Journal of Information Systems Engineering and Management
2025, 10(27s)
e-ISSN: 2468-4376
https://www.jisem-journal.com/

Research Article

Mathematical Analysis of a Seasonal Malaria Chemoprevention (SMC) Intervention in Children Under 5 Years: Application to Senegal

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ARTICLE INFO

Received: 18 Dec 2024

Revised: 15 Feb 2025

Accepted: 28 Feb 2025

ABSTRACT

Malaria remains a major cause of morbidity and mortality among children under 5 years old in Senegal. To alleviate this burden, Seasonal Malaria Chemoprevention (SMC) administers antimalarial drugs during the high transmission season. Currently, in Senegal, SMC targets children aged 3 months to under 10 years. This study, based on a mathematical SIR-SI model, evaluates the effectiveness of this intervention, focusing specifically on children under 5 years old. We developed a coupled SIR-SI model that integrates the transmission dynamics between humans and mosquitoes, incorporating the SMC treatment rate (η) into the differential equations to model the chemoprevention effect. The Jacobian matrix was calculated for both disease-free and endemic equilibria, and eigenvalues were analyzed to assess their stability. Our results show that the basic reproduction number R_0, calculated using the next-generation matrix method, depends on key parameters such as transmission rates, recovery rates, mosquito mortality rates, and particularly the SMC treatment rate (η). Increasing this rate significantly reduces R_0, thereby stabilizing the disease-free equilibrium. Numerical simulations, based on biologically realistic parameters, confirm that SMC effectively reduces R_0 and limits malaria transmission. While our findings suggest that targeting children under 5 years old could be sufficient to significantly reduce transmission, a comparative analysis including the 0-5 and 0-10 age groups would be necessary to further validate this assertion, considering local dynamics and recent shifts in malaria burden toward older age groups. This study highlights the critical role of SMC in malaria control and provides a scientific basis for refining and optimizing intervention strategies in Senegal.

Keywords: Malaria transmission dynamics - Seasonal malaria chemoprevention (SMC) - SIR-SI Mathematical model - Basic reproduction number (R_0) - Children under 5 Years.

1. INTRODUCTION

Malaria remains one of the leading causes of morbidity and mortality in many tropical regions, particularly in sub-Saharan Africa. Among the most vulnerable groups, children under the age of 5 account for a significant proportion of malaria-related deaths. In Senegal, where malaria is endemic in certain areas and its transmission highly seasonal, combating this disease remains a major public health priority.

To address this challenge, various interventions have been implemented, including the use of insecticide-treated nets, indoor residual spraying, and artemisinin-based combination therapies (ACTs). Among these strategies, Seasonal Malaria Chemoprevention (SMC) has emerged as a key intervention. Recommended by the WHO since 2012, SMC involves administering antimalarial drugs to healthy children during the high transmission season to reduce their risk of infection. Currently, in Senegal, this intervention targets children aged 3 months to under 10 years.

However, extending SMC coverage to children under 10 raises questions regarding cost, logistics, and effectiveness. The hypothesis that limiting coverage to children under 5 years old could suffice to effectively control transmission deserves further investigation.

To this end, we developed a coupled SIR-SI mathematical model that incorporates both human and vector dynamics to analyze the impact of SMC on malaria transmission. This model not only evaluates the effects of the intervention but also explores the optimization of coverage strategies. This study aims to provide evidence-based recommendations to improve resource allocation and maximize the effectiveness of SMC in Senegal.

2. STATE OF THE ART

Malaria remains one of the leading causes of morbidity and mortality in tropical regions, particularly in sub-Saharan Africa, where it persists as an endemic disease despite significant efforts to control and eliminate it. This persistence is attributed to environmental, social, and biological factors that facilitate the transmission of the *Plasmodium falciparum* parasite. Several strategies have been implemented to combat malaria, including the use of insecticide-treated nets (ITNs), indoor residual spraying (IRS), artemisinin-based combination therapies (ACTs), and seasonal malaria chemoprevention (SMC). Among these interventions, ACTs play a key role in reducing the infectiousness of malaria patients. Flegg et al. (2011) proposed standardized methods for measuring parasite clearance, demonstrating that ACTs reduce transmission, although their effectiveness varies by endemicity levels **[1]**. For instance, Okell et al. (2008) reported a 53% reduction in prevalence in low-transmission areas (initial prevalence of 3.7%), while the reduction was only 11% in high-transmission areas (initial prevalence of 57.1%) **[2]**. Additionally, Bretscher et al. (2017) showed that adding prolonged protection (≥30 days) and effective transmission blocking (ACT + primaquine) maximizes efficacy, particularly in moderate-to-high transmission areas **[3]**. In this context, SMC, introduced by the WHO in 2012, has become a key intervention in areas with highly seasonal transmission. Cairns et al. (2012) estimated that SMC could prevent millions of cases and thousands of child deaths annually **[4]**. In Senegal, Cissé et al. (2016) reported a 60% reduction in confirmed cases, a 69% decrease in antimalarial treatments, and a 45% drop in severe cases among children targeted by SMC **[5]**. These findings are corroborated by De Cola et al. (2022), who observed a significant reduction in malaria risk in Burkina Faso and Nigeria, as measured by rapid diagnostic tests (RDTs) **[6]**. However, while the effectiveness of these interventions is well-documented, their implementation requires a deep understanding of transmission dynamics. Epidemiological models, such as the SIR framework introduced by Kermack and McKendrick, are essential for simulating intervention effects and guiding public health policies. For instance, Chitnis et al. (2012) demonstrated that combining ITNs and IRS effectively reduces transmission, though it quickly rebounds after interventions cease **[7]**. Such models also enable the exploration of interactions between different strategies to maximize their impact. In this regard, White et al. (2017) developed a mathematical model integrating data on drug resistance and SMC coverage, demonstrating that maintaining high coverage is crucial for maximizing the benefits of this intervention. This work underscores the importance of model-based approaches in guiding prevention efforts **[8]**.

Limitations of existing models (in Senegal) and Objectives of the Present Work
Despite these advancements, significant gaps remain in understanding the combined impact of interventions, particularly in specific contexts such as Senegal. Existing models rarely comprehensively integrate the combined dynamics of human and vector transmission or the impact of seasonal interventions like SMC. To address these needs, this study aims to develop a coupled SIR-SI mathematical model capable of analyzing the impact of SMC on malaria transmission among children under 5 years old in Senegal.

Although SMC in Senegal currently targets children aged 0 to 120 months, we focus on children under 5 years old (0–59 months) for two main reasons. First, this age group is particularly vulnerable to malaria due to their immature immune systems. Second, this choice ensures comparability with other studies focused on this specific age group. By narrowing the analysis to this cohort, this study provides relevant insights to optimize resource allocation and improve the effectiveness of interventions in Senegal.

3. METHODOLOGY

This study focuses on the modeling, analysis, and simulation of malaria dynamics, with a particular emphasis on the impact of the SMC intervention. Our model is structured into compartments. The human compartment includes individuals susceptible to infection, those who are infected, and those who have recovered. Similarly, the mosquito compartment includes mosquitoes susceptible to infection and those already infected.

The key parameters used in the model are as follows:

- β_h: transmission rate from infected mosquitoes to humans
- β_m: transmission rate from infected humans to mosquitoes
- γ: recovery rate in humans
- μ: mortality rate of mosquitoes
- η: efficacy of SMC (seasonal malaria chemoprevention), which plays a crucial role in our model

We analyzed our model by examining the Jacobian matrix at the disease-free equilibrium and endemic equilibrium points. Our objective was to determine the stability of these equilibrium points. To achieve this, we calculated the eigenvalues of the Jacobian matrix and studied its trace and determinant. Finally, we calculated the basic reproduction number, denoted as Ro.

In parallel, we conducted numerical simulations using the R software to visualize infection dynamics over time and compare scenarios with and without the SMC intervention, thereby assessing the effectiveness of this control strategy.

Prior to this, the STL decomposition (Seasonal and Trend decomposition using Loess) was applied to the time series data collected as part of the National Malaria Control Program (NMCP Senegal). This method decomposed malaria cases into three main components: trend, seasonality, and remainder. The analysis was conducted on global data concerning children under 5 years of age in Senegal for the period from 2016 to 2019.The resulting components were analyzed to highlight long-term trends, identify recurring seasonal cycles, and detect anomalies not explained by trend or seasonality. This approach provides a detailed view of the temporal dynamics of the disease, offering critical insights to refine malaria control strategies for this particularly vulnerable age group.

3.1 How do malaria cases among children under 5 evolve over time?

The graph below presents a heatmap illustrating the monthly distribution of malaria cases among children under 5 years old, by region, in Senegal between 2016 and 2019. The color intensity reflects the number of cases, ranging from white (low or no cases) to dark red (a very high number of cases).

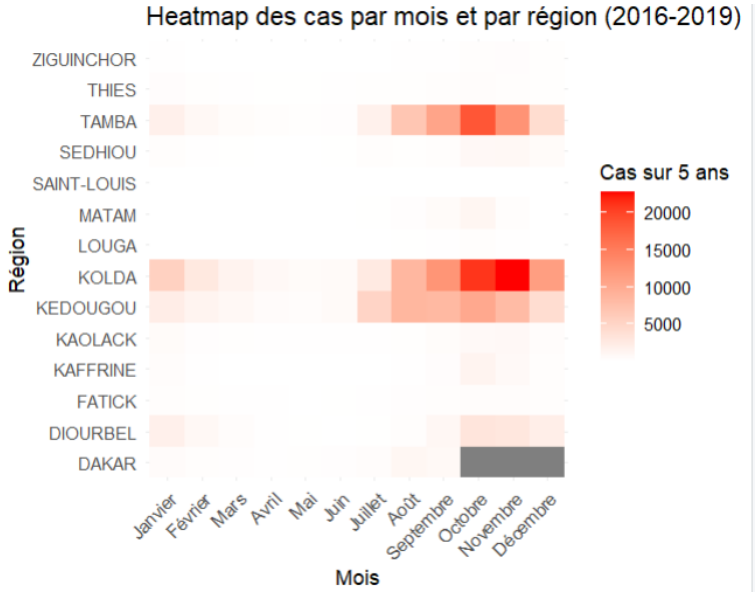

Fig.1 Heatmap of Monthly Malaria Cases by Region in Children Under 5

The heatmap highlights an alarming concentration of malaria cases in the regions of Kolda, Tambacounda, and Kédougou, particularly at the end of the rainy season. These areas should be prioritized for malaria control interventions in Senegal. The observed regional and seasonal variability underscores the need for a targeted and adaptable approach to optimize the effectiveness of prevention and control strategies.

The following figure shows the STL decomposition of malaria cases over time, applied to the NMCP database (monthly data) from 2016 to 2019.

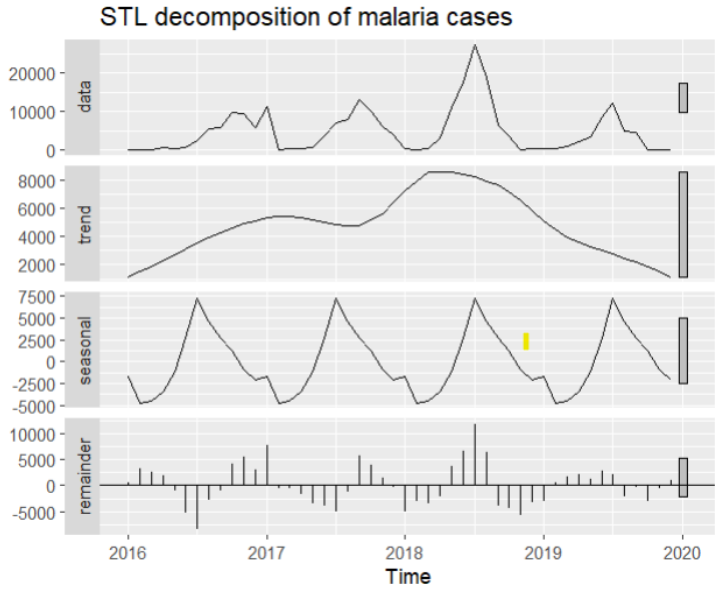

Fig 2: STL decomposition of malaria cases in children under 5 in Senegal

In summary, the data reveal an upward trend in malaria cases up to 2018, influenced by regular seasonal variations. Anomalies are limited, suggesting that the trend and seasonality adequately explain the fluctuations.

The following graph shows the trend component of malaria cases over time, extracted from the STL decomposition we performed earlier.

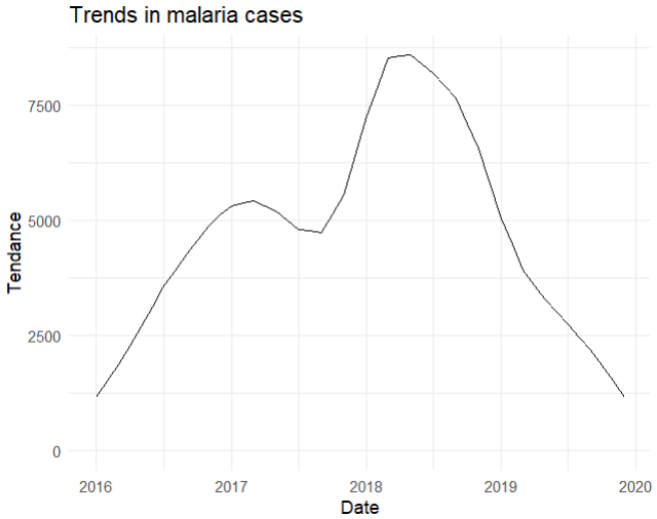

Fig.3: Trends in malaria cases in the under-5s

This graph indicates a phase of significant increase in malaria cases followed by a phase of decline. The data suggest that after peaking in 2018, efforts to reduce malaria cases have been effective. However, it is important to study the underlying factors driving these changes to better understand the disease dynamics and anticipate future trends.

The graph below, however, shows that malaria cases are strongly influenced by regular seasonal cycles, with predictable periods where cases increase significantly.

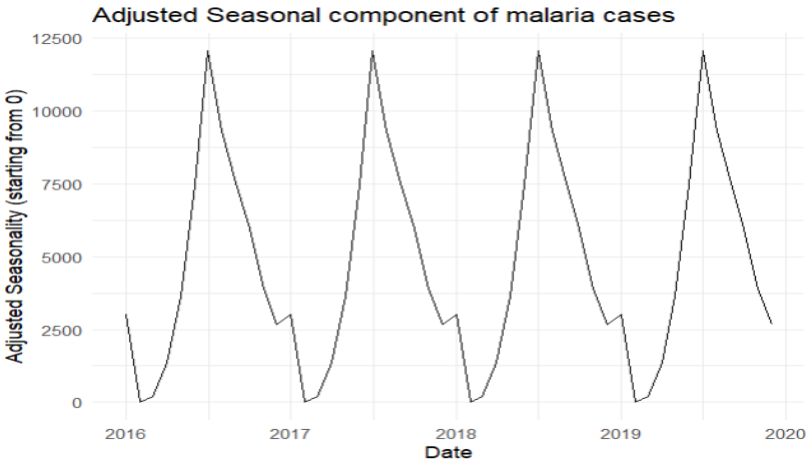

Fig.4 seasonal component of malaria cases in the under-5s

This graph serves as a valuable tool for planning public health resources and interventions, particularly in the context of Seasonal Malaria Chemoprevention (SMC). By identifying periods of the year when malaria risk is highest, it enables better targeting of SMC campaigns, intensifying prevention efforts during seasons conducive to disease transmission, such as the rainy season. This ensures optimal resource utilization and enhanced effectiveness of interventions.

These graphs (fig1, fig2, fig3, and fig4), by highlighting critical periods of malaria risk, also underscore the importance of robust analytical tools to guide control strategies. It is within this context that our SIR-SI model integrates seamlessly, offering a mathematical approach to simulate malaria transmission dynamics between humans and mosquitoes.

By incorporating specific parameters, such as the SMC treatment rate, our model allows for the evaluation of the impact of this intervention in reducing infections. It also helps explore various scenarios to optimize SMC schedules and adapt strategies based on observed local dynamics, such as the seasonality highlighted in this graph.

Thus, the SIR-SI model goes beyond descriptive analysis to serve as a predictive tool, enabling the maximization of intervention effectiveness and ensuring better allocation of resources in the fight against malaria.

3.2 Mathematical analysis of the model

The model we will study is as follows (see Fig.5):

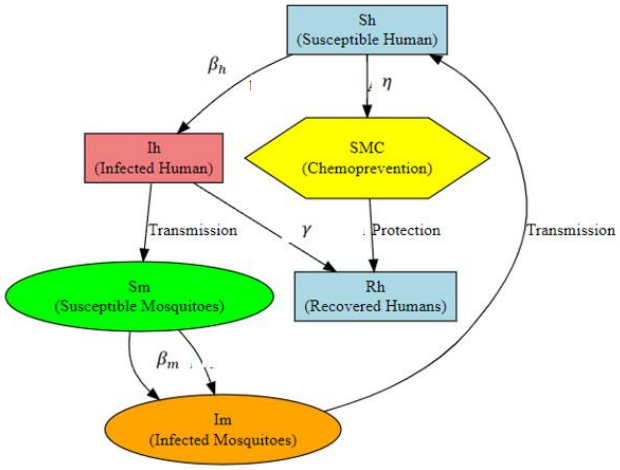

Fig.5: Diagram of malaria transmission dynamics with the integration of SMC as an intervention

This model, illustrated in Fig.5, represents the dynamics of malaria transmission with the integration of Seasonal Malaria Chemoprevention (SMC) as an intervention. Below is a detailed explanation of the components and interactions in the model:

Model Components:

- S_h (Susceptible Humans): Represents human individuals susceptible to malaria infection.
- I_h (Infected Humans): Represents humans currently infected with the malaria parasite.
- R_h (Recovered Humans**):** Represents humans who have recovered from the infection and have temporary immunity.
- SMC (Chemoprevention): An intervention aimed at protecting susceptible humans (Sh) from infection by administering preventive treatment.
- S_m (Susceptible Mosquitoes): Represents mosquitoes susceptible to infection from infected humans.
- I_m (Infected Mosquitoes): Represents mosquitoes that are infected and capable of transmitting the parasite to humans.

Interactions and Dynamics:

- **Transmission Between Humans and Mosquitoes:**
  - Susceptible mosquitoes (S_m) become infected (I_m) when they bite infected humans (I_h).
  - Susceptible humans (S_h) become infected (I_h) after being bitten by infected mosquitoes (I_m).
- **SMC Intervention:**
  - Susceptible humans (S_h) can receive preventive treatment (SMC) at a rate η, reducing their risk of infection.
  - Chemoprevention protects susceptible humans, moving them directly to the recovered state (R_h), where they benefit from temporary immunity.
- **Immunity and Recovery (γ):**
  - Infected humans (I_h) can recover and transition to the recovered state (R_h) at a rate γ, gaining temporary immunity before becoming susceptible again (S_h).
- **Mosquito Dynamics:**
  - Infected mosquitoes (I_m) can transmit the parasite to susceptible humans (S_h).
  - Susceptible mosquitoes (S_m) can become infected through contact with infected humans (I_h).

Key Model Parameters:

- $\boldsymbol{\beta_h}$**:** Transmission rate of malaria from infected mosquitoes (I_m) to susceptible humans (S_h).
- $\boldsymbol{\beta_m}$**:** Transmission rate of malaria from infected humans (I_h) to susceptible mosquitoes (S_m).
- $\boldsymbol{\eta}$**:** Rate at which susceptible individuals (S_h) receive chemoprevention.
- $\boldsymbol{\gamma}$**:** Recovery rate of infected humans (I_h) to the recovered state (R_h).

The SIR model for humans with SMC and the SI model for mosquitoes (Fig.5) is defined by the following differential equations:

$$\begin{cases} \frac{dS_h}{dt} = -\beta_h S_h I_m - \eta S_h \\ \frac{dI_h}{dt} = \beta_h S_h I_m - \gamma I_h \\ \frac{dR_h}{dt} = \gamma I_h + \eta S_h \\ \frac{dS_m}{dt} = -\beta_m S_m I_h \\ \frac{dI_m}{dt} = \beta_m S_m I_h - \mu I_m \end{cases}$$

Equilibrium Analysis

Disease-Free Equilibrium (DFE)

$S_h = 1, \quad I_h = 0, \quad R_h = 0, \quad S_m = 1 \quad I_m = 0$

In the DFE, all rates of change of the variables are zero.

$\frac{dS_h}{dt} = \frac{dI_h}{dt} = \frac{dR_h}{dt} = \frac{dS_m}{dt} = \frac{dI_m}{dt} = 0$

Substituting these conditions into the differential equations

$\frac{dS_h}{dt} = -\beta_h S_h I_m - \eta S_h = 0$

$\frac{dI_h}{dt} = \beta_h S_h I_m - \gamma I_h = 0$

$\frac{dR_h}{dt} = \gamma I_h + \eta S_h = 0$

$\frac{dS_m}{dt} = -\beta_m S_m I_h = 0$

$\frac{dI_m}{dt} = \beta_m S_m I_h - \mu I_m = 0$

Let's solve these equations in the DFE (Deterministic Finite Environment)

$\frac{dS_h}{dt} = 0: \quad -\beta_h S_h I_m - \eta S_h = 0 \Longrightarrow S_h(\eta + \beta_h I_m) = 0$

$S_h = 1$ et $I_m = 0$ (because $\eta + \beta_h \cdot 0 \neq 0$)

$\frac{dI_h}{dt} = 0: \quad \beta_h S_h I_m - \gamma I_h = 0 \Longrightarrow \gamma I_h = 0 \Longrightarrow I_h = 0$

$\frac{dR_h}{dt} = 0: \quad \gamma I_h + \eta S_h = 0 \Longrightarrow \eta \cdot 1 = 0$

$\frac{dS_m}{dt} = 0: \quad -\beta_m S_m I_h = 0 \Longrightarrow I_m = 0$

$S_m = 1$

$\frac{dI_m}{dt} = 0$: $\beta_m S_m I_h - \mu I_m = 0 \implies I_m = 0$

The equilibrium point without disease is:

$$(S_h, I_h, R_h, S_m, I_m) = (1, 0, 0, 1, 0)$$

The Jacobian matrix J is the matrix of partial derivatives of the differential equations with respect to the state variables

$$J_{DFE} = \begin{pmatrix} -\eta & 0 & 0 & 0 & -\beta_h \\ 0 & -\gamma & 0 & 0 & \beta_h \\ \eta & \gamma & 0 & 0 & 0 \\ 0 & -\beta_m & 0 & 0 & 0 \\ 0 & \beta_m & 0 & 0 & -\mu \end{pmatrix}$$

$Tr(J_{DFE}) = -(\eta + \gamma + \mu)$

we calculate the determinant using Laplace's method

$$J_{DFE} = \begin{pmatrix} -\eta & 0 & 0 & 0 & -\beta_h \\ 0 & -\gamma & 0 & 0 & \beta_h \\ \eta & \gamma & 0 & 0 & 0 \\ 0 & -\beta_m & 0 & 0 & 0 \\ 0 & \beta_m & 0 & 0 & -\mu \end{pmatrix}$$

$$\det(J_{DFE}) = \sum_{j=1}^{5} (-1)^{1+j} a_{ij} M_{1j}$$

where M_{ij} is the minor of the element α_{ij} that is, the determinant of the matrix obtained by removing the $j - th$ column

Step 1: Laplace expansion along the first row

$\det(J_{DFE}) = (-1)^{1+1}(-\eta)M_{11} + (-1)^{1+5}(-\beta_h)M_{15}$

Let's simplify this expression:

$\det(J_{DFE}) = -\eta M_{11} - (-\beta_h)M_{15} \implies \det(J_{DFE}) = -\eta M_{11} + \beta_h M_{15}$

Let's calculate the minors M_{11} and M_{15}

Calculation M_{11}: It is the matrix obtained by removing the first row and the first column from J_{DFE}

$$\begin{vmatrix} -\gamma & 0 & 0 & \beta_h \\ \gamma & 0 & 0 & 0 \\ -\beta_m & 0 & 0 & 0 \\ \beta_m & 0 & 0 & -\mu \end{vmatrix}$$

This matrix is triangular (all elements below the main diagonal are zero), so its determinant is the product of the diagonal elements: $M_{11} = (-\gamma) \cdot 0 \cdot 0 \cdot (-\mu) = 0$

Calculation M_{15} : It is the matrix obtained by removing the first row and the fifth column from J_{DFE}

$$\begin{vmatrix} 0 & -\gamma & 0 & 0 \\ \eta & \gamma & 0 & 0 \\ 0 & -\beta_m & 0 & 0 \\ 0 & \beta_m & 0 & 0 \end{vmatrix}$$

This matrix is also triangular (all elements to the right of the main diagonal are zero), so its determinant is also the product of the diagonal elements: $M_{15} = 0 \cdot \gamma \cdot 0 \cdot 0 = 0$

Finally

$$\det(J_{DFE}) = -\eta \cdot 0 + \beta_h \cdot 0 = 0$$

The determinant of the Jacobian matrix J_{DFE} at the disease-free equilibrium point is zero.

This result indicates that the disease-free equilibrium is at the boundary between stability and instability. In other words, this equilibrium is neutral in terms of linear stability. An equilibrium is considered neutral when, after a slight disturbance, the system does not return to its initial state but also does not diverge exponentially. Trajectories near this equilibrium may remain close without necessarily converging to it.

For a more in-depth analysis, it is necessary to examine the eigenvalues of the Jacobian matrix. If one or more eigenvalues have zero real parts, it is difficult to conclude local stability solely from linear analysis. Conversely, positive real parts of the eigenvalues would indicate instability, while negative real parts would indicate asymptotic stability. However, if all the eigenvalues have negative real parts except one that is zero, this suggests marginal or conditional stability.

In epidemiology, for a model like the SIR-SI with SMC, this means two things: first, without additional interventions or parameter changes, the system can remain in a disease-free equilibrium, but it is vulnerable to disturbances. Small disturbances could potentially push the system in an unstable direction, thereby triggering an epidemic. Second, this equilibrium is fragile and might require continuous interventions to maintain the absence of disease.

Eigenvalue Analysis of the Jacobian Matrix

To gain a better understanding of the stability of the disease-free equilibrium, we need to analyze the eigenvalues of the Jacobian matrix.

$$J_{DFE} = \begin{pmatrix} -\eta & 0 & 0 & 0 & -\beta_h \\ 0 & -\gamma & 0 & 0 & \beta_h \\ \eta & \gamma & 0 & 0 & 0 \\ 0 & -\beta_m & 0 & 0 & 0 \\ 0 & \beta_m & 0 & 0 & -\mu \end{pmatrix}$$

To find the eigenvalues, we need to solve the characteristic equation: $det(J_{DFE} - \lambda I) = 0$

where I is the identity matrix and λ represents the eigenvalues

$$J_{DFE} - \lambda I = \begin{pmatrix} -\eta - \gamma & 0 & 0 & 0 & -\beta_h \\ 0 & -\gamma - \lambda & 0 & 0 & \beta_h \\ \eta & \gamma & -\lambda & 0 & 0 \\ 0 & -\beta_m & 0 & -\lambda & 0 \\ 0 & \beta_m & 0 & 0 & -\mu - \lambda \end{pmatrix}$$

The determinant of this matrix is:

$$\begin{vmatrix} -\eta - \gamma & 0 & 0 & 0 & -\beta_h \\ 0 & -\gamma - \lambda & 0 & 0 & \beta_h \\ \eta & \gamma & -\lambda & 0 & 0 \\ 0 & -\beta_m & 0 & -\lambda & 0 \\ 0 & \beta_m & 0 & 0 & -\mu - \lambda \end{vmatrix}$$

To simplify, note that some blocks of this matrix are independent of the others:

For block 1: $\begin{pmatrix} -\eta - \gamma & -\beta_h \\ 0 & -\mu - \lambda \end{pmatrix}$

The eigenvalues are the solutions of: $(\eta + \lambda)(\mu + \lambda) = 0$ $\lambda = -\eta$ or $\lambda = -\mu$

For block 2: $\begin{pmatrix} -\gamma-\lambda & \beta_h \\ \gamma & -\lambda \end{pmatrix}$

The eigenvalues are the solutions of: $det\begin{pmatrix} -\gamma-\lambda & \beta_h \\ \gamma & -\lambda \end{pmatrix} = 0$

That gives: $(\gamma+\lambda)\lambda + \gamma\beta_h = 0$, $\lambda^2 + \gamma\lambda + \gamma\beta_h = 0$

The solutions to this quadratic equation are:

$$\lambda = \frac{-(\gamma)\pm\sqrt{\gamma^2-4\gamma\beta_h}}{2}$$

The eigenvalues will depend on the parameters γ and β_h

Missing Eigenvalue, that is, the eigenvalue corresponding to the off-diagonal part (i.e., to the element $\beta_m$and 0) is $\lambda = 0$

The eigenvalues are therefore:

$$\lambda_1 = -\eta$$

$$\lambda_2 = -\mu$$

$$\lambda_3, \lambda_4 = \frac{-(\gamma)\pm\sqrt{\gamma^2-4\gamma\beta_h}}{2}$$

$$\lambda_5 = 0$$

To conclude on stability:

- If all eigenvalues except one have negative real parts, the equilibrium may be stable, but the zero eigenvalue indicates neutrality or marginal stability.
- If any eigenvalue has a positive real part, the equilibrium is unstable.

In our case: λ_1 and λ_2 are negative if $\eta > 0$ and $\mu > 0$.

The values of λ_3 and λ_4 depend on γ and β_h.

The presence of the zero eigenvalue λ_5 indicates marginal stability. Perturbations can push the system away from equilibrium, but without clear indications of convergence towards equilibrium or rapid divergence, a more in-depth analysis, such as a nonlinear analysis, would be necessary.

Endemic equilibrium, EE

To study the endemic equilibrium of our system of differential equations, we need to find the constant values of the variables S_h, I_h, R_h, S_m and I_m for which the time derivatives are zero. This means we need to solve the system of equations by setting each derivative equal to zero.

Our system of differential equations is as follows:

$$\begin{cases} \frac{dS_h}{dt} = -\beta_h S_h I_m - \eta S_h \\ \frac{dI_h}{dt} = \beta_h S_h I_m - \gamma I_h \\ \frac{dR_h}{dt} = \gamma I_h + \eta S_h \\ \frac{dS_m}{dt} = -\beta_m S_m I_h \end{cases}$$

$$\frac{dI_m}{dt} = \beta_m S_m I_h - \mu I_m$$

For the endemic equilibrium, we need to set each derivative to zero:

$$\begin{cases} -\beta_h S_h I_m - \eta S_h = 0 \\ \beta_h S_h I_m - \gamma I_h = 0 \\ \gamma I_h + \eta S_h = 0 \\ -\beta_m S_m I_h = 0 \end{cases}$$

$$\beta_m S_m I_h - \mu I_m = 0$$

We will solve this system to find the equilibrium values $S_h^*, \mathrm{I}_h^*, R_h^*, S_m^*, I_m^*$

In the first equation, $-\beta_h S_h I_m - \eta S_h = 0 \implies (-\beta_h I_m - \eta) S_h = 0$

Thus, $S_h \neq 0$ since there is at least one infected individual, which implies $I_m = -\frac{\eta}{\beta_h}$

Since I_m must be positive, this solution is not physically realistic. We seek non-trivial solutions.

$S_h \neq 0,\ I_h \neq 0, S_m \neq 0$ and $I_m \neq 0$.

Linearization of the System

To linearize the system around the equilibrium points, we need to calculate the Jacobian matrix of the system.

$$J = \begin{pmatrix} -\beta_h I_m - \eta & 0 & 0 & 0 & -\beta_h S_h \\ \beta_h I_m & -\gamma & 0 & 0 & \beta_h S_h \\ \eta & \gamma & 0 & 0 & 0 \\ 0 & -\beta_m S_m & 0 & -\beta_m I_h & 0 \\ 0 & \beta_m S_m & 0 & \beta_m I_h & -\mu \end{pmatrix}$$

To study the stability, we need to evaluate this matrix at the endemic equilibrium and analyze the eigenvalues of the Jacobian matrix.

$Tr(J) = -\beta_h I_m - \eta - \gamma - \beta_m I_h - \mu \quad \Leftrightarrow \quad Tr(J) < 0$ (Trace of J is negative)

Calculation of the Determinant

Let's determine the determinant:

$$\begin{vmatrix} -\beta_h I_m - \eta & 0 & 0 & 0 & -\beta_h S_h \\ \beta_h I_m & -\gamma & 0 & 0 & \beta_h S_h \\ \eta & \gamma & 0 & 0 & 0 \\ 0 & -\beta_m S_m & 0 & -\beta_m I_h & 0 \\ 0 & \beta_m S_m & 0 & \beta_m I_h & -\mu \end{vmatrix}$$

For a $5x5$ Jacobian matrix, traditional methods of solving, such as Laplace's expansion or cofactors, remain cumbersome. Additionally, for a thorough analysis, it is necessary to evaluate the eigenvalues of the Jacobian matrix at the endemic equilibrium. To achieve greater accuracy, we will use numerical tools like R to compute the eigenvalues and assess stability by simulating the model with biologically realistic parameters (see R code). This will allow us to analyze the stability of the endemic equilibrium for the given parameters.

Summary of Results Obtained with R

After defining the mathematical model and calculating the Jacobian matrix at the endemic equilibrium, we used R to determine the eigenvalues of this matrix in order to analyze the stability of the equilibrium.

Parameter Values Used

- Human-to-mosquito transmission rate $\beta_h = 0.3$
- Mosquito-to-human transmission rate $\beta_m = 0.2$

- Treatment rate by SMC $\eta = 0.1$
- Recovery rate $\gamma = 0.1$
- Mosquito mortality rate $\mu = 0.1$
- Number of infected humans at endemic equilibrium $I_h = 0.1$
- Number of infected mosquitoes at endemic equilibrium $I_m = 0.1$

Calculations at Endemic Equilibrium

- Number of susceptible humans $(S_h) : -\frac{\gamma}{\eta} I_h = -\frac{0.1}{0.1} \times 0.1 = -0.1$
- Number of susceptible mosquitos $(S_m) : -\frac{\mu\eta}{\beta_m \beta_h I_h} = -\frac{0.1 \times 0.1}{0.2 \times 0.3 \times 0.1} = -1.6667$

Jacobian Matrix:

The Jacobian matrix at the endemic equilibrium is:

$$J = \begin{bmatrix} -0.03 & 0 & 0 & 0 & -0.03 \\ 0.03 & -0.1 & 0 & 0 & -0.03 \\ 0.1 & 0.1 & 0 & 0 & 0 \\ 0 & 0.3333 & 0 & -0.2 & 0 \\ 0 & -0.3333 & 0 & 0.2 & -0.1 \end{bmatrix}$$

Eigenvalues

The eigenvalues calculated with R are:

$\lambda_1 = -0.23427 + 0.26198i$

$\lambda_2 = -0.23427 + 0.26198i$

$\lambda_3 = -0.1,$

$\lambda_4 = 0,$

$\lambda_5 = -0.03007.$

Stability Analysis

- The eigenvalues $\lambda_1, \lambda_2, \lambda_3$ et λ_5 have negative real parts
- The eigenvalue λ_4 is zero, indicating the need for a more in-depth analysis for this value.

The analysis shows that most eigenvalues have negative real parts, suggesting that the endemic equilibrium is locally stable. The presence of a zero eigenvalue ($\lambda_4 = 0$) requires further investigation to determine its contribution to the system's stability. A nonlinear analysis or more detailed numerical simulations may be necessary for a definitive conclusion.

Calculation of R_0

To calculate R_0 (the basic reproduction number) for the SIR-SI model with SMC intervention, the Next Generation Matrix (NGM) method will be used.

New infections for humans and mosquitoes are:

- New human infections: $\beta_h S_h I_m$
- New mosquito infections: $\beta_m S_m I_h$

The transitions for each compartment are:

- Transition for humans: $-\eta S_h,\ \beta_h S_h I_m - \gamma I_h,\ \gamma I_h + \eta S_h$
- Transition for mosquitoes: $-\beta_m S_m I_h,\ \beta_m S_m I_h - \mu I_m$

The matrix F contains the terms for new infections, and the matrix V contains the terms for transitions.

The next generation matrix is given by $K = FV^{-1}$ and R_0 is the largest eigenvalue of the matrix K

$$F = \begin{bmatrix} \beta_h S_h & 0 \\ 0 & \beta_m S_m \end{bmatrix} \qquad V = \begin{bmatrix} \gamma + \eta & 0 \\ 0 & \mu \end{bmatrix} \qquad V^{-1} = \begin{bmatrix} \frac{1}{\gamma+\eta} & 0 \\ 0 & \frac{1}{\mu} \end{bmatrix}$$

We can then write: $R_0 = \rho(F \cdot V^{-1})$

$$K = F \cdot V^{-1} = \begin{bmatrix} \beta_h S_h & 0 \\ 0 & \beta_m S_m \end{bmatrix} \cdot \begin{bmatrix} \frac{1}{\gamma+\eta} & 0 \\ 0 & \frac{1}{\mu} \end{bmatrix} = \begin{bmatrix} \frac{\beta_h S_h}{\gamma+\eta} & 0 \\ 0 & \frac{\beta_m S_m}{\mu} \end{bmatrix}$$

R_0 is given by the spectral radius of the matrix K, which is the largest eigenvalue of K.

The eigenvalues of K are:

$$\lambda_1 = \frac{\beta_h S_h}{\gamma+\eta} \qquad \lambda_2 = \frac{\beta_m S_m}{\mu}$$

Thus, R_0 is:

$$R_0 = \max\left(\frac{\beta_h S_h}{\gamma+\eta}, \frac{\beta_m S_m}{\mu}\right)$$

For the human component, if η increases, then the denominator $\gamma + \eta$ increases.

Consequently $\frac{\beta_h S_h}{\gamma+\eta}$ decreases.

The mosquito component $\frac{\beta_m S_m}{\mu}$ is not directly affected by η

In summary, increasing η tends to reduce R_0 if the human infection ((represented by $\frac{\beta_h S_h}{\gamma+\eta}$) is the dominant component. This means that seasonal malaria chemoprevention (SMC) can effectively reduce the spread of the disease by decreasing the human infection contribution to R_0 .

3.3 SIMULATIONS

The simulations in Fig. 6, Fig. 7, and Fig. 8 were performed using the R software.

Before SMC

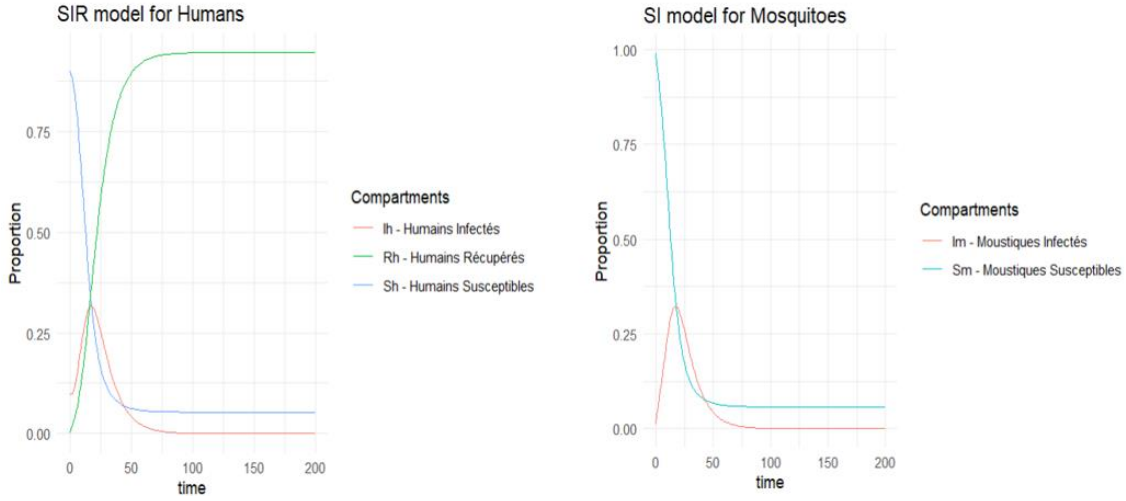

Fig.6: results before SMC

After intervention by SMC

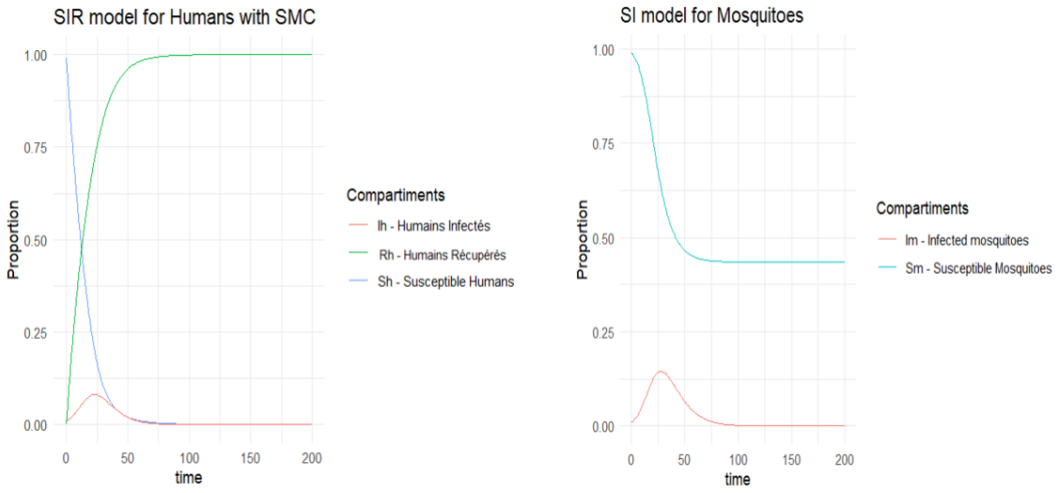

Fig.7: results after intervention by SMC

Before the SMC (Fig.6 left):

- **Susceptible (S_h - blue curve)**: A large proportion of the human population is initially susceptible to infection. This proportion rapidly decreases at the beginning of the epidemic, indicating a fast transmission of the disease in the population.
- **Infected (I_h - red curve):** The number of infected individuals quickly rises at first, reaching a peak before gradually decreasing. This suggests that, without intervention, malaria spreads rapidly among humans.
- **Recovered (R_h - green curve):** The proportion of recovered individuals gradually increases, eventually dominating the population, which means that many people recover or become immune, but only after a large number of individuals have been infected**.**

After SMC (Fig.7 left):

- **Susceptible (S_h - blue curve):** The proportion of susceptible individuals decreases much more slowly. This indicates that SMC (Seasonal Malaria Chemoprevention) is protecting a large portion of the human population from infection.
- **Infected (I_h - red curve):** The infection peak is much lower and fades quickly. This shows that the SMC intervention significantly reduces the number of people infected by malaria.
- **Recovered (R_h - green curve):** The number of recoveries continues to rise, but with a much lower rate of initial infections. This demonstrates the protective effect of SMC, reducing the need for recovery by preventing infection in the first place.

Conclusion for Humans:

- **Before SMC**, the infection spreads rapidly, with a large number of individuals infected in a short time.
- **After SMC**, the infection is well controlled, with a marked reduction in new infection cases and a much slower spread.

SI Model for Mosquitoes (Before SMC Fig.6 vs After SMC Fig7)

Before SMC (Fig.6 right):

- **Susceptible (S_m - blue curve)**: Susceptible mosquitoes decrease rapidly, as they become infected once malaria spreads.
- **Infected (I_m - red curve)**: The peak of infected mosquitoes is relatively high, and although it decreases after some time, a significant number of mosquitoes remain infected, promoting continued transmission of malaria to humans.

After SMC (Fig.7 right):

- **Susceptible (S_m - blue curve)**: The proportion of susceptible mosquitoes decreases more slowly, and fewer mosquitoes become infected.
- **Infected (I_m - red curve)**: The peak of infected mosquitoes is much lower than in the first case, and the proportion of infected mosquitoes remains low throughout. This demonstrates that SMC, by reducing human infections, also reduces mosquito infections, thereby decreasing overall transmission.

Conclusion for Mosquitoes:

- **Before SMC**, mosquitoes become rapidly infected, contributing to maintaining high transmission levels of malaria.
- **After SMC**, there is a significant reduction in infected mosquitoes, indicating that the intervention also impacts the mosquito transmission reservoir.

Regular interventions by SMC

The regular interventions of Seasonal Malaria Chemoprevention (SMC), illustrated in Fig. 8, play a crucial role in reducing malaria transmission.

Fig.8: results after regular intervention by SMC

- Susceptible population (S_h - Blue Curve):
  - The proportion of susceptible individuals (those at risk of being infected) decreases rapidly at the beginning, but it doesn't reach zero.
  - After the initial drop, the curve follows a regular oscillation pattern, showing a cyclical nature. This suggests that despite regular SMC interventions, a portion of the population remains susceptible. The periodic rise and fall might indicate periods when SMC is administered, and its effect wanes over time until the next intervention.
- Recovered population (Rh - Green Curve):
  - The recovered proportion increases sharply at the beginning, indicating that the intervention is effective in either preventing or mitigating the severity of infections, leading to recovery.

- Similar to the susceptible group, the recovered population shows a cyclical behavior, fluctuating over time. The oscillation reflects the temporary protection offered by the SMC, which wears off, requiring regular re-administration to maintain the level of protection in the population.

- Infected population (I_h- Red Curve):
  - The proportion of infected individuals remains very low throughout the time period. This indicates that the regular SMC interventions are highly effective in keeping infection levels under control.
  - The small rise and fall in infection rates also follow the oscillation pattern, but at a much lower scale compared to the susceptible and recovered populations. This fluctuation likely corresponds to brief periods when the effect of SMC diminishes, allowing minor increases in infections before the next round of intervention brings them back down.

Key Takeaways:

- **Cyclical nature of SMC protection:** The oscillations in the susceptible and recovered populations reflect the fact that SMC interventions need to be administered regularly. The protection it offers decreases over time, and thus without continued intervention, the population would become more susceptible again.
- **Low infection levels:** The infected population remains extremely low due to the regular application of SMC, suggesting that it is successful in preventing widespread transmission of malaria.
- **Intervention success:** Despite the cyclic increase in the susceptible population, the overall effect of regular SMC administration is to maintain a high level of recovery and immunity in the population, preventing large-scale outbreaks of malaria.

This graph demonstrates that while SMC is not a one-time solution, its regular application effectively controls the infection rate, even though a portion of the population cycles through susceptibility and recovery.

4. DISCUSSION

The results of this study confirm the proven effectiveness of Seasonal Malaria Chemoprevention (SMC) in reducing malaria transmission among children under 5 years old. Our simulations demonstrate that regular and meticulously planned administration of SMC keeps infection levels at extremely low thresholds, significantly reducing the risk of major epidemic outbreaks. These findings highlight the importance of focusing this intervention on children under 5 years old, who represent the most vulnerable age group due to their immature immune systems and increased susceptibility to the disease.

The results of our modeling suggest that targeting children under 5 years old could be sufficient to significantly reduce malaria transmission. This strategic choice would allow for a more efficient and rational use of available resources while maintaining a substantial impact on case reduction. Furthermore, this approach aligns with other international studies that also focus on this key population, further strengthening the scientific validity and operational relevance of this strategy.

Additionally, the analysis reveals that the effectiveness of SMC could be further enhanced through a combination with complementary interventions, such as the use of insecticide-treated nets or indoor residual spraying (thereby increasing the parameter μ, representing the mosquito mortality rate). This integrated approach would simultaneously target the human and vector components of the basic reproduction number (R0), both of which play critical roles in transmission dynamics. Coordinated management of these components could accelerate and sustain the reduction of the malaria burden.

In conclusion, focusing specifically on children under 5 years old, integrated into a combined approach and based on rigorous planning, could maximize the effectiveness of SMC, optimize resource allocation, and strengthen malaria control efforts in endemic regions.

Limitation of this study

This study is strictly based on numerical simulations using a deterministic SIR-SI model. While these simulations provide valuable insights, they rely on theoretical assumptions and do not incorporate real-world variability or observed field data, which could influence the applicability of the results.

CONCLUSION

This study highlights the effectiveness of Seasonal Malaria Chemoprevention (SMC) in reducing malaria transmission among children under 5 years old in Senegal. Using an SIR-SI mathematical model, we demonstrated that targeting this age group maintains infection levels at very low thresholds. Our results suggest that, under certain conditions, focusing SMC coverage on children under 5 could be sufficient to significantly reduce transmission.

However, the current decision to extend SMC to children up to 10 years old is supported by previous studies that have identified a shift in the distribution of malaria cases toward older age groups in Senegal. These findings, backed by field data, emphasize the need to consider local dynamics and epidemiological specificities. While our model demonstrates notable effectiveness for children under 5, an explicit comparative modeling between the 0-5 and 0-10 age groups would be essential to confirm and deepen this assertion.

Moreover, the success of SMC depends on regular and meticulously planned administration, particularly during high-transmission periods such as the rainy season. The cyclical nature of infections observed in our simulations underscores the importance of repeated interventions to ensure sustained disease control. These results provide a strong scientific basis for refining prevention strategies and highlight the critical importance of integrating local data into public health decision-making processes.

Perspectives:

- **Explicit Comparison Between Age Groups (0-5 years and 0-10 years):**
  Developing a comparative modeling study between the age groups targeted by SMC (0-5 years and 0-10 years) is essential. This would provide a better understanding of the impact of extending coverage on transmission dynamics and help confirm or refute the relevance of this strategy.
- **Cost-Effectiveness Analysis:**
  Assess the economic impact of focusing coverage on children under 5 years compared to extending it to children under 10 years. This analysis would optimize the allocation of resources available for malaria control.
- **Simulation of Policy Changes in Administration:**
  Evaluate the effects of different administration strategies, such as adjusting the timing or frequency of treatments, based on seasonal specificities and local transmission dynamics.

Acknowledgments

I wish to express my heartfelt gratitude to all the institutions, organizations, and individuals who contributed, directly or indirectly, to the completion of this work.

First and foremost, I sincerely thank the National Malaria Control Program (NMCP) of Senegal for their support, invaluable data, and unwavering commitment to the fight against malaria.

I am also deeply grateful to the MARCAD program, led by Professor Oumar Gaye, for its unwavering and constant support. I would also like to express my gratitude to Professor Karim Konate for his valuable support of my research and the opportunities he has provided me to develop and enhance my skills in mathematical modeling applied to public health. My appreciation also goes to the AMMnet network, led by Jaline Gerardin, which facilitated enriching scientific exchanges and collaborations within a community dedicated to infectious disease modeling. This network played a key role in broadening my scientific perspectives and deepening my expertise.

I would like to thank the MAMOD AFRICA team, led by Emilie Pothin of SwissTPH, for inviting me to participate in a one-month training program in Senegal through AIMS. This experience was pivotal in strengthening my malaria modeling skills.

Special thanks go to Lucy Okell and her team at the Medical Research Council (MRC) of Imperial College London for their warm hospitality, scientific support, and knowledge sharing, which significantly enriched my methodological approach and analytical perspective.

I also wish to express my deep gratitude to Professor Ousmane Faye, whose generosity knows no bounds. His support and selfless assistance have had a significant impact on my work, helping me overcome numerous challenges.

Finally, I acknowledge Cheikh Anta Diop University, my home institution, for providing the academic framework that was essential to the success of this work.

To all these institutions and individuals, I extend my sincere thanks for their contributions to the advancement of my work and their role in the fight against malaria.

No funding / No financial support was received for this article.

The authors declare that there is no conflict of interest

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