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Research paper

Impact of Malaria Vaccination on Malaria Infection in Côte d'Ivoire: Mathematical Modeling of Malaria Cases in The Context of Childhood Vaccination

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Abstract

In Côte d'Ivoire, a malaria routine vaccination targeting a specific age group of children began in 2024. In this article, we propose a mathematical model of malaria cases by age group that takes this vaccination into account; this model will allow us to study the impact of this vaccination on malaria dynamics in Côte d'Ivoire. We have shown that it is very costly to reach a disease-free equilibrium and have also determined the basic reproduction number for such an equilibrium. However, we have observed that the vaccination coverage rate strongly influences malaria dynamics. Graphical analysis and numerical simulations corroborate these results. This mathematical model allows us to make predictions that will be important for decision-making and planning.

Keywords: *SIRS-SI Model; Basic Reproduction Rate; Disease-Free Equilibrium; Numerical Simulation; Predictions.*

1. Introduction

Malaria is a vector born disease (The primary vector in Africa is Anopheles gambiae) caused by Plasmodium. Plasmodium Falciparum is the most deadly malaria parasite and Africa has widespread the transmission. It is transmitted to humans through the bite of a mosquito of the Anopheles genus, itself infected with the Plasmodium parasite after biting a person suffering from malaria [1]. Warm temperatures, high humidity, and seasonal rainfall create ideal environments for mosquito breeding and parasite development. Late diagnosis, limited access to antimalarial treatments, and shortages of preventive tools (e.g., insecticide-treated nets) increase mortality. According to the latest global malaria report published by the World Health Organization (WHO) [2], the number of malaria cases is estimated to be 263 million and the number of deaths 597,000 worldwide by 2023. Sub-Saharan Africa accounts for around 95% of global malaria cases and deaths, with children under 5 being most affected. In 2021 in Cote d'Ivoire, the national malaria incidence was estimated at 231 cases per 1 000 people per year (i.e., 23.1 %) in the population at risk and for children under 5 years old, the incidence is substantially higher: about 441 cases per 1 000 children under 5 per year [3]. For several years now, parasites have been developing resistance to antimalarial molecules, and mosquitoes are becoming less sensitive to insecticides [1]. The fight against malaria is therefore adapting to these resistances; it is in this spirit that vaccination has joined the list of prevention measures. The vaccine being rolled out in Côte d'Ivoire is R21/Matrix-M malaria vaccine. The initial target age group is infants / very young children, specifically those aged 0 to 23 months (i.e., under 2 years old). The immunization schedule used in the country's program consists of four doses, administered at roughly 6 months, 8 months, 9 months, and 15 months of age.

To stem the tide, Côte d'Ivoire was the first African country to administer R21, the second vaccine recommended by the World Health Organization (WHO) after RTS S, to children under the age of two. This free vaccination campaign began in 2024, targeting children aged 0 to 23 months. The protection provided by the R21 vaccine used in Côte d'Ivoire is approximately 2 years [4]. This suggests that the vaccination strategy implemented in Côte d'Ivoire enables children under the age of 5, the age group with the highest mortality rate, to be immunized [5]. Complementary to existing measures, vaccination is a major step in the fight against malaria for Côte d'Ivoire, which aims to reach 250 000 children by 2024. The country has received 655 600 doses of malaria vaccine [5].

1.1. Objective

Our objective is to study the effectiveness of the malaria vaccination strategy in Côte d'Ivoire targeting children under 5 years of age. We hope to highlight the initial trends of this vaccination strategy on the dynamics of malaria in children under 5. We will also propose strategies for improving the current malaria situation in Côte d'Ivoire.

1.2. Methodology

The first mathematical model of malaria was developed in 1910 by Sir Ronald Ross, a British bacteriologist and entomologist. In [6], he proposed a mathematical compartmental model to explain that it was not necessary to kill all the mosquitoes for malaria to disappear. All that was needed was to reduce the mosquito population below a certain threshold. The mathematical models of malaria that followed were strongly inspired by Ross's model. In the progress of malaria modelling, most of the results obtained were inspired by the previous ones. Very recently, in 2024, Ademe Kebede Gizaw et al. in [7] carried out a study of the stability of a deterministic model of the spread of malaria with age classes and without vaccination. Also in 2024, Pride Duve et al. in [8], explored a theoretical mathematical model of malaria with vaccination and immigrants sick with malaria. They concluded that malaria could be contained with vaccination and the absence of infected immigrants. In 2024, in [9], Akindele Akano Onifade et al. developed a mathematical model of malaria incorporating the testing of resistant strains as a control strategy. A sensitivity analysis enabled them to study the influence of their model's parameters on the fight against the disease.

Building on previous modelling efforts, we propose a SIRS-SI model describing the spread of malaria in Côte d'Ivoire. This model includes four human compartments with two age classes (susceptible humans to be over 5 years old, susceptible humans to be under 5 years old, infected humans, and vaccinated humans). It also includes two mosquito compartments. Our model takes into account the effect of vaccination on children aged 0 to 23 months in Côte d'Ivoire. In section 2, we provide a more detailed presentation of the development of this mathematical model. In section 3, the mathematical properties necessary for the study of our model are developed: the existence and positivity of the solution, the determination of the disease-free equilibrium point and the calculation of the basic reproduction rate. Our aim is to show the influence of vaccination coverage rate on malaria dynamics in Côte d'Ivoire. So, we continue with section 6 in which we determine the values of some constants of our model. This enables us to perform numerical simulations that allow us to observe the influence of childhood vaccination on the dynamics of malaria.

2. The Mathematical Model

From July 2024, with the introduction of vaccination in children aged between 0 and 23 months, the rate of infections in children aged 0-5 should fall considerably over time, given the immunity of at least 2 years conferred by the vaccine. We propose a 6-compartment model describing the dynamics of malaria in Côte d'Ivoire with the introduction of vaccination conferring immunity to children up to the age of 5. The total population of humans and the total population of female mosquitoes at time t, expressed in days, are denoted by $N_h(t)$ and $N_m(t)$ respectively.

$N_h(t)$ the total human population at time t is divided into three compartments:

1) $S_a h(t)$: Susceptible humans over 5 years of age who may contract the malaria at time t,
2) $S_c h(t)$: Susceptible humans under 5 years of age who may contract the malaria at time t,
3) $I_h(t)$: Infected humans i.e., people who have contracted the malaria at time t,
4) $V_h(t)$: Humans vaccinated against malaria at time t.

An empirical study carried out in Côte d'Ivoire established the proportion of female Anopheles gambiae s.l. mosquitoes in individuals of its species to be at least 80 %.

$N_m(t)$: the total population of female mosquitoes at time t is divided into two compartments :

$S_m(t)$: Susceptible mosquitoes i.e., mosquitoes that can contract the disease at time t,

$I_m(t)$: Infected mosquitoes i.e., mosquitoes that can transmit the virus at time t.

The following graph shows the dynamics of the disease.

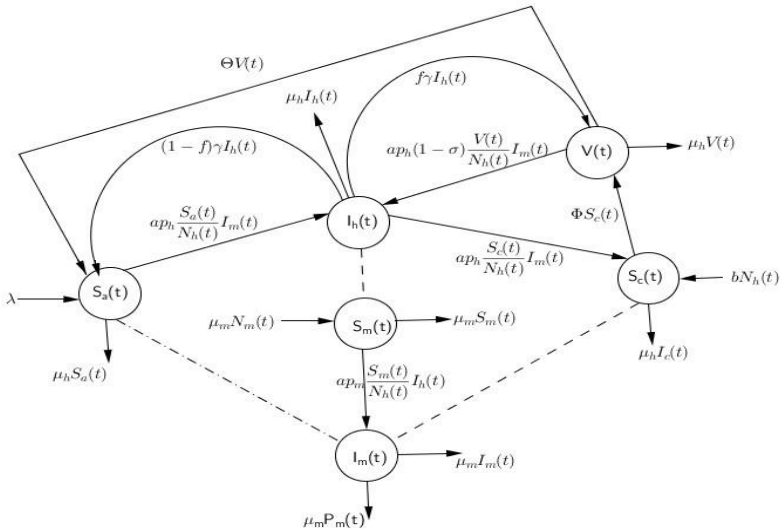

Fig. 1: Malaria Dynamics During the Vaccination Campaign.

Where

Table 1: The Constants of the Vaccination Model

Model parameters	Meanings
λ	the number of susceptible humans over the age of 5 recruited per day (emigration)
μ_h	the death rate of humans per day
p_h	probability of a bite causing infection in a human
p_m	probability of a bite causing infection in a mosquito
a	the number of bites per mosquito per day
b	the recruitment rate of children aged 0 to 23 among humans
Φ	the proportion of children aged 0 to 23 months vaccinated per day among humans
Θ	the duration of immunity conferred by the vaccine in children
σ	the vaccine efficacy rate
γ	the recovery rate of infected humans
f	the proportion of children aged 0 to 23 months among humans who have recovered
μ_m	the birth rate of mosquitoes in the total mosquito population per day or death rate of mosquitoes per day

The above graph is modelled by the following system of differential equations:

$$\begin{cases} \frac{dS_a(t)}{dt} = \lambda + \theta V(t) + (1-f)\gamma I_h(t) - ap_h \frac{I_m(t)S_a(t)}{N_h(t)} - \mu_h S_a(t) \\ \frac{dS_c(t)}{dt} = bN_h(t) + f\gamma I_h(t) - ap_h \frac{I_m(t)S_c(t)}{N_h(t)} - \phi S_c(t) - \mu_h S_c(t) \\ \frac{dI_h(t)}{dt} = ap_h \frac{I_m(t)}{N_h(t)}[S_a(t) + S_c(t) + (1-\sigma)V(t)] - \gamma I_h(t) - \mu_h I_h(t) \\ \frac{dV(t)}{dt} = \phi S_c(t) - ap_h(1-\sigma)\frac{V(t)I_m(t)}{N_h(t)} - \theta V(t) - \mu_h V(t) \\ \frac{dS_m(t)}{dt} = \mu_m N_m(t) - ap_m \frac{I_h(t)S_m(t)}{N_h(t)} - \mu_m S_m(t) \\ \frac{dI_m(t)}{dt} = ap_m \frac{I_h(t)S_m(t)}{N_h(t)} - \mu_m I_m(t) \end{cases} \quad (1)$$

The initial conditions of system (1) are the following $S_a(0) > 0$, $S_c(0) > 0$, $I(0) > 0$, $V(0) = 0$, $S_m(0) > 0$ and $I_m(0) > 0$

3. Mathematical Investigation of The Model with Vaccination

3.1. A unique positive solution

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Theorem 3.1: *For any initial value* $(S_a(0), S_c(0), I_h(0), V(0), S_m(0), I_m(0)) \in \mathbb{R}_+^6$*, the system (1) admits a single positive solution.*

Proof. Since the coefficients of our model are Lipschitzian, model (1) has a unique solution. Let us now prove the positivity of this solution. To establish the theorem, it is therefore sufficient to show that the set $\mathbb{R}_+^6$ is positively invariant for the system (1).

If x and y are compartments of the model (1), the notation $\frac{dx(s)}{ds}|_{y(s)=0}$ gives the expression of $\frac{dx(s)}{ds}$ by giving the $y(s)$ component the value 0.

As shown in and if for $\tau \geq 0$, the hypothesis $(S_a(\tau), S_c(\tau), I_h(\tau), V(\tau), S_m(\tau), I_m(\tau)) \in \mathbb{R}_+^6$ gives $\frac{dS_a(\tau)}{d\tau}|_{S_a(\tau)=0} \geq 0$, $\frac{dS_c(\tau)}{d\tau}|_{S_c(\tau)=0} \geq 0$, $\frac{dI_h(\tau)}{d\tau}|_{I_h(\tau)=0} \geq 0$, $\frac{dV(\tau)}{d\tau}|_{V(\tau)=0} \geq 0$, $\frac{dS_m(\tau)}{d\tau}|_{S_m(\tau)=0} \geq 0$ and $\frac{dI_m(\tau)}{d\tau}|_{I_m(\tau)=0} \geq 0$ then for all $t \geq 0$, $(S_a(t), S_c(t), I_h(t), V(t), S_m(t), I_m(t)) \in \mathbb{R}_+^6$.Let $\tau \geq 0$. Assuming $(S_a(\tau), S_c(\tau), I_h(\tau), V(\tau), S_m(\tau), I_m(\tau)) \in \mathbb{R}_+^6$, we obtain the following results.

$\frac{dS_a(\tau)}{d\tau}|_{S_a(\tau)=0} = \lambda + \theta V(\tau) + (1-f)\gamma I_h(\tau) \geq 0$. Which gives us that for all $t \geq 0$, $S_a(t) \geq 0$.

$\frac{dS_c(\tau)}{d\tau}|_{S_c(\tau)=0} = b[S_a(\tau) + I_h(\tau) + V(\tau)] + f\gamma I_h(\tau) \geq 0$. Which gives us that for all $t \geq 0$, $S_c(t) \geq 0$.

$\frac{dI_h(\tau)}{d\tau}|_{I_h(\tau)=0} = ap_h \frac{I_m(\tau)}{N_h(\tau)}[S_a(\tau) + S_c(\tau) + (1-\sigma)V(\tau)] \geq 0$. So for all $t \geq 0$, $I_h(t) \geq 0$.

$\frac{dV(\tau)}{d\tau}|_{V(\tau)=0} = \phi S_c(\tau) \geq 0$. So for all $t \geq 0$, $V(t) \geq 0$.

Similarly $\frac{dS_m(\tau)}{d\tau}|_{S_m(\tau)=0} = \mu_m I_m(\tau) \geq 0$. Which gives us that for all $t \geq 0$, $S_m(t) \geq 0$.

$\frac{dI_m(\tau)}{d\tau}|_{I_m(\tau)=0} = p_m \frac{I_h(\tau)S_m(\tau)}{N_h(\tau)} \geq 0$. So for all $t \geq 0$, $I_m(t) \geq 0$.

This proves that $\mathbb{R}_+^6$ is positively invariant for the system (1). This gives us the desired result. □

3.2. On the existence of a Disease Free Equilibrium point (DFE) and the computing of the basic reproduction number R0

3.2.1. Discussion on the DFE

$E^0 = (S_a^0, S_c^0, 0, V^0, S_m^0, 0)$ is a DFE of the model (1) if it checks

$$\begin{cases} bS_a^0 + (b + \mu_h - \phi)S_c^0 + bV^0 = 0 \\ \phi S_c^0 - (\theta + \mu_h)bV^0 = 0 \\ \mu_h S_a^0 - \theta V^0 = \lambda. \end{cases} \quad (2)$$

The determinant of system (2) is

$$\Delta = (\theta + \mu_h)(\phi + \mu_h)(b - \mu_h)$$

- If $b = \mu_h$, then $\Delta = 0$ If $b = \mu_h$, then $\Delta = 0$ and there is no disease free equilibrium state;
- if $b \neq \mu_h$, then $\Delta \neq 0$ and the system (2) admits a single solution given by

$$S_a^0 = \frac{\lambda[(\theta+\mu_h)(b-\mu_h-\phi)+b\phi]}{\Delta} \quad (3)$$

$$S_c^0 = -\frac{b\lambda(\theta+\mu_h)}{\Delta} \quad (4)$$

$$V^0 = -\frac{b\lambda\phi}{\Delta} \quad (5)$$

In this case:

- if $b > \mu_h$, then $\Delta > 0$ and there is no disease free equilibrium state because S_c^0 and V^0 are negative;
- if $b < \mu_h$, then $\Delta < 0$ and S_a^0, S_c^0, V^0 are positive. In this case, there is only one state of equilibrium without disease, given by expressions (3), (4) and (5).

Note, however, that the condition $b < \mu_h$ means that the recruitment rate of adult individuals (number of individuals entering the population per unit of time) is lower than the death rate. This assumption is unrealistic, so we can assume that our model does not allow for disease free equilibrium state.

Discussion:

The difficulty in obtaining a DFE can be explained by the fact that vaccination coverage is limited to a small segment of the population. Furthermore, this model does not take into account the use of certain measures such as impregnated mosquito nets.

3.2.2. On the sensitivity of the basic reproduction rate to vaccination

The DFE can exist with a highly unrealistic condition. It is therefore not possible to get this DFE. However, to complete our mathematical study, we calculate the basic reproduction rate.

Definition: The basic reproduction number $\mathcal{R}_0$ is the average number of secondary infections resulting from a single primary infection in an otherwise susceptible population.

With the condition $b < \mu_h$, the system (1) admits a single disease free equilibrium E^0. In this case, the next generation matrix method (and) is used to compute the basic reproduction number $\mathcal{R}_0$ as the spectral radius of the matrix FV^{-1} where F is the matrix of transmission terms and V is the matrix of transition terms. We get

$$\mathcal{R}_0 = \rho(FV^{-1}) = \sqrt{\frac{a^2 p_m p_h S_m^0 (S_a^0 + S_c^0 + (1-\sigma)V^0)}{(\mu_h+\gamma)\mu_m(S_a^0+S_c^0+V^0)}}.$$

$$\mathcal{R}_0 = \sqrt{\frac{a^2 p_m p_h S_m^0}{(\mu_h+\gamma)\mu_m}}\sqrt{1 - \frac{\sigma b\phi}{(\theta+\mu_h)(\phi+\mu_h)}}.$$

We can write

$$\mathcal{R}_0 = \widehat{\mathcal{R}_0}\sqrt{1 - \frac{\sigma b\phi}{(\theta+\mu_h)(\phi+\mu_h)}}.$$

With

$$\widehat{\mathcal{R}_0} = \sqrt{\frac{a^2 p_m p_h S_m^0}{(\mu_h+\gamma)\mu_m}}$$

Remarks:

- In the absence of vaccination ($\phi = 0$) or vaccine ineffectiveness ($\sigma = 0$), $\mathcal{R}_0 = \widehat{\mathcal{R}_0}$, which is the basic reproduction number of the model without a vaccine as in [1].

- The functions $\phi \mapsto \sqrt{1-\frac{\sigma b \phi}{(\theta+\mu_h)(\phi+\mu_h)}}$ and $\sigma \mapsto \sqrt{1-\frac{\sigma b \phi}{(\theta+\mu_h)(\phi+\mu_h)}}$ are respectively decreasing functions. On the one hand, this means that if vaccination coverage increases, the basic reproduction number decreases. On the other hand, this means that if the vaccine's effectiveness increases, the basic reproduction number decreases.

4. Numerical Simulations

A qualitative study of sensitivity to vaccination and Predictions on the evolution of malaria in Côte d'Ivoire with the vaccination campaign

According to the general census of the population of Côte d'Ivoire conducted in 2021 [14], 30 795 immigrants arrived in Côte d'Ivoire that year. That is an average of 2 566 people per month. According to [15], the population of Côte d'Ivoire is estimated at 32 490 020 inhabitants. The same source states that this population includes 3 696 301 children aged 0 to 5. The number of individuals affected by malaria in july 2024 is 881 241. Malaria vaccination begins in July 2024 with a pilot phase which have permitted to vaccine approximately 250,000 children in 38 high-transmission health districts [16]. Taking all this information into account, we consider July 2024 as the starting point for our model with $t = 0$. We thus obtain $N(0) = 32490020$, $S_a(0) = 27662478$, $S_c(0) = 3696301$, $I_h(0) = 886763$ and $V(0) = 250000$. Given the duration of immunity granted after one dose of vaccine (see [17]), the vaccination schedule adopted in Côte d'Ivoire (see [16]) could provide vaccine immunity to children up to the age of 5. So we can consider that $\theta = \frac{1}{5\times12} \simeq 0{,}017$. We also consider the following data.

Table 2: Values of Parameters of the Model for Numerical Simulations

Parameters	Values	References
θ	0,017	[16]
f	0,11	[16]
b	0,339	[15]
ϕ	0,046	[14]-[16]
γ	0,83	[18]
σ	0,75	[16]
a	0,4	[19]
p_h	0,3	[20]
p_m	0,3	[20]
μ_h	0,092	[20]
μ_m	0,12	[20]
λ (per month)	2566	[14]

Côte d'Ivoire aims to protect 1 million children under the age of 2 by the end of 2025. To achieve this goal, we have calculated that φ, the proportion of children aged 0 to 23 months vaccinated per month among humans, must be at least 0,043. We obtain the following trajectory over a period of 17 months after July 2024, the start of the malaria vaccination campaign in Côte d'Ivoire.

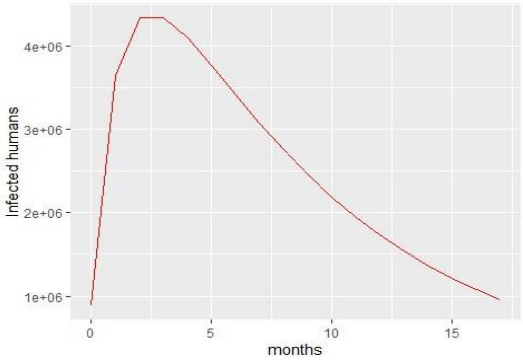

Fig. 2: Trajectory of Infected Humans in Côte d'Ivoire Starting in July 2024 with the Goal of Vaccinating One Million Children Under the age of 2 by the end of 2025. $\phi \approx 0{,}046$.

The previous trajectory corresponds to a monthly vaccination rate among children equal $\phi \approx 0{,}046$. With more intensive vaccination, corresponding to a tenfold increase in vaccination coverage, the trajectory of infections becomes less alarming.
The peak of infection is lower and is reached earlier. The following figure illustrates this situation.

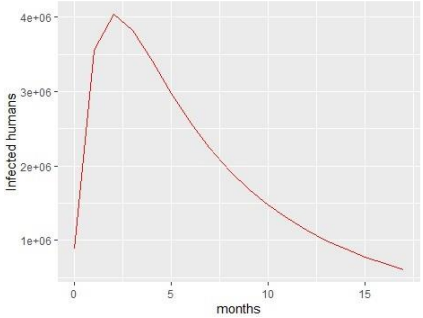

Fig. 3: Trajectory of Infected Humans in Côte d'Ivoire Starting in July 2024 with a higher monthly vaccination coverage among children. $\phi = 0{,}46$.

With monthly vaccination coverage among children at 0.6, we achieve even more significant control over the peak of the epidemic. A lower peak facilitates overall hospital care for patients. This is important because hospital capacity has certain limitations. We can observe this decline in the peak in the figure below.

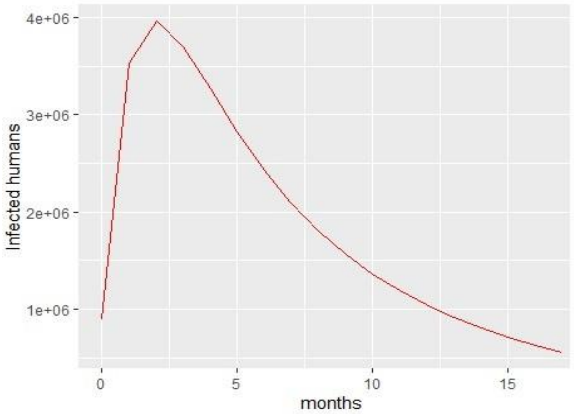

Fig. 4: Trajectory of Infected Humans in Côte d'Ivoire Starting in July 2024 with even higher vaccination coverage among c*hildren. $\phi = 0,6$.

We conclude this qualitative study of the influence of vaccination coverage among children under 2 years of age on malaria dynamics in Côte d'Ivoire with a prediction that takes into account a higher monthly vaccination rate. We obtain an even lower peak in the epidemic, which suggests that vaccination coverage has a certain influence on the malaria epidemic that is very favorable to us.

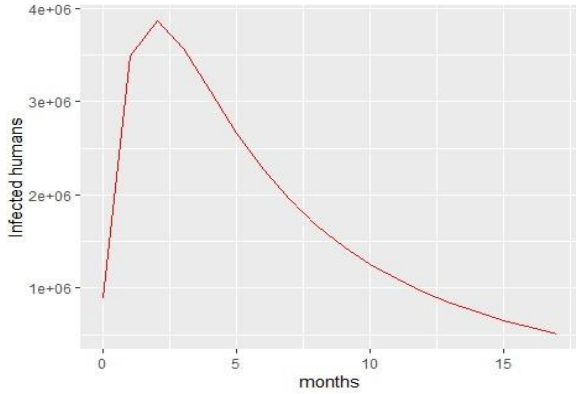

Fig. 5: Trajectory of Infected Humans with current vaccination coverage but higher vaccine effectiveness. $\phi = 0,8$.

The following figure, except for vaccine efficacy, relates to current data in Côte d'Ivoire, as in Fig. 2. We have imagined a scenario with higher vaccine efficacy in which it has a value of 0.9 instead of its actual value of 0.75. In the current situation, we observe that this increase has had very little impact on the dynamics of the epidemic compared to an increase in vaccination coverage.

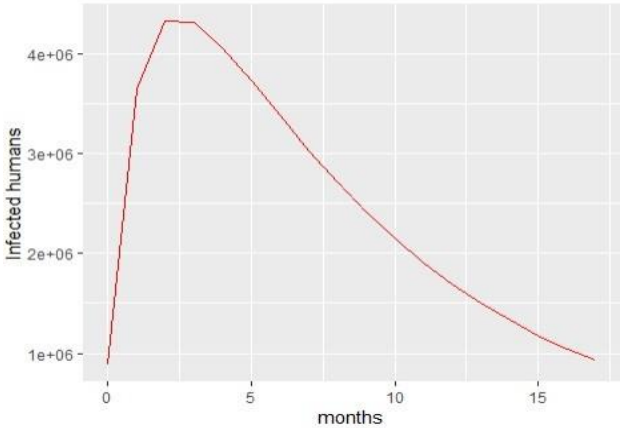

Fig. 6: Trajectory of infected humans with current data and $\sigma = 0,9$.

5. Conclusion

In this study, we conducted a mathematical analysis of malaria dynamics in 5 d'Ivoire, incorporating vaccination of children under two years of age. The deterministic mathematical model we constructed allowed us to demonstrate that a disease-free equilibrium can only be achieved under unrealistic conditions that could lead to the extinction of humanity. However, numerical simulations enabled us to observe that vaccination coverage has a considerable impact on disease dynamics: by significantly increasing this coverage, better disease control can be achieved. We therefore argue that childhood vaccination is a cost-effective strategy for our country, which does not have substantial

resources allocated to health. This vaccination targets only an age group with high malaria mortality; however, it proves effective for the entire population. This effectiveness is all the greater when vaccination coverage is broad. This is why we urge our health authorities to allocate the necessary resources to achieve good vaccination coverage.
However, the mathematical model we propose has limitations. This model does not incorporate barrier measures to combat malaria. It could be improved by taking into account the seasonal nature of mosquito proliferation, which is much more prevalent during the rainy season in Côte d'Ivoire. Our model could thus be improved by involving entomologists, geographers and health professionals in its study.

Acknowledgement

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