k' S_k(t) - \sigma S_k(t), \\ \dfrac{dE_k(t)}{dt} = \alpha_k S_k(t)I(t) - b_k E_k(t) - \beta_k E_k(t) - \sigma E_k(t), \\ \dfrac{dI_k(t)}{dt} = \beta_k E_k(t) - c_k I_k(t) - \sigma I_k(t), \end{cases} \tag{1}$$

with initial conditions

$$S(0) \geq 0,\ E(0) \geq 0,\ I(0) \geq 0,\ R(0) \geq 0,\ S_k(0) \geq 0,\ E_k(0) \geq 0,\ I_k(0) \geq 0. \tag{2}$$

The general dynamics of human population is represented by the equation:

$$\frac{dN}{dt} = aN_0 - a'S - bE - cI - \delta R.$$

Given initial conditions (2) must satisfy inequality: $N(0) \geq 0$. Thus, total population size $N(t)$ remains positive and limited during the entire time $t > 0$. The dynamics of mosquito population is as follows

$$\frac{dN_k}{dt} = aN_{0_k} - a'S_k - bE_k - cI_k - \sigma(S_k + E_k + I_k).$$

The model uses the following parameters:

- $N(t)$ — size of human population;
- $S(t)$ — size of subpopulation of susceptible individuals;
- $E(t)$ — size of subpopulation of exposed people;
- $I(t)$ — size of subpopulation of infected people;
- $R(t)$ — size of subpopulation of recovered people;
- a — birth rate in human population;
- a' — mortality rate among subpopulation S;
- b — mortality rate among subpopulation E;
- c — mortality rate among infected subpopulation I;
- δ — mortality rate among recovered subpopulation R;
- β — intensity of people's transition from subpopulation E to I with the onset of isease symptoms;
- γ — intensity of people's recovery, i.e. transition from subpopulation I to R;
- μ — rate of people's return from recovered to susceptible;
- α — probability of transmitting an infectious mosquito bite to a susceptible person;
- $N_k(t)$ — total mosquito population;
- $S_k(t)$ — number of mosquitoes that can be infected;
- $E_k(t)$ — number of mosquitoes susceptible to the disease;
- $I_k(t)$ — number of infected mosquitoes;
- $a_k(t)$ — birth rate in mosquito population;
- $a'_k(t)$ — mortality in susceptible mosquito population;
- $b_k(t)$ — mortality of exposed mosquito population;
- $c_k(t)$ — mortality of infected mosquito population;
- $\alpha_k(t)$ — probability of mosquito moving from susceptible to exposed group;
- $\beta_k(t)$ — coefficient of mosquitoes that begin to show disease symptoms;
- $dv \in (0, 1)$ — level of vaccination of susceptible part of population;
- σ — decrease level of mosquito population as a result of anti-epidemiological measures.

2.1. Region of Admissible Values

A mathematical model represented by a system of differential equations (1) describes changes in human and mosquito populations. Therefore, it is important to make sure that all solutions with nonnegative initial conditions (2) will remain nonnegative for any t. All solutions of the proposed system that have initial data in region Ω.

Theorem 1. *Let* $(S, E, I, R, S_k, E_k, I_k)$ *be any solution of system* (1) *with positive initial conditions* (2). *For any time* $t \geq 0$ *there exists:*

$$\Omega = \left\{(S, E, I, R, S_k, E_k, I_k) \in \mathbb{R}^7_+, V_1 \leq \frac{aN_0}{a' + b + c + \delta}, V_2 \leq \frac{a_k N_{0_k}}{a'_k + b_k + c_k + \sigma}\right\}.$$

Then Ω *is positively invariant and absorbing for system* (1) *with initial conditions* (2).

Proof. To prove the theorem, we use the Lyapunov functions. Consider the Lyapunov function $V(t) = (V_1(t), V_2(t))$. Suppose that functions $V_1(t)$, $V_2(t)$ are defined for $\forall\ t \geq 0$, they are also differentiable and continuously differentiable on set Ω containing the origin.

The time derivative of function $V(t)$ is equal to

$$\frac{dV(t)}{dt} = \begin{cases} \dfrac{dV_1(t)}{dt} = aN_0 - (a' + b + c + \delta)V_1 - a'S - bE - cI - \delta R, \\ \dfrac{dV_2(t)}{dt} = a_k N_{0_k} - (a'_k + b_k + c_k + \sigma)V_2 - a'_k S_k - b_k E_k - c_k I_k - \sigma N_k. \end{cases} \tag{3}$$

For system (3), it is obvious that

$$\begin{aligned} \frac{dV_1(t)}{dt} &\leq aN_0 - (a' + b + c + \delta)V_1, \\ \frac{dV_2(t)}{dt} &\leq a_k N_{0_k} - (a'_k + b_k + c_k + \sigma)V_2. \end{aligned} \tag{4}$$

By the properties of the Lyapunov function, we obtain the following conditions:

$$\begin{cases} \dfrac{dV_1}{dt} \leq aN_0 - (a' + b + c + \delta)V_1 \leq 0 \ \text{ for } \ V_1 \geq \dfrac{aN_0}{a' + b + c + \sigma}, \\ \dfrac{dV_2}{dt} \leq a_k N_{0_k} - (a'_k + b_k + c_k + \sigma)V_2 \leq 0 \ \text{ for } \ V_2 \geq \dfrac{a_k N_{0_k}}{a'_k + b_k + c_k + \sigma}. \end{cases} \tag{5}$$

From the conditions of (5), it follows that $\dfrac{dV(t)}{dt} \leq 0$, which means that Ω is a positively invariant and absorbing set.

From the above equations and conditions (3), we obtain the inequalities for V_1 and V_2:

$$\begin{aligned} 0 \leq V_1(t) &\leq \frac{aN_0}{a' + b + c + \delta} + e^{-(a' + b + c + \delta)t}\left(V_{0_1} - \frac{aN_0}{a' + b + c + \delta}\right), \\ 0 \leq V_2(t) &\leq \frac{a_k N_{0_k}}{a'_k + b_k + c_k + \sigma} + e^{-(a'_k + b_k + c_k + \sigma)t}\left(V_{0_2} - \frac{a_k N_{0_k}}{a'_k + b_k + c_k + \sigma}\right). \end{aligned}$$

For $t \longrightarrow +\infty$ we get

$$\begin{aligned} 0 \leq V_1(t) &\leq \frac{aN_0}{a' + b + c + \delta}, \\ 0 \leq V_2(t) &\leq \frac{a_k N_{0_k}}{a'_k + b_k + c_k + \sigma}, \end{aligned}$$

and we can conclude that Ω is an absorbing set. Indeed, the following inequalities hold for $t \longrightarrow +\infty$:

$$\limsup_{t\to+\infty} V_1 \leq \frac{aN_0}{a' + b + c + \delta},$$
$$\limsup_{t\to+\infty} V_2 \leq \frac{a_k N_{0_k}}{a'_k + b_k + c_k + \sigma}.$$

Thus, Ω is positively invariant, and all solutions are bounded in interval $[0, \infty)$.

3. Some Equilibria

For the model, we study two equilibria of a system of differential equations (1):

1. Equilibrium without disease E_s;
2. Endemic equilibrium E_e.

Solving the following system of differential equations

$$\begin{cases} -\alpha S(t)I_k(t) + aN(t) - a'S(t) - dvS(t) & = 0 \\ \alpha S(t)I_k(t) + \mu R(t) - bE(t) - \beta E(t) & = 0, \\ \beta E(t) - cI(t) - \gamma I(t) & = 0, \\ \gamma I(t) - \delta R(t) - \mu R(t) + dvS(t) & = 0, \\ -\alpha_k S_k(t)I(t) + a_k N_k(t) - a'_k S_k(t) - \sigma S_k(t) & = 0, \\ \alpha_k S_k(t)I(t) - b_k E_k(t) - \beta_k E_k(t) - \sigma E_k(t) & = 0, \\ \beta_k E_k(t) - c_k I_k(t) - \sigma I_k(t) & = 0, \end{cases} \tag{6}$$

find two equilibrium points:

1. Equilibrium without disease free equilibrium $E_s = (\frac{a}{a'+dv}N_0, 0, 0, 0, \frac{a_k}{a'_k+dv}N_{0_k}, 0, 0)$, t .e. this is a solution to a system in which there are no disease cases in both populations;
2. Endemic equilibrium of system $E_e = (S^*, E^*, I^*, R^*, S^*_k, E^*_k, I^*_k)$, implying the presence of a disease and all subpopulations are present in population.

To find equilibrium, from the first equation of system (6) we get $S = \dfrac{aN_0}{\alpha I_k + a' + dv}$, from the third equation we get $E = \dfrac{c+\gamma}{\beta} I$ or $I = \dfrac{\beta}{c+\gamma} E$, then from the fourth equation: $R = \dfrac{\gamma}{\delta+\mu} I + \dfrac{dv}{\sigma+\mu} S$, from the fifth equation: $S_k = \dfrac{a_k N_{0_k}}{\alpha_k I + a'k + \sigma}$, from the sixth equation: $E_k = \dfrac{\alpha_k S_k}{b_k + \beta_k + \sigma} I$, from the seventh equation: $I_k = \dfrac{\beta_k E_k}{c_k + \sigma}$, from the second equation: $E = \dfrac{\alpha}{b+\beta} S I_k + \dfrac{\mu}{b+\beta} R$.

Substituting the first, third, fourth, fifth, sixth and seventh equations of system (6) into the second equation of the system, we obtain

$$E = \frac{aa_k\alpha\alpha_k\beta_k N_0 N_{0_k}(\gamma + c)(\delta + \mu)I + \mu a N_0(\gamma + c)K_1}{K_2(a_k\alpha\alpha_k\beta_k N_{0_k} I + (a' + dv)K_1)},$$

where

$$K_1 = (c_k + \sigma)(\beta_k + b_k + \sigma)(\alpha_k I + a'_k + \sigma),$$
$$K_2 = (b + \beta)(\delta + \mu)(c + \gamma) - \mu\gamma\beta.$$

Establishing equality with the third equation obtained in system (6), we get an equation of the second degree, which has two solutions, and the solution that satisfies the conditions is:

$$I = \frac{-(\beta a N_0 \alpha_k(\alpha\beta_k a_k N_k(\delta + \mu) + \mu(c_k + \sigma)(\beta_k + b_k + \sigma)))}{2K_2(\alpha\alpha_k\beta_k a_k N_{k_0} + \alpha_k(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma))} +$$
$$+ \frac{-(K_2(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma)(a'_k + \sigma)) + \sqrt{\Delta}}{2K_2(\alpha\alpha_k\beta_k a_k N_{k_0} + \alpha_k(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma))},$$

where

$$\begin{aligned}\Delta = {} & [K_2(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma)(a'_k + \sigma) + \\ & + K_2(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma)(a'_k + \sigma)]^2 - \\ & - 4K_2(\alpha\alpha_k\beta_k a_k N_{k_0} + \alpha_k(a' + dv)(c_k + \sigma) \times \\ & \times (\beta_k + b_k + \sigma))(\beta a N_0 \mu(c_k + \sigma)(\beta_k + b_k + \sigma)(a'_k + \sigma)).\end{aligned}$$

Therefore, the endemic equilibrium of model (1) is defined as a vector $E_e = (S^*, E^*, I^*, R^*, S_k^*, E_k^*, I_k^*)$ with components:

$$I^* = \frac{-(\beta a N_0 \alpha_k(\alpha\beta_k a_k N_k(\delta + \mu) + \mu(c_k + \sigma)(\beta_k + b_k + \sigma)))}{2K_2(\alpha\alpha_k\beta_k a_k N_{k_0} + \alpha_k(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma))} +$$
$$+ \frac{-(K_2(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma)(a'_k + \sigma)) + \sqrt{\Delta}}{2K_2(\alpha\alpha_k\beta_k a_k N_{k_0} + \alpha_k(a' + dv)(c_k + \sigma)(\beta_k + b_k + \sigma))},$$
$$S^* = \frac{aN_0}{\alpha I_k^* + a' + dv},$$
$$E^* = \frac{c + \gamma}{\beta} I^*,$$
$$R^* = \frac{\gamma}{\delta + \mu} I^* + \frac{dv}{\delta + \mu} S^*,$$
$$S_k^* = \frac{a_k N_{0_k}}{\alpha_k I^* + a'_k}\sigma,$$
$$E_k^* = \frac{\alpha_k}{b_k + \beta_k - \sigma} S_k^* I^*,$$
$$I_k^* = \frac{\beta_k}{c_k + \sigma} E_k^*.$$

Equilibrium E_e is an endemic point of the model, where all subgroups of two populations are represented.

4. Basic Reproduction Number R_0

Determine basic reproduction number R_0 for modified model $SEIRS_kE_kI_k$ presented above. This number is used to study the epidemic process evolution and

can be interpreted as an average number of new malaria cases caused by one infected person in a fully susceptible population. To calculate R_0, we use a *method of next-generation matrix* described in Calistus, 2022, Chander and Tulkens, 1997, Chang et al., 2020, Cooper et al., 2020. For the presented model, the calculation of R_0 can be represented as follows:

$$\begin{aligned}\frac{dx}{dt} &= F(x) - V(x),\\ x &= (S, E, I, R, S_k, E_k, I_k)^T.\end{aligned}$$

Using a next generation matrix method, the following calculations are required. First, we define matrices F and V:

$$\mathcal{F} = \begin{pmatrix} \alpha_k S_k(t) I(t) \\ 0 \\ \alpha S(t) I_k(t) \\ 0 \end{pmatrix}, \quad \mathcal{V}^+ = \begin{pmatrix} \mu R(t) \\ \beta E(t) \\ 0 \\ \beta_k E_k(t) \end{pmatrix}, \quad \mathcal{V}^- = \begin{pmatrix} -(b+\beta)E(t) \\ -(c+\gamma)I(t) \\ -(b_k+\beta_k)E_k(t) - \sigma E_k \\ -c_k I_k(t) - \sigma I_k(t) \end{pmatrix},$$

hence we get that

$$\mathcal{V} = \mathcal{V}^+ + \mathcal{V}^- = \begin{pmatrix} \mu R(t) - (b+\beta)E(t) \\ \beta E(t) - (c+\gamma)I(t) \\ -(b_k+\beta_k)E_k(t) - \sigma E_k \\ \beta_k E_k(t) - c_k I_k(t) - \sigma I_k \end{pmatrix}.$$

Define matrices

$$D\mathcal{F}(E_s) = \begin{pmatrix} 0 & \alpha_k S_k^0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \alpha S^0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$D\mathcal{V}(E_s) = \begin{pmatrix} -(b+\beta) & 0 & 0 & 0 \\ \beta & -(c+\gamma) & 0 & 0 \\ 0 & 0 & -(b_k+\beta_k+\sigma) & 0 \\ 0 & 0 & \beta_k & -(c_k+\sigma) \end{pmatrix}.$$

Hence,

$$F = \begin{bmatrix} 0 & \alpha_k S_k^0 \\ 0 & 0 \end{bmatrix}, \quad F' = \begin{bmatrix} 0 & \alpha S^0 \\ 0 & 0 \end{bmatrix},$$
$$V = \begin{bmatrix} -(b+\beta) & 0 \\ \beta & -(c+\gamma) \end{bmatrix}, \quad V' = \begin{bmatrix} -(b_k+\beta_k+\sigma) & 0 \\ \beta_k & -(c_k+\sigma) \end{bmatrix}.$$

Calculate R_0 using formula $R_0 = \rho(-FV^{-1})$, where

$$V^{-1} = \frac{1}{det(V)} t_{(com(V))},$$

and

$$det(V) = (b+\beta)(c+\gamma), \quad t_{(com(V))} = \begin{bmatrix} -(c+\gamma) & 0 \\ -\beta & -(b+\beta) \end{bmatrix}.$$

Substituting $det(V)$ and $t_{(com(V))}$ into expression V^{-1}, we get

$$V^{-1} = \frac{1}{(b+\beta)(c+\gamma)} \begin{bmatrix} -(c+\gamma) & 0 \\ -\beta & -(b+\beta) \end{bmatrix},$$
$$(V')^{-1} = \frac{1}{(b_k+\beta_k+\sigma)(c_k+\sigma)} \begin{bmatrix} -(c_k+\sigma) & 0 \\ -\beta_k & -(b_k+\beta_k+\sigma) \end{bmatrix}.$$

These formulas are valid:

$$FV^{-1} = \begin{bmatrix} -\frac{\alpha_k\beta S_k^0}{(b+\beta)(c+\gamma)} & -\frac{\alpha_k S_k^0}{c+\gamma} \\ 0 & 0 \end{bmatrix},$$
$$FV'^{-1} = \begin{bmatrix} -\frac{\alpha\beta_k S^0)}{(c_k+\sigma)(b_k+\beta_k+\sigma)} & -\frac{\alpha S^0}{(c_k+\sigma)} \\ 0 & 0 \end{bmatrix},$$

calculate R_h and R_k:

$$R_h = \rho(-FV^{-1}) = \frac{\alpha_k\beta S_k^0}{(b+\beta)(c+\gamma)}, \quad R_k = \rho(-FV'^{-1}) = \frac{\alpha\beta_k S^0}{(c_k+\sigma)(b_k+\beta_k+\sigma)},$$

from which we obtain the basic reproduction number R_0 in the form:

$$R_0 = R_h \times R_k = \frac{\alpha_k\beta S_k^0 \alpha\beta_k S^0}{c_k+\sigma)(b_k+\beta_k+\sigma)(b+\beta)(c+\gamma)},$$

where $(S^0, S_k^0) = (\frac{a}{a'+dv}N_0, \frac{a_k}{a_k'+\sigma}N_{0_k})$, and as a result write the final formula for R_0:

$$R_0 = \frac{\alpha\beta\alpha_k\beta_k a a_k N_0 N_{0_k}}{(a_k'+\sigma)(c_k+\sigma)(a'+dv)(b+\beta)(c+\gamma)(b_k+\beta_k+\sigma)}.$$

R_0 gives information about the disease course. If $R_0 \leq 1$, the number of infected people will decrease, and the disease will eventually pass. If $R_0 \geq 1$, the number of infected people increases, the disease can spread to the entire population and become endemic. Numerical analysis will show how the disease proceeds in the population at different values of R_0.

5. Equilibrium Stability

First, we analyze the stability of equilibrium without disease using the system of equations (1) using basic reproductive number R_0.

Theorem 2. *Disease-free equilibrium E_s is locally asymptotically stable if $R_0 \leq 1$ and $\frac{B_1B_2B_3+B_1B_5}{B_1^2B_4+B_3^2} > 1$, and unstable if $R_0 > 1$. Expressions for B_1, B_2, B_3, B_4 and B_5 are given in the proof.*

Proof. The Jacobi matrix of system (1) is written as

$J(S, E, I, R, S_k, E_k, I_k) =$

$$\begin{pmatrix} -\alpha I_k - a' - dv & 0 & 0 & 0 & 0 & 0 & -\alpha S \\ \alpha I_k & -b-\beta & 0 & \mu & 0 & 0 & \alpha S \\ 0 & \beta & -c-\gamma & 0 & 0 & 0 & 0 \\ dv & 0 & \gamma & -\delta-\mu & 0 & 0 & 0 \\ 0 & 0 & -\alpha_k S_k & 0 & -\alpha_k I - a_k' - \sigma & 0 & 0 \\ 0 & 0 & \alpha_k S_k & 0 & \alpha_k I & -b_k-\beta_k-\sigma & 0 \\ 0 & 0 & 0 & 0 & 0 & \beta_k & -c_k-\sigma \end{pmatrix}.$$

The Jacobi matrix at disease-free equilibrium point E_s is equal to

$$J(E_s) = \begin{pmatrix} -a'-dv & 0 & 0 & 0 & 0 & 0 & -\alpha\frac{aN_0}{a'+dv} \\ 0 & -b-\beta & 0 & \mu & 0 & 0 & \alpha\frac{aN_0}{a'+dv} \\ 0 & \beta & -c-\gamma & 0 & 0 & 0 & 0 \\ dv & 0 & \gamma & -\delta-\mu & 0 & 0 & 0 \\ 0 & 0 & -\alpha_k\frac{a_kN_{0_k}}{a'_k+\sigma} & 0 & -a'_k-\sigma & 0 & 0 \\ 0 & 0 & \alpha_k\frac{a_kN_{0_k}}{a'_k+\sigma} & 0 & 0 & -(b_k+\beta_k+\sigma) & 0 \\ 0 & 0 & 0 & 0 & 0 & \beta_k & -c_k-\sigma \end{pmatrix}.$$

Let's find the eigenvalues of this matrix by equating its determinant to zero, that is,

$$\begin{vmatrix} -a'-dv-\lambda & 0 & 0 & 0 & 0 & 0 & -\alpha\frac{aN_0}{a'+dv} \\ 0 & -b-\beta-\lambda & 0 & \mu & 0 & 0 & \alpha\frac{aN_0}{a'+dv} \\ 0 & \beta & -c-\gamma-\lambda & 0 & 0 & 0 & 0 \\ dv & 0 & \gamma & -\delta-\mu-\lambda & 0 & 0 & 0 \\ 0 & 0 & -\alpha_k\frac{a_kN_{0_k}}{a'_k-\sigma} & 0 & -a'_k-\sigma-\lambda & 0 & 0 \\ 0 & 0 & \alpha_k\frac{a_kN_{0_k}}{a'_k+\sigma} & 0 & 0 & -(b_k+\beta_k+\sigma)-\lambda & 0 \\ 0 & 0 & 0 & 0 & 0 & \beta_k & -c_k-\sigma-\lambda \end{vmatrix}$$

we obtain the following characteristic equation:

$$\lambda^7 + B_1\lambda^6 + B_2\lambda^5 + B_3\lambda^4 + B_4\lambda^3 + B_5\lambda^2 + B_6\lambda + B_7 = 0,$$

where

$$\begin{aligned}
B_1 &= \beta_k + b_k + c_k + 3\sigma + a'_k + \gamma + c + \delta + \mu + a' + dv + b + \beta, \\
B_2 &= (\beta_k + b_k + \sigma)(c_k + \sigma) + (b_k + \beta_k + c_k + 2\sigma)(a'_k + \sigma) + (\gamma + c + \delta + \mu + \\
&\quad + a' + dv + \beta + b)(\beta_k + b_k + c_k + 3\sigma + a'_k) + (a' + dv)(\beta + b) + \\
&\quad + (a' + dv + \beta + b)(\gamma + c + \delta + \mu) + (\gamma + c)(\delta + \mu), \\
B_3 &= (a'_k + \sigma)(\beta_k + b_k + \sigma)(c_k + \sigma) + (\gamma + c + \delta + \mu + a' + dv + \beta + b) \\
&\quad ((\beta_k + b_k + \sigma)(c_k + \sigma) + (b_k + \beta_k + c_k + 2\sigma)(a'_k + \sigma)) + ((a' + dv)(\beta + b) + \\
&\quad + (a' + dv + \beta + b)(\gamma + c + \delta + \mu) + \\
&\quad + (\gamma + c)(\delta + \mu))(\beta_k + b_k + c_k + 3\sigma + a'_k) + ((a' + dv)(\beta + b)(\gamma + c + \delta + \mu) + \\
&\quad + (\gamma + c)(\delta + \mu)(a' + dv + \beta + b)) + \beta\gamma\mu, \\
B_4 &= (\gamma + c + \delta + \mu + a' + dv + \beta + b)(a'_k + \sigma)(\beta_k + b_k + \sigma)(c_k + \sigma) + \\
&\quad + ((a' + dv)(\beta + b) + (a' + dv + \beta + b)(\gamma + c + \delta + \mu) + \\
&\quad + (\gamma + c)(\delta + \mu))((\beta_k + b_k + \sigma)(c_k + \sigma) + (b_k + \beta_k + c_k + 2\sigma)(a'_k + \sigma)) + \\
&\quad + (a' + dv)(\beta + b)(\gamma + c + \delta + \mu) + (\gamma + c)(\delta + \mu)(a' + dv + \beta + b) + \\
&\quad + ((a' + dv)(\beta + b) + (a' + dv + \beta + b)(\gamma + c + \delta + \mu) + \\
&\quad + (\gamma + c)(\delta + \mu))(\beta_k + b_k + c_k + 3\sigma + a'_k) + (a' + dv)(\beta + b)(\gamma + c)(\delta + \mu) - \\
&\quad - \frac{\alpha\beta\alpha_k\beta_k a a_k N_0 N_{0_k}}{(a'_k + \sigma)(a' + dv)} + \beta\gamma\mu(b_k + \beta_k + c_k + 2\sigma) + \beta\gamma\mu(a' + a_k + dv + \sigma),
\end{aligned}$$

$$
\begin{aligned}
B_5 &= (a'_k+\sigma)(\beta_k+b_k+\sigma)(c_k+\sigma)((a'+dv)(\beta+b)+(a'+dv+\beta+b)\\
&\quad (\gamma+c+\delta+\mu)+(\gamma+c)(\delta+\mu))+((a'+dv)(\beta+b)(\gamma+c+\delta+\mu)+\\
&\quad +(\gamma+c)(\delta+\mu)(a'+dv+\beta+b))((\beta_k+b_k+\sigma)(c_k+\sigma)+\\
&\quad +(a'_k+\sigma)(\beta_k+b_k+c_k+2\sigma))+(a'+dv)(b+\beta)(c+\gamma)(\delta+\mu)\\
&\quad (b_k+\beta_k+c_k+3\sigma+a'_k)-\frac{2\alpha\beta\alpha_k\mu aa_k dvN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}-\\
&\quad -\frac{\alpha\beta\alpha_k\beta_k aa_kN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}(\delta+\mu)+\beta\gamma\mu(b_k+\beta_k+\sigma)(c_k+\sigma)-(a'+a_k+dv+\sigma)\\
&\quad (\frac{\alpha\beta\alpha_k\beta_k aa_kN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}+\beta\gamma\mu(b_k+\beta_k+c_k+2\sigma)+\beta\gamma\mu(a'+dv)(a'_k+\sigma),\\
B_6 &= ((a'+dv)(b+\beta)(c+\gamma+\delta+\mu)+(c+\gamma)(\delta+\mu)(a'+dv+b+\beta))\\
&\quad ((a'_k+\sigma)(\beta_k+b_k+\sigma)(c_k+\sigma)+(\beta_k+b_k+\sigma)(c_k+\sigma)+(a'_k+\sigma)\\
&\quad (\beta_k+b_k+c_k+2\sigma))(a'+dv)(\beta+b)(\gamma+c)(\delta+\mu)-\\
&\quad -\frac{\alpha\beta\alpha_k\mu aa_k dvN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}(2c_k+a'_k+\beta_k+b_k+4\sigma)\\
&\quad -\frac{\alpha\beta\alpha_k\mu aa_k dvN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}(2c_k+a'_k+\beta_k+b_k+4\sigma)-\\
&\quad -(a'-a_k+dv+\sigma)\frac{\alpha\beta\alpha_k\beta_k aa_kN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}(\delta+\mu)+\beta\gamma\mu(b_k+\beta_k+\sigma)(c_k+\sigma)-\\
&\quad -(a'_k+\sigma)(a'+dv)\frac{\alpha\beta\alpha_k\beta_k aa_kN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}+\beta\gamma\mu(b_k+\beta_k+c_k+2\sigma),\\
B_7 &= (a'+dv)(b+\beta)(c+\gamma)(\delta+\mu)(a'_k+\sigma)(\beta_k+b_k+\sigma)(c_k+\sigma)-\\
&\quad -(a'_k+\sigma)(a'+dv)\frac{\alpha\beta\alpha_k\beta_k aa_kN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}(\delta+\mu)+\beta\gamma\mu(b_k+\beta_k+\sigma)(c_k+\sigma)-\\
&\quad -\frac{\alpha\beta\alpha_k\mu aa_k dvN_0N_{0_k}}{(a'_k+\sigma)(a'+dv)}(c_k+\sigma)(a'_k+\beta_k+b_k+2\sigma).
\end{aligned}
$$

The characteristic equation can have seven roots, which can be obtained by solving the following equation:

$$\lambda^7+B_1\lambda^6+B_2\lambda^5+B_3\lambda^4+B_4\lambda^3+B_5\lambda^2+B_6\lambda+B_7=0.$$

It is impossible to write the solutions explicitly, so to determine the nature of the stability of equilibrium point E_s, we use the Routh-Hurwitz criterion to study the

stability. To do this, we write an auxiliary matrix

$$\begin{vmatrix} 1 & B_2 & B_4 & B_6 & 0 & 0 \\ B_1 & B_3 & B_5 & B_7 & 0 & 0 \\ \dfrac{B_1B_2-B_3}{B_1} & \dfrac{B_1B_4-B_5}{B_1} & \dfrac{B_1B_6-B_7}{B_1} & 0 & 0 & 0 \\ B_3-\dfrac{B_1(B_1B_4-B_5)}{B_1B_2-B_3} & B_5-\dfrac{B_1(B_1B_6-B_7)}{B_1B_2-B_3} & B_7 & 0 & 0 & 0 \\ B_1' & B_2' & 0 & 0 & 0 & 0 \\ B_3' & B_7 & 0 & 0 & 0 & 0 \\ \dfrac{B_3'B_2'-B_1'B_7}{B_3'} & 0 & 0 & 0 & 0 & 0 \\ B_7 & 0 & 0 & 0 & 0 & 0, \end{vmatrix},$$

where

$$B_1' = \frac{B_1B_4-B_5}{B_1} - \frac{(B_1B_2-B_3)(B_5(B_1B_2-B_3)-B_1(B_1B_6-B_7))}{B_1(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5))},$$
$$B_2' = \frac{B_1B_6-B_7}{B_1} - \frac{B_7(B_1B_2-B_3)^2}{B_1(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5))},$$
$$B_3' = B_5 - \frac{B_1(B_1B_6-B_7)}{B_1B_2-B_3} - \frac{B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5)}{B_1B_2-B_3}\frac{B_2'}{B_1'}.$$

Applying the Routh-Hurwitz criterion, we obtain that system (1) is asymptotically stable at equilibrium E_s if these inequalities are satisfied:

$$B_1 > 0,$$
$$B_7 > 0,$$
$$\frac{B_1B_2-B_3}{B_1} > 0,$$
$$B_3 - \frac{B_1(B_1B_4-B_5)}{B_1B_2-B_3} > 0,$$
$$\frac{B_1B_4-B_5}{B_1} - \frac{(B_1B_2-B_3)(B_5(B_1B_2-B_3)-B_1(B_1B_6-B_7))}{B_1(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5))} > 0,$$
$$\frac{B_1B_6-B_7}{B_1} - \frac{B_7(B_1B_2-B_3)^2}{B_1(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5))} > 0,$$
$$B_5 - \frac{B_1(B_1B_6-B_7)}{B_1B_2-B_3} - \frac{B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5)}{B_1B_2-B_3}\frac{B_2'}{B_1'} > 0,$$
$$\frac{B_3'B_2'-B_1'B_7}{B_3'} > 0.$$

Then from $\frac{B_1B_2-B_3}{B_1} > 0$ and $B_1 > 0$ it follows that $B_1B_2 - B_3 > 0$. The fourth inequality is equivalent to $B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5) > 0$, or $B_1B_2-B_3 > 0$. The fifth inequality is equivalent to $B_1(B_1B_4-B_5)(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5))-B_1(B_1B_2-B_3)(B_5(B_1B_2-B_3)-B_1(B_1B_2-B_3)-B_1B_6-B_7)) > 0$, or $B_1^2(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5) > 0$. The sixth inequality is equivalent to $B_1(B_1B_6-B_7)(B_3(B_1B_2-B_3)-B_1(B_1B_4-B_5))-B_1B_7(B_1B_2-B_3)^2 > 0$, or $B_1' > 0$. The seventh inequality is equivalent to $B_5B_1'(B_1B_2-B_3)-B_1B_1'(B_1B_6-$

$B_7) - B_2'(B_3(B_1B_2 - B_3) - B_1(B_1B_4 - B_5)) > 0$. Then the last inequality can be simplified as $B_3'B_2' - B_1'B_7 > 0$, or $B_3' > 0$.

Therefore, we get the system:

$$\begin{aligned}
B_1 &> 0,\\
B_7 &> 0,\\
B_1B_2 - B_3 &> 0,\\
B_3(B_1B_2 - B_3) - B_1(B_1B_4 - B_5) &> 0,\\
B_1(B_1B_4 - B_5)(B_3(B_1B_2 - B_3) - B_1(B_1B_4 - B_5))- &\\
-B_1(B_1B_2 - B_3)(B_5(B_1B_2 - B_3) - B_1(B - 1B_6 - B_7)) &> 0,\\
B_1(B_1B_6 - B_7)(B_3(B_1B_2 - B_3) - B_1(B_1B_4 - B_5)) - B_1B_7(B_1B_2 - B_3)^2 &> 0,\\
B_5B_1'(B_1B_2 - B_3) - B_1B_1'(B_1B_6 - B_7) - B_2'(B_3(B_1B_2 - B_3)- &\\
-B_1(B_1B_4 - B_5)) &> 0,\\
B_3'B_2' - B_1'B_7 &> 0,
\end{aligned}$$

then seven eigenvalues have negative real parts, which follows from the Routh-Hurwitz criterion. Thus, all eigenvalues of the characteristic equation have negative real parts if and only if $R_0 < 1$ and $B_1B_2B_3 + B_1B_5 > B_1^2B_4 + B_3^2$, i.e. $\frac{B_1B_2B_3+B_1B_5}{B_1^2B_4+B_3^2} > 1$, then the disease-free equilibrium E_s is locally asymptotically stable.

Theorem 3. *Endemic equilibrium point E_e is locally asymptotically stable if $R_0 > 1$ and $\frac{D_1D_2D_3+D_1D_5}{D_1^2D_4+D_3^2} > 1$, where expressions for D_1, D_2, D_3, D_4 and D_5 are given in the proof.*

Proof. The Jacobi matrix of system (1) is written as:
$J(S, E, I, R, S_k, E_k, I_k) =$

$$\begin{pmatrix}
-\alpha I_k - a' - dv & 0 & 0 & 0 & 0 & 0 & -\alpha S\\
\alpha I_k & -b-\beta & 0 & \mu & 0 & 0 & \alpha S\\
0 & \beta & -c-\gamma & 0 & 0 & 0 & 0\\
dv & 0 & \gamma & -\delta-\mu & 0 & 0 & 0\\
0 & 0 & -\alpha_k S_k & 0 & \alpha_k I - a_k' - \sigma & 0 & 0\\
0 & 0 & \alpha_k S_k & 0 & \alpha_k I & -(b_k+\beta_k+\sigma) & 0\\
0 & 0 & 0 & 0 & 0 & \beta_k & -c_k-\sigma
\end{pmatrix}.$$

The Jacobi matrix at endemic equilibrium $E_e = (S^*, E^*, I^*, R^*, S_k^*, E_k^*, I_k^*)$ can be written as
$J(E_e) =$

$$\begin{pmatrix}
-\alpha I_k^* - a' - dv & 0 & 0 & 0 & 0 & 0 & -\alpha S^*\\
\alpha I_k^* & -b-\beta & 0 & \mu & 0 & 0 & \alpha S^*\\
0 & \beta & -c-\gamma & 0 & 0 & 0 & 0\\
dv & 0 & \gamma & -\delta-\mu & 0 & 0 & 0\\
0 & 0 & -\alpha_k S_k^* & 0 & -\alpha_k I^* - a_k' - \sigma & 0 & 0\\
0 & 0 & \alpha_k S_k^* & 0 & \alpha_k I^* & -(b_k+\beta_k+\sigma) & 0\\
0 & 0 & 0 & 0 & 0 & \beta_k & -c_k-\sigma
\end{pmatrix}.$$

Let us find the eigenvalues of this matrix, equating its determinant to zero, we obtain the following characteristic equation:

$$\lambda^7 + D_1\lambda^6 + D_2\lambda^5 + D_3\lambda^4 + D_4\lambda^3 + D_5\lambda^2 + D_6\lambda + D_7 = 0,$$

where

$$
\begin{aligned}
D_1 &= (\beta + b + \gamma + c + \alpha_k I^* + a'_k + 2\sigma + \beta_k + b_k + c_k + \sigma + \alpha I^*_k + a' + dv),\\
D_2 &= (\beta_k + b_k + \sigma)(\beta + b + \gamma + c + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\beta + b)(\gamma + c) + (\beta + b + \gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\delta + \mu)(\alpha_k I^* + a'_k + \sigma) + (\beta_k + b_k + \sigma)(\beta + b + \gamma + c + \alpha_k I^* + a'_k +\\
&\quad + 2\sigma + \beta_k + b_k)(c_k + \sigma + \alpha I^*_k + a' + dv) + (c_k + \sigma)(\alpha_k I^* + a' + dv),\\
D_3 &= (\beta_k + b_k + \sigma)((\beta + b)(\gamma + c) + (\beta + b + \gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\delta + \mu)(\alpha_k I^* + a'_k + \sigma) + \beta\alpha\gamma) + (c_k + \sigma + \alpha I^*_k + a' + dv)\\
&\quad ((\beta_k + b_k + \sigma)(\beta + b + \gamma + c + \alpha_k I^* + a'_k + \sigma) + (\beta + b)(\gamma + c) +\\
&\quad + (\beta + b + \gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) + (\delta + \mu)(\alpha_k I^* + a'_k + \sigma)) +\\
&\quad + (\beta + b + \gamma + c + \alpha_k I^* + a'_k + 2\sigma + \beta_k + b_k)((c_k + \sigma)(\alpha_k I^* + a' + dv)),\\
D_4 &= \beta\alpha\beta_k\alpha_k S^{*2} + \beta\gamma\mu\beta_k + \beta\gamma\mu b_k + 2\beta\gamma\mu\sigma + \beta\gamma\mu\alpha_k I^* + \beta\gamma\mu a'_k +\\
&\quad + (\beta_k + b_k + \sigma)((\beta + b)(\gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\beta + b + \gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma)) +\\
&\quad + (\beta + b)(\gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma) + (c_k + \sigma + \alpha I^*_k + a' + dv)\\
&\quad ((\beta_k + b_k + \sigma)((\beta + b)(\gamma + c) + (\beta + b + \gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\delta + \mu) + (\alpha_k I^* + a'_k + \sigma) + \beta\alpha\gamma)) + ((\beta_k + b_k + \sigma)(\beta + b + \gamma + c +\\
&\quad + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\beta + b)(\gamma + c) + (\beta + b + \gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) +\\
&\quad + (\delta + \mu)(\alpha_k I^* + a'_k + \sigma))((c_k + \sigma)(\alpha_k I^* + a' + dv)),\\
D_5 &= (\beta_k + b_k + \sigma)(\beta + b)(\gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma) - \beta\alpha S^*\beta_k\alpha_k^2 S^*_k I^* +\\
&\quad + \beta\alpha S^{*2}\beta_k\alpha_k(\alpha_k I^* + a'_k + \sigma) + \beta\gamma\mu(\beta_k + b_k + \sigma)(\alpha_k I^* + a'_k + \sigma) +\\
&\quad + (c_k + \sigma + \alpha I^*_k + a' + dv)(\beta\alpha\beta_k\alpha_k S^{*2} + \beta\gamma\mu\beta_k + \beta\gamma\mu b_k + 2\beta\gamma\mu\sigma +\\
&\quad + \beta\gamma\mu\alpha_k I^* + \beta\gamma\mu a'_k + (\beta_k + b_k + \sigma)((\beta + b)(\gamma + c)(\delta + \mu + \alpha_k I^* +\\
&\quad + a'_k + \sigma) + (\beta + b + \gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma)) + (\beta + b)(\gamma + c)\\
&\quad (\delta + \mu)(\alpha_k I^* + a'_k + \sigma)) + ((\beta_k + b_k + \sigma)((\beta + b)(\gamma + c) +\\
&\quad + (\beta + b + \gamma + c)(\delta + \mu + \alpha_k I^* + a'_k + \sigma) + (\delta + \mu)(\alpha_k I^* + a'_k + \sigma) + \beta\alpha\gamma))\\
&\quad ((c_k + \sigma)(\alpha_k I^* + a' + dv)) + \alpha^2\beta\alpha_k\beta_k S^*_k S^* I^*_k.\\
D_6 &= ((\beta_k + b_k + \sigma)(\beta + b)(\gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma) - \beta\alpha S^*\beta_k\alpha_k^2 S^*_k I^* +\\
&\quad + \beta\alpha S^{*2}\beta_k\alpha_k(\alpha_k I^* + a'_k + \sigma) + \beta\gamma\mu(\beta_k + b_k + \sigma)(\alpha_k I^* + a'_k + \sigma))\\
&\quad (c_k + \sigma + \alpha I^*_k + a' + dv) + ((c_k + \sigma)(\alpha_k I^* + a' + dv))((\beta_k + b_k + \sigma)(\beta + b)\\
&\quad (\gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma) - \beta\alpha S^*\beta_k\alpha_k^2 S^*_k I^* +\\
&\quad + \beta\alpha S^{*2}\beta_k\alpha_k(\alpha_k I^* + a'_k + \sigma) + \beta\gamma\mu(\beta_k + b_k + \sigma)(\alpha_k I^* + a'_k + \sigma)) +\\
&\quad + \alpha\beta\alpha_k\beta_k S^*_k S^*(\alpha_k I^* + a'_k +\\
&\quad + \sigma + \mu dv + \alpha I^*_k(\alpha + \mu) + \alpha_k I^*\alpha I^*_k),\\
D_7 &= ((\beta_k + b_k + \sigma)(\beta + b)(\gamma + c)(\delta + \mu)(\alpha_k I^* + a'_k + \sigma) - \beta\alpha S^*\beta_k\alpha_k^2 S^*_k I^* +\\
&\quad + \beta\alpha S^{*2}\beta_k\alpha_k(\alpha_k I^* + a'_k + \sigma) + \beta\gamma\mu(\beta_k + b_k + \sigma)(\alpha_k I^* + a'_k + \sigma))\\
&\quad ((c_k + \sigma)(\alpha_k I^* + a' + dv)) + \alpha\beta\alpha_k^2\beta_k\mu dv I^* S^*_k S^* + \alpha^2\beta\alpha_k^2\beta_k I^* S^*_k S^* I^*_k(\alpha + \mu) +\\
&\quad + \alpha\beta\alpha_k\beta_k S^*_k S^*(\alpha_k I^* + a'_k + \sigma)(\mu dv + \alpha I^*_k(\alpha + \mu)).
\end{aligned}
$$

Matrix eigenvalues are solutions of the characteristic equation. The equation has seven roots. We use the Routh-Hurwitz criterion.

We write an auxiliary matrix

$$\begin{vmatrix} 1 & D_2 & D_4 & D_6 & 0 & 0 \\ D_1 & D_3 & D_5 & D_7 & 0 & 0 \\ \dfrac{D_1D_2-D_3}{D_1} & \dfrac{D_1D_4-D_5}{D_1} & \dfrac{D_1D_6-D_7}{D_1} & 0 & 0 & 0 \\ D_3-\dfrac{D_1(D_1D_4-D_5)}{D_1D_2-D_3} & D_5-\dfrac{D_1(D_1D_6-D_7)}{D_1D_2-D_3} & D_7 & 0 & 0 & 0 \\ D_1' & D_2' & 0 & 0 & 0 & 0 \\ D_3' & D_7 & 0 & 0 & 0 & 0 \\ \frac{D_3'D_2'-D_1'D_7}{D_3'} & 0 & 0 & 0 & 0 & 0 \\ D_7 & 0 & 0 & 0 & 0 & 0, \end{vmatrix},$$

where

$$D_1' = \frac{D_1D_4-D_5}{D_1} - \frac{(D_1D_2-D_3)(D_5(D_1D_2-D_3)-D_1(D_1D_6-D_7))}{D_1(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))},$$

$$D_2' = \frac{D_1D_6-D_7}{D_1} - \frac{D_7(D_1D_2-D_3)^2}{D_1(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))},$$

$$D_3' = D_5 - \frac{D_1(D_1D_6-D_7)}{D_1D_2-D_3} - \frac{D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5)}{D_1D_2-D_3}\frac{D_2'}{D_1'}.$$

Applying the Routh-Hurwitz criterion, we obtain that system (1) is asymptotically stable at equilibrium point E_e if these inequalities are satisfied:

$$D_1 > 0,$$

$$D_7 > 0,$$

$$\frac{D_1D_2-D_3}{D_1} > 0,$$

$$D_3 - \frac{D_1(D_1D_4-D_5)}{D_1D_2-D_3} > 0,$$

$$\frac{D_1D_4-D_5}{D_1} - \frac{(D_1D_2-D_3)(D_5(D_1D_2-D_3)-D_1(D_1D_6-D_7))}{D_1(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))} > 0,$$

$$\frac{D_1D_6-D_7}{D_1} - \frac{D_7(D_1D_2-D_3)^2}{D_1(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))} > 0,$$

$$D_5 - \frac{D_1(D_1D_6-D_7)}{D_1D_2-D_3} - \frac{D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5)}{D_1D_2-D_3}\frac{D_2'}{D_1'} > 0,$$

$$\frac{D_3'D_2'-D_1'D_7}{D_3'} > 0.$$

It follows from $\frac{D_1D_2-D_3}{D_1} > 0$ and $D_1 > 0$ that $D_1D_2-D_3 > 0$. The fourth inequality is equivalent to $D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5) > 0$, or $D_1D_2-D_3 > 0$. The fifth inequality is equivalent to $(D_1D_4-D_5)(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))-(D_1D_2-D_3)(D_5(D_1D_2-D_3)-D_1(D_1D_6-D_7)) > 0$, or $D_1(D_3(D_1D_2-D_3)-(D_1D_4-D_5)) > 0$. The sixth inequality is equivalent to $(D_1D_6-D_7)(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))-D_7(D_1D_2-D_3)^2 > 0$, or $D_1(D_3(D_1D_2-D_3)-(D_1D_4-D_5)) > 0$. The seventh

inequality is equivalent to $D_5D_1'(D_1D_2-D_3)-D_1D_1'(D_1D_6-D_7)-D_2'(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))>0$, or $D_1'>0$. Then the last inequality can be simplified as $D_3'D_2'-D_1'D_7>0$, or $D_3'>0$.

Therefore, we get the system:

$$\begin{aligned}
D_1 &> 0,\\
D_7 &> 0,\\
D_1D_2-D_3 &> 0,\\
D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5) &> 0,\\
D_1(D_1D_4-D_5)(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))-&\\
-D_1(D_1D_2-D_3)(D_5(D_1D_2-D_3)-D_1(D_1D_6-D_7)) &> 0,\\
D_1(D_1D_6-D_7)(D_3(D_1D_2-D_3)-D_1(D_1D_4-D_5))-D_1D_7(D_1D_2-D_3)^2 &> 0,\\
D_5D_1'(D_1D_2-D_3)-D_1D_1'(D_1D_6-D_7)-D_2'(D_3(D_1D_2-D_3)-&\\
-D_1(D_1D_4-D_5)) &> 0\\
D_3'D_2'-D_1'D_7 &> 0,
\end{aligned}$$

Seven eigenvalues have negative real parts if they satisfy the Routh-Hurwitz criterion. Thus, all eigenvalues of a characteristic equation have negative real parts if and only if $R_0>1$ and $D_3D_1D_2+D_1D_5>D_3^2+D_1^2D_4$, which is true when $\frac{D_1D_2D_3+D_1D_5}{D_1^2D_4+D_3^2}>1$, then endemic equilibrium E_e is locally asymptotically stable.

6. Numerical Simulations

Numerical modeling allows us to better understand the dynamics of the malaria epidemic. Let us study the dynamics of development of each population subgroup depending on the disease severity. In this part, we will focus on the simulation parameters associated with vaccination by presenting several graphical representations of the disease dynamics with different values of the parameters and different values of R_0. Computer simulation is carried out using the *Matlab* software. The parameters used for numerical simulation are presented in Tables 1 and 2.

Table 1. Parameters for the simulation, which results are presented in Fig. 2

α	α_k	β	β_k	γ	μ	a	a'	a_k	a_k'	b	b_k	c	c_k	d	σ	dv	R_0
In Fig. 2.6 (first set of parameters)																	
0.72	2.0	0.5	0.5	0.5	0.01	0.8	0.01	0.4	0.2	0.2	0.1	0.4	0.25	0.01	0.00	0.00	7.26
In Fig. 2.6 (second set of parameters)																	
0.72	2.0	0.5	0.5	0.5	0.01	0.8	0.01	0.4	0.2	0.2	0.1	0.4	0.25	0.01	0.75	0.25	0.32

In Fig. 2 we present four series of numerical experiments for which $R_0=7.26$ (first two lines) and $R_0=0.32$ (last two lines). It can be noted that the disease exists in populations (host and vector). Without vaccination or methods of reducing mosquito population, susceptible subpopulation is declining. At the same time, the representative curves of subpopulations (exposed, infected, and recovered) converge to equilibrium values, and we note a significant presence of the disease in the population. Vaccination was carried out in human population (second line of graph and first figure), which shows that the disease has practically disappeared, and the

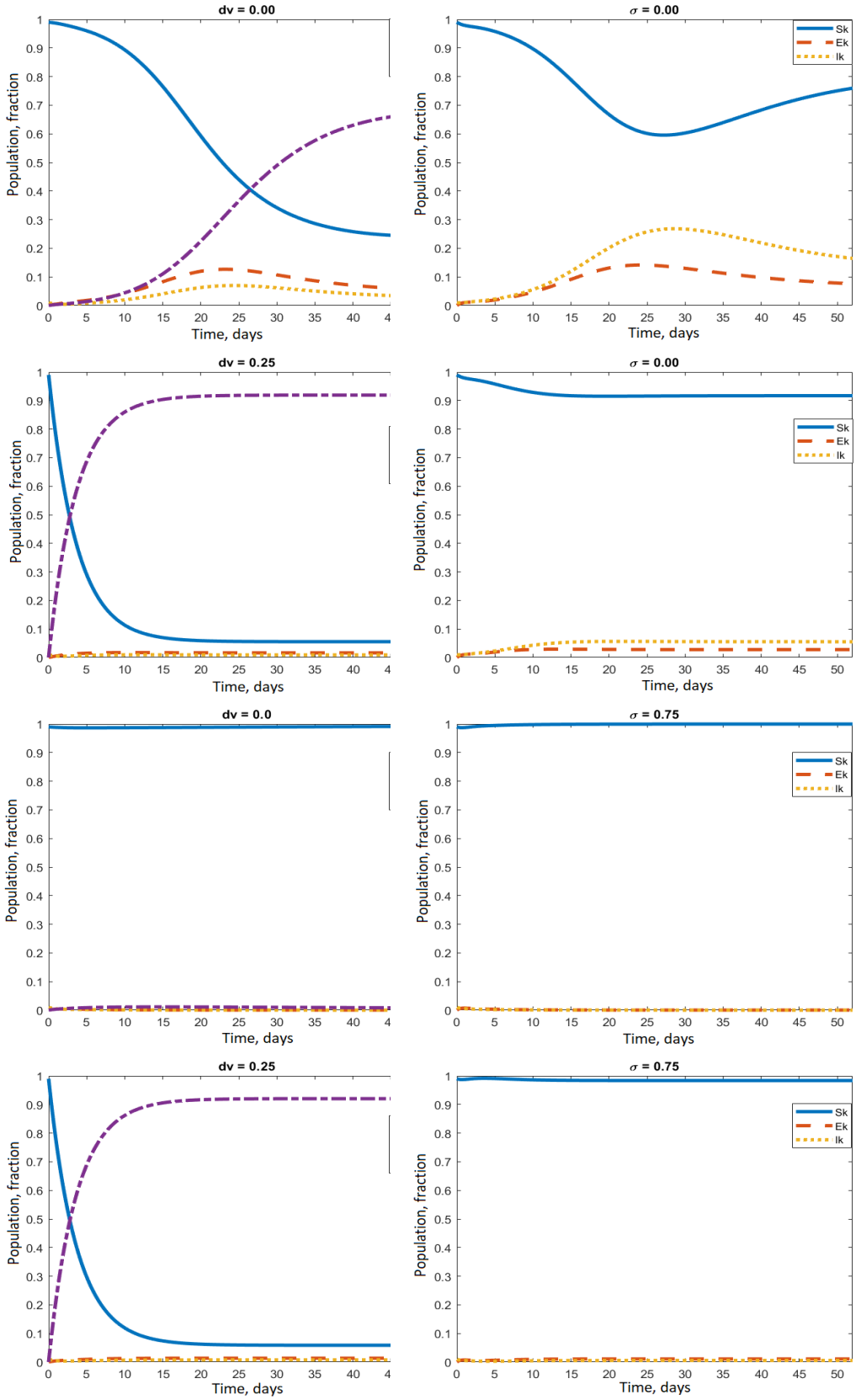

Fig. 2. Epidemic process for different values of R_0 ($R_0 = 7.26$ and $R_0 = 0.32$)

curves of other subpopulations converge to equilibrium values. The last two lines of the graph show that with vaccination and a method of preventing mosquito development, one can observe that the representative curves of the population (host and vector) quickly stabilize, and the disease disappears from the population.

Table 2. Parameters for the simulation, which results are presented in Fig. 3

α	α_k	β	β_k	γ	μ	a	a'	a_k	a'_k	b	b_k	c	c_k	d	σ	dv	R_0
In Fig. 2.7 (first set of parameters)																	
0.8	2.5	0.4	0.6	0.45	0.02	0.4	0.25	0.5	0.25	0.15	0.2	0.25	0.3	0.05	0.00	0.00	10.36
In Fig. 2.7 (second set of parameters)																	
0.8	2.5	0.4	0.6	0.45	0.02	0.4	0.25	0.5	0.25	0.15	0.2	0.25	0.3	0.05	0.25	0.6	2.59

In Fig. 3 there are four series of simulations for which $R_0 = 10.36$ (first two lines of graphs) and $R_0 = 2.59$ (last two lines of graphs). It can be noted that the disease lasts in host and vector populations relatively long. At the same time, a representative curve of susceptible subpopulation decreases. At the same time, representative curves of the subpopulations (exposed, infected, and recovered) converge to equilibrium values, and a significant disease presence can be noted in the population. If control measures are not taken, there is a risk that the disease will remain in the population because the calculated basic reproduction number indicates that at least one infected person can infect several people. If human people has been vaccinated with a parameter of $dv = 0.6$ (second line of graph, first figure), then despite the fact that the disease still exists in the population, an infection rate decreases due to vaccination of the population. The last two lines show that with the help of vaccination and a method of preventing mosquito development (parameter $\sigma = 0.25$), representative curves of populations (host and vector) gradually converge to equilibrium values.

In general, the results of numerical simulations show that a method of eliminating or preventing mosquito development is very effective in suppressing a rapid epidemic development, but it is very difficult and expensive for applying it in practice.

7. Conclusions

Malaria is a tropical infectious disease. Nowadays, scientists have failed to develop an effective vaccine to combat this disease which can be very dangerous and may cause many deaths in the human population. The mathematical modeling of this disease plays a crucial role in understanding the dynamics of transmission and appropriate prevention strategies. In this paper, we study the $SEIRS_kE_kI_k$ model with vaccination and strategies of decreasing of mosquitos population. For the model, we examine two stable equilibria: a disease-free equilibrium, in which the disease is not presented in the populations; and an endemic equilibrium, when there is a non-zero infected subpopulation. We establish the stability of these two equilibria using the theory of Lyapunov functions. It is proved that the dynamic process is completely determined by the number of basic reproductions R_0. If $R_0 \leq 1$, the disease-free equilibrium is locally asymptotically stable. If $R_0 > 1$, there is a globally asymptotically stable endemic equilibrium. The results of the simulations show how the disease spreads in the population. The spread of this disease can be prevented

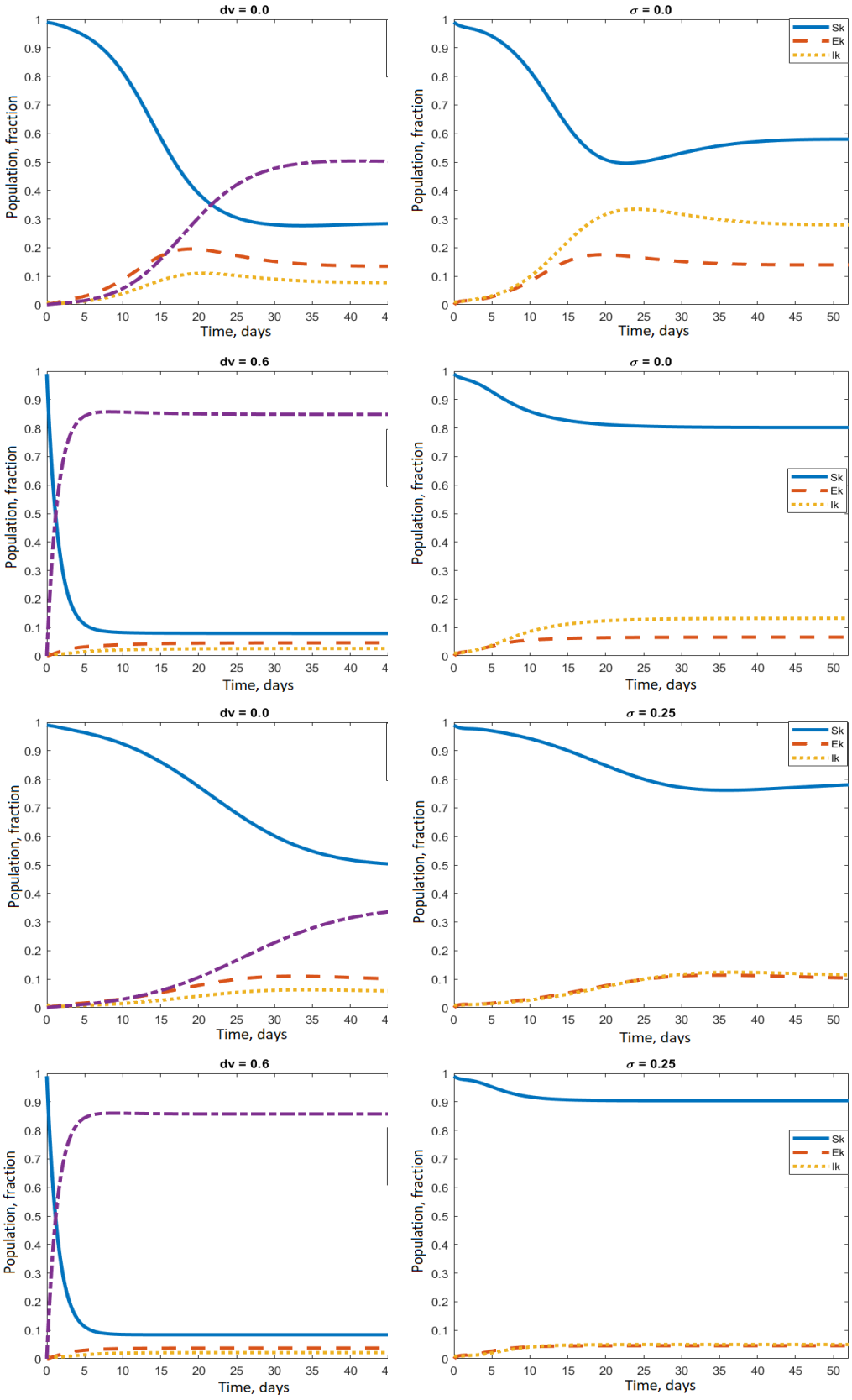

Fig. 3. Epidemic process for different values of R_0 ($R_0 = 10.36$ and $R_0 = 2.59$)

through vaccination strategies and methods of reducing the mosquito population. The numerical results show the impact of vaccination of the human population, with good vaccine the disease will disappear in the population.

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