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Mathematical modeling of malaria transmission dynamics in children under five years of age facing innovative interventions in the Democratic Republic of the Congo

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Abstract

Background

Malaria remains the leading cause of morbidity and mortality in the Democratic Republic of Congo (DRC), particularly among children under five years of age, who account for 67% of malaria-related deaths. Given the stationary trend in incidence despite current efforts, the National Strategic Plan (NSP) 2024-2028 introduces innovative interventions requiring rigorous prospective evaluation. This study aims to model transmission dynamics under different coverage scenarios to guide resource allocation for disease control and elimination in this vulnerable group.

Methods

We developed a deterministic discrete-time compartmental model of SEIR (Humans) and SEI (Mosquitoes) type, parameterized using data from the District Health Information Software 2 (DHIS2) from 2017 to 2023, covering 519 health zones. Transmission intensity was quantified by the basic reproduction number (R_0), calculated using the next-generation matrix method, after adjusting the crude incidence for reporting, testing, and care-seeking.

Results

In the absence of intervention scale-up, morbidity saturates at critical endemic levels. With current coverage rates (21% for vaccine and chemoprevention), R_0 values remain well above unity: R21 vaccine ($R_0=4.55$), IPTi/PMC ($R_0=4.66$), and ITNs ($R_0=3.71$). Achieving 80% coverage for individual interventions is insufficient to interrupt transmission. Only the combined scenario ("Mix-intervention") at 80% coverage achieves an R_0 of 0.48.

Conclusion

Interrupting malaria transmission among children under five in the DRC is mathematically feasible. However, it requires a synergy of innovative interventions reaching a critical coverage threshold.

Keywords: Malaria, SEIR modeling, DRC, R21/Matrix-M, R_0 .

1. INTRODUCTION

Malaria remains a major cause of morbidity and mortality, disproportionately affecting children under five years of age in sub-Saharan Africa. In the DRC, children in this age group are the most vulnerable, representing an alarming proportion of deaths attributable to this disease. Between 2017 and 2023, the annual incidence of malaria among children under five increased from 499 to 530 per 1,000 population, while mortality rose from 40 to 64 per 100,000 population. These statistics reflect the magnitude of the challenge and the urgency of strengthening malaria control strategies [1,2]. The DRC remains one of the most affected countries worldwide, accounting for 12.3% of global cases and 11.6% of malaria deaths in 2022. In 2023, 13,440,922 children under five suffered from malaria, representing 49% of all reported cases, including 1,253,679 severe cases. The number of recorded deaths among these children reached 14,930, accounting for 67% of malaria-related deaths [3,4].

Recently introduced innovative interventions, such as the malaria vaccine (MV) and seasonal malaria chemoprophylaxis (SMC), have shown significant potential to reduce transmission and the burden of malaria. A study conducted in three African countries reported a 30% reduction in severe cases among vaccinated children [5]. However, unequal access to these interventions, their limited implementation, and the variability of needs across epidemic zones pose major

challenges. Precise epidemiological stratification and mathematical modeling are therefore essential to optimize control strategies.

This study uses mathematical modeling to analyze and predict malaria dynamics among children under 5 years in the DRC, based on historical data (2017 to 2023) and future projections. It aims to evaluate the impact of innovative interventions planned in the NSP of the National Malaria Control Program (NMCP) 2024-2028 under different scenarios, to inform strategic decision-making and optimize resource planning for malaria control in this particularly vulnerable group.

Innovative interventions planned in the NSP of the NMCP/DRC for children under 5 years: The **R21/Matrix-M malaria vaccine**, developed by the University of Oxford, was approved in 2023. This vaccine, combining the R21 antigen specific to the *Plasmodium* parasite and the Matrix-M adjuvant from Novavax, offers an enhanced and durable immune response against malaria. It specifically targets the sporozoite of *Plasmodium*, which is the form of parasite when it enters the human host. Trials have demonstrated high efficacy, reducing symptomatic cases by 75% within 12 months following the three-dose series administered before the high transmission season. Additionally, a fourth annual dose maintains this efficacy. These results are comparable to those of the RTS, S vaccine. The vaccine also proved its efficacy in a phase 3 multicenter trial, with a significant 66% reduction in clinical cases after the third dose [6]. In the DRC, the Demographic and Health Survey (DHS-DRC III 2023-24) reveals that basic vaccination coverage is relatively low, with only 21% of children fully vaccinated. Despite this limited coverage, the data show a high incidence of malaria among children under 5 years, making this population eligible for the introduction of the R21 vaccine in high-transmission areas [7]. Perennial malaria chemoprevention (PMC), with intermittent preventive treatment in infants (IPTi-SP), has shown a significant reduction in clinical malaria (30.3% [95% CI 19.8%-39.4%]), anemia (21.3% [95% CI 8.3%-32.5%]), and malaria-related hospital admissions in infants (38.1% [95% CI 12.5%-56.2%]). Initially recommended for infants under 12 months, it is now advised up to 24 months in areas with moderate to high transmission. In 2024, a pilot plan was implemented, and its scale-up is planned for 2025 [8]. Seasonal malaria chemoprevention (SMC) consists of IPTi administered to children aged 3 to 59 months during the transmission season. It can prevent up to 75% of severe malaria cases and could reduce mortality. Recent studies have shown similar results with combined SP+AQ treatments and other drug combinations. The observational study on the effectiveness of SMC conducted at the scale of West and Central Africa in five countries (Burkina Faso, Chad, Gambia, Mali, and

Nigeria) and published in *The Lancet* in 2020, shows an overall estimate of SMC protective efficacy in reducing clinical malaria incidence within 28 days following administration of 88.2% (95% CI 78.7-93.4). Areas with low to high malaria transmission, such as Haut Katanga and Lualaba, are particularly targeted for this intervention [9].

Insecticide-treated nets (ITNs) constitute a major intervention for malaria prevention in the DRC, providing protection against mosquito bites and reducing malaria transmission. Although effective, ITNs face challenges such as insecticide resistance and low durability. To counter resistance, next-generation nets have been introduced, combining pyrethroids with a synergist. ITNs have demonstrated a 17% reduction in infant mortality and a nearly 50% reduction in uncomplicated malaria episodes. However, usage remains uneven, with only 37% of households having one net per two people [10].

The study objectives were: to determine the epidemiological stratification in terms of malaria incidence and mortality among children under 5 years in the DRC, from 2017 to 2023; to describe the targeting of innovative malaria control interventions among children under 5 years in the DRC, in 2024; to predict the dynamics of malaria among children under 5 years from 2024 to 2050, based on data from 2017 to 2023; to develop an effective predictive model, enabling estimation of future malaria morbidity as a function of different scenarios of intensification or cessation of innovative interventions.

2. METHODS

2.1. Study setting

This study was conducted in 519 health zones (HZ) across the 26 provinces of the DRC that routinely report malaria surveillance data through the DHIS2. The 2023 population, projected from DHIS2 data using the national annual population growth rate of 2.9% (National Institute of Statistics), was estimated at 123,835,800 inhabitants, of whom 38.4% lived in urban areas and 61.6% in rural areas. Figure 1 shows the geographical distribution of the 26 provincial health divisions and the 519 HZ included in the study.

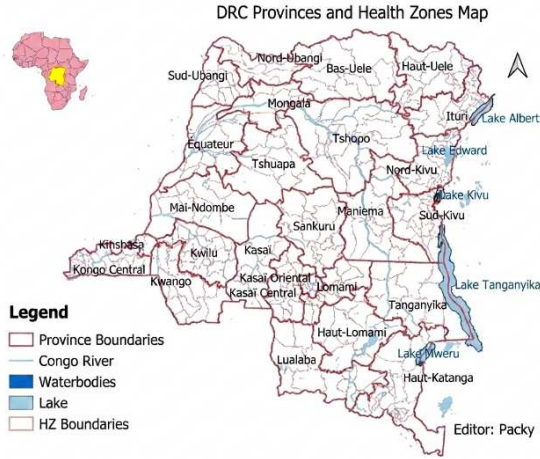


Figure 1. Map of the DRC with 26 DPS and 519 HZ

2.2. Study type and period

This is a modeling study conducted to simulate malaria transmission and predict morbidity and mortality among children under 5 years of age. Data from 2017 to 2023 were used to parameterize a compartmental model adapted from that of Ross. The efficacy of innovative malaria control interventions for children in this age group, as planned in the NSP 2024-2028 of the NMCP, was applied under various scenarios (parameter modification) to obtain a projection at time t .

2.3. Model type

A SEIR (Susceptible-Exposed-Infectious-Recovered) compartmental model was applied to the human population ($N^h = S^h + E^h + I^h + R^h$) and an SEI (Susceptible-Exposed-Infectious) model for the mosquito population ($N^a = S^a + E^a + I^a$). Susceptible humans can be infected by infectious mosquitoes, and vice versa, following infection rates (λ^h, λ^a). Mosquitoes, unlike humans, do not recover after infection.

2.4. Model formulation and parameterization

A discrete-time modeling approach inspired by the work of Jia Li (2013) was used. The difference equations describe the dynamics of the human and anopheline classes, accounting for infection rates (λ^h, λ^a), incubation rates (γ^h, γ^a), recovery rates (η^h), and survival probabilities of humans and anophelines (α_k^h, α_b^a) for each class. Key parameters include the average number of bites per mosquito, the probability of transmission per bite (β^h, β^a), and the relationship between human and mosquito population densities.

2.5. Model equations

The following dynamic equations were used to model the interactions between humans and mosquitoes:

❖ **Humans :**

$$S^h(t+1) = \Lambda + (1 - \lambda^h)\alpha_1^h S^h(t) + \theta^h \alpha_8^h R^h(t)$$

$$E^h(t+1) = \lambda^h \alpha_2^h S^h(t) + (1 - \gamma^h)\alpha_3^h E^h(t)$$

$$I^h(t+1) = \gamma^h \alpha_4^h E^h(t) + (1 - \eta^h)\alpha_5^h I^h(t)$$

$$R^h(t+1) = \eta^h \alpha_6^h I^h(t) + (1 - \theta^h)\alpha_7^h R^h(t)$$

❖ **Mosquitoes:**

$$S^a(t+1) = b^a \alpha_b^a (N^a(t)) N^a(t) + (1 - \lambda^a(t)) S^a(t) \alpha_1^a$$

$$E^a(t+1) = \lambda^a(t) \alpha_2^a S^a(t) + (1 - \gamma^a) E^a(t) \alpha_3^a$$

$$I^a(t+1) = \gamma^a \alpha_4^a E^a(t) + I^a(t) \alpha_5^a$$

The mathematical interactions between the human (SEIR) and mosquito (SEI) compartments are represented schematically in Figure 2, which illustrates the transmission pathways of Plasmodium between humans and Anopheles mosquitoes, as well as the transitions between epidemiological states within each population.

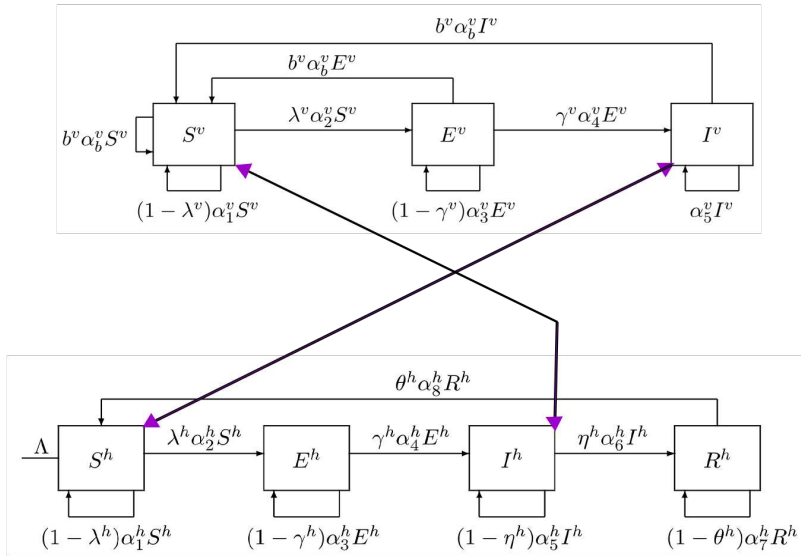


Figure 2: Compartmental model of parasite transmission between humans and mosquitoes

❖ Calculation of R_0

In mathematical epidemiology, the primary focus is on measuring the intensity of disease transmission. This measure, called the reproduction rate and denoted by R_0 , enables epidemiologists to determine whether the disease tends to disappear or persist (reach endemic

proportions). If R_0 is less than 1, it can be assumed that the disease will eventually die out after a certain time; if R_0 is greater than 1, an expansion and persistence of the disease must be feared [11].

The calculation of R_0 in discrete-time systems relies on the so-called next-generation matrix approach [12,13,14]. This approach, for SIR-type models, explains the evolution or projection of individuals from time t to time $t + 1$ on the one hand through the survival of infectious individuals and on the other hand through their fertility.

Our previous system can therefore be written in the form: $X(t + 1) = (F + T)X(t)$

Where F represents new infections and T represents transitions between classes.

The Jacobian matrix J evaluated at the disease-free equilibrium, denoted DFE and given by $(E^a, I^a, E^h, I^h, S^a, S^h, R^h) = (0, 0, 0, 0, S_0^a, S_0^h, 0)$, is of the form

$$J = \begin{pmatrix} F+T & 0 \\ . & C \end{pmatrix},$$

Where the fertility matrix F is given by

$$F = \begin{pmatrix} 0 & 0 & 0 & \frac{r\beta^h S_0^a \alpha_2^h S_0^a}{S_0^h} \\ 0 & 0 & 0 & 0 \\ 0 & G'(0)r\beta^a \alpha_2^h & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

And T as the transition matrix is given by

$$T = \begin{pmatrix} (1 - \gamma^a)\alpha_3^a & 0 & 0 & 0 \\ \gamma^a \alpha_4^a & \alpha_5^a & 0 & 0 \\ 0 & 0 & (1 - \gamma^h)\alpha_3^h & 0 \\ 0 & 0 & \gamma^h \alpha_4^h & (1 - \eta^h)\alpha_5^h \end{pmatrix}$$

The matrix C , for its part, has the form

$$C = \begin{pmatrix} c_{11} & 0 & 0 \\ 0 & \alpha_1^h & \theta^h \alpha_8^h \\ 0 & 0 & (1 - \theta^h)\alpha_7^h \end{pmatrix},$$

Where

$$c_{11} = \beta^a \alpha_b^a (S_0^a) + b^a S_0^a \alpha_b^{a'} (S_0^a) + \alpha_1^a$$

After all assumptions of non-negativity and others as described in Simple discrete-time malarial models [15], we find the estimation of the reproduction rate as :

$$R_0 := \sqrt{\frac{G'(0)r\beta^h \gamma^h \alpha_2^h \alpha_4^h}{(1 - (1 - \gamma^h)\alpha_3^h)(1 - (1 - \eta^h)\alpha_5^h)} \frac{r\beta^a \gamma^a \alpha_2^a \alpha_4^a}{(1 - (1 - \gamma^a)\alpha_3^a)(1 - \alpha_5^a)} \frac{S_0^a}{S_0^h}}$$

Note from the above that the average duration of infection in humans is:

$$\bar{\tau}^h = \frac{\gamma^h \alpha_2^h \alpha_4^h}{(1 - (1 - \gamma^h)\alpha_3^h)(1 - (1 - \eta^h)\alpha_5^h)},$$

The average number of bites per human from all mosquitoes is:

$$\bar{r}^h = G'(0)r \frac{S_0^v}{S_0^h}.$$

We write the average probability of transmission: $\bar{\beta}^h = \beta^h$

Then, the reproduction number of infections in humans can be expressed as :

$$R_0^h = \bar{r}^h \bar{\beta}^h \bar{\tau}^h.$$

Similarly, we define the average duration of infection in mosquitoes as

$$\bar{\tau}^a = \frac{\gamma^a \alpha_2^a \alpha_4^a}{(1 - (1 - \gamma^a) \alpha_3^a)(1 - \alpha_5^a)}.$$

and write $\bar{r}^a = r$ and $\bar{\beta}^a = \beta^a$.

Then, the reproduction number of infections in mosquitoes can be expressed as:

$$R_0^a := \bar{r}^a \bar{\tau}^a \bar{\beta}^a.$$

Hence, we can rewrite the reproduction number of the infection as: $R_0 = \sqrt{R_0^h R_0^a}$.

2.6. Study parameters

Table I. Definition and description of the epidemiological and entomological parameters used in the mathematical model of malaria transmission among children under five years of age in the Democratic Republic of the Congo.

#	Population	Symbol	Description
1	Human	λ^h	Infection rate of susceptible humans.
2	Human	γ^h	Incubation rate of exposed humans before becoming infectious. N. B: Malaria symptoms generally appear between 10 and 15 days after the bite of an infected mosquito. However, this delay may vary depending on the type of Plasmodium parasite and the health status of the infected person. In some cases, symptoms may appear earlier or later, ranging from 8 to 30 days [16]. The probability that a person bitten by an infected anopheline mosquito develops malaria is very high. In general, it is estimated that more than 90% of people bitten by an infected mosquito will contract the disease [17,18,19].
3	Human	η^h	Recovery (cure) rate of infectious humans.
4	Human	θ^h	Rate of immunity loss by recovered humans. N. B: The frequency of malaria episodes in children under 5 years in sub-Saharan Africa may vary depending on several factors, including the specific region, environmental conditions, and prevention measures in place. In general, in highly endemic areas, a child may contract malaria several times per year. According to some studies, children may have between 2 to 5 malaria episodes per year in the most affected regions [20,21].
5	Human	α_1^h	Survival rate of susceptibles N.B: In the DRC, the mortality rate of children under 5 years is alarming. In 2022, it was estimated at approximately 76 deaths per 1,000 live births. This high rate is mainly due to factors such as malnutrition, infectious diseases, and limited access to healthcare [22].

6	Human	α_2^h	Survival rate of susceptibles who became exposed Since exposure to the disease following a bite from an infected anopheline is immediate, we will consider this survival rate as equivalent to the previous one, i.e α_1^h .
7	Human	α_3^h	Survival rate of exposed
8	Human	α_4^h	Survival rate of exposed who became infectious
9	Human	α_5^h	Survival rate of infectious
10	Human	α_6^h	Survival rate of infectious who recovered
11	Human	α_7^h	Survival rate of recovered
12	Human	α_8^h	Survival rate of recovered who became susceptible again
13	Human	Λ	Population constante at time 0
14	Mosquito	b^a	Mosquito birth rate Anopheline mosquitoes, vectors of malaria, go through several developmental stages: egg, larva, nymph and adult. The female anopheline generally lays between 50 and 200 eggs on the water surface after a blood meal. The development time from eggs to adult emergence may vary depending on environmental conditions, particularly temperature and water availability, and generally takes between 10 and 14 days [23]. In general, most eggs laid by anopheline mosquito's hatch, but the exact rate may vary depending on environmental conditions and predators. On average, approximately 80% to 90% of eggs laid by anopheline mosquito's hatch and transform into larvae [24].
15	Mosquito	γ^a	Probability that an incubating mosquito becomes infectious. The probability that a female Anopheles mosquito becomes infected after biting a person carrying the Plasmodium

			parasite depends on several factors, including parasite density in the human host, the specific Plasmodium species, and environmental conditions. Although studies indicate that this probability may vary, it is generally accepted to be between 10% and 30% under natural conditions [25].
16	Mosquito	λ^a	Mosquito infection rate. The probability that a mosquito bites a person infected with malaria and is not contaminated is relatively low. When a female anopheline mosquito bites an infected person, there is a high likelihood that it will ingest Plasmodium parasites present in the blood. These parasites then develop in the mosquito, making it capable of transmitting malaria to other people during subsequent bites [26].
17	Mosquito	β^a	Birth rate of new mosquitoes
18	Mosquito	α_b^a	Survival rate of new mosquitoes. The lifespan of a female anopheline generally ranges from 2 weeks to 1 month, depending on environmental conditions [26].
19	Mosquito	α_1^a	Survival rate of susceptible adults
20	Mosquito	α_2^a	Survival rate of exposed adults
21	Mosquito	α_3^a	Survival rate of infectious disease from time 0 to time 1
22	Mosquito	α_4^a	Survival rate of infectious diseases from time 1 to time 2
23	Mosquito	α_5^a	Survival rate of infectious from time 2 to time 3

The table summarizes the biological and epidemiological parameters included in the SEIR–SEI mathematical model, together with their definitions and supporting assumptions derived from published literature. Human parameters describe infection, recovery, immunity, and survival processes, whereas mosquito parameters describe mosquito demography, infection, and survival dynamics.

2.7. Statistical parameters

Table II. Statistical parameter values and assumptions used to parameterize the mathematical model of malaria transmission among children under five years of age in the Democratic Republic of the Congo.

#	Parameter	Symbol	Value
1	Survival rate of susceptibles	α_1^h	The mortality rate of children under 5 years in the DRC is estimated at 76 per 1,000, or approximately 8 children per 100. The survival rate, the complement of the mortality rate, is therefore calculated as: $\alpha_1^h = 1 - (76/1000) = 92,4$
2	Survival rate	$\alpha^h = \alpha_1^h = \dots = \alpha_8^h$	The natural survival rate being not significantly different among susceptibles, exposed, infectious, and recovered, in the context of our study, this rate will be considered as a constant equivalent to the survival rate of susceptibles.
3	Incubation rate of exposed humans before becoming infectious.	γ^h	We assumed that the probability of developing malaria after a bite from an infected anopheline mosquito (γ^h) ranges from 91% to 97%, reflecting an incubation period of 10 to 30 days.

4	Rate of immunity loss by recovered humans.	θ^h	Considering ω^h as the frequency of malaria episodes with a mean value of 3, $\theta^h = \frac{\omega^h}{1 + \omega^h} = \frac{3}{1 + 3} = 75\%$
5	Mosquito birth rate	b^a	In the DRC, given the environmental conditions highly favorable to anopheline egg hatching, we estimate this rate at approximately 90%. $b^a = 0.9 = 90\%$
6	Probability that an incubating mosquito becomes infectious.	γ^a	The transition rate from an exposed to infectious anopheline is high. In this work, we will use a rate as used by Jia Li [26]. $\gamma^a = 0.8 = 80\%$
7	Average number of bites by a mosquito during its lifetime on the human population.	r	On average, an anopheline mosquito can bite between 10 and 50 people during its lifetime, depending on access to human hosts and competition with other mosquitoes. Per night, a female may bite 1 to 3 times, although she may avoid biting the same individual multiple times, depending on the availability of other hosts [26]. In this study, we used a value of 30 bites per mosquito.
8	Mosquito survival rate	$\alpha_1^a = \alpha_2^a = \dots = \alpha_5^a = 0.8 = 80\%$	Generally, the daily survival rate of Anopheles mosquitoes ranges from 0.8 to 0.95 (80 to 95%). This means that a mosquito has an 80 to 95% chance of surviving from one day to the next under normal conditions.

This table summarizes the statistical values assigned to the epidemiological and entomological parameters used in the SEIR–SEI model. The selected values are based on published literature and biological assumptions, and were used to parameterize the model simulations and estimate the basic reproduction number (R_0).

2.8. Variable selected in the model

Table III. Dependent variable

#	Variables	Symbol	Formula
1	Infection rate in humans (incubation rate) or incidence rate	λ^h	This rate will be expressed as the number of malaria cases.

2.9. Data collection

We used two techniques to collect data. The first involved downloading routine data from the DHIS2 database, and the second consisted of a documentary review of annual NMCP reports, epidemiological and entomological surveys, and various scientific publications addressing the topic under study.

2.10. Data processing and analysis

2.10.1. Quality control

We performed quality control before data analysis to assess the consistency of time, data, extreme values, and missing data. To highlight extreme values and missing data by variable and by year from 2017 to 2023, we generated scatter plots with values on the y-axis and years in different colors. For this purpose, simple imputation was applied by replacing atypical or missing values with the median of the series, given its robustness considering the disparity of distributions (symmetric and asymmetric).

To detect potential inconsistencies in the data, nested data elements were used. In this context, we cross-referenced the cascade of confirmed malaria cases and tested cases using the greater-than-or-equal-to ($\geq$) relationship. An audit was conducted by telephone calls to the NMCP coordinators of the concerned provinces, who in turn corrected the data in DHIS2. Data downloaded from DHIS2 in Excel 2019 were organized. Analysis was performed using SPSS 25, R 4.2.2, Microsoft Office Excel 2019, QGIS, and Python. Crude incidence was obtained by dividing the number of malaria cases in HZ by the population of that zone considered at risk. This crude incidence was subsequently adjusted at three levels, taking into account presumed cases, reporting, testing, and care-seeking.

3. RESULTS

3.1. Dynamics of malaria morbidity and efficacy of innovative interventions on predicted morbidity

Table IV. Baseline values of epidemiological and entomological parameters used in the mathematical model for simulating malaria transmission among children under five years of age in the Democratic Republic of the Congo.

Parameter	Value	Parameter	Value
λ^h	0,94	r	30
γ^h	0,9	b^a	0,9
η^h	0,99	λ^a	0,9
θ^h	0,75	γ^a	0,8
α_1^h	0,9	β^a	0,3
α_2^h	0,7	δ^a	0,9
α_3^h	0,6	α_1^a	0,5
α_4^h	0,8	α_2^a	0,5
α_5^h	0,8	α_3^a	0,5
α_6^h	0,8	α_4^a	0,5
α_7^h	0,8	α_5^a	0,5
α_8^h	0,8	S^a / S^h	40
β^h	0,03		

Abbreviations: λ^h = human infection rate; γ^h = human recovery rate; η^h = human survival probability; θ^h = immunity loss rate; λ^a = mosquito infection rate; γ^a = probability that an exposed mosquito becomes infectious; b^a = mosquito birth rate; S^a/S^h = mosquito-to-human population ratio. Parameter values were derived from the literature and the assumptions described in Tables I and II.

These values were drawn from various publications that addressed the question of malaria transmission between humans and anopheline mosquitoes and are reported in Tables 1 and 2.

3.1.1. Current simulation without intervention

4. Figure 3. Trends in malaria morbidity among children under five in the DRC, 2017–2050

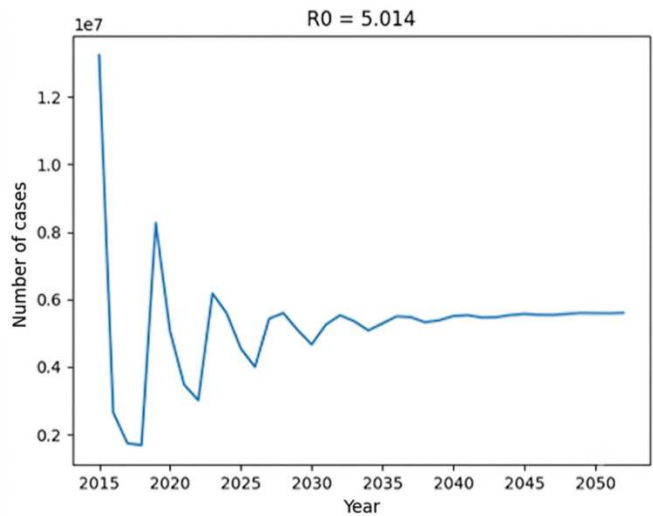


Figure 3. Trends in malaria morbidity among children under five in the DRC, 2017–2050

Figure 3 presents the predicted trend in malaria morbidity among children under five years of age in the DRC under the baseline scenario, assuming that no additional malaria control interventions are implemented beyond current conditions. The simulation, based on data from 2017 to 2023, projects malaria cases up to 2050. As shown in Figure 3, malaria cases progressively increase before reaching an endemic plateau around 2040, with an estimated basic reproduction number (R_0) of 5.014. These projections were obtained using the baseline parameter values presented in Table IV. Only the predicted dynamics in the human population (children under five years of age) are displayed.

4.1.1. Application of innovative interventions (current situation)

Table V. Changes in the basic reproduction number (R_0) under current coverage levels of malaria control interventions in children under five years of age.

Intervention	Efficacy	Coverage	Parameter	Current value	Value after intervention	New R_0
R21 Vaccine	75%	21%	λ^h	94%	94% - 16% = 78%	4.55
			λ^a	90%	90% - 16% = 74%	4.55
IPTi	30,3% (PMC) and 88,3% (SMC : SPAQ)	21% (PMC) and 80% (SMC)	λ^h	94%	94% - 12% = 82%	4.66
			λ^a	90%	90% - 12% = 78%	4.66
ITN	50%	69%	α_1^a	80%	80% - 35% = 45%	3.71
Mix-intervention			λ^h	94%	94% - 16% - 12% = 66%	
			λ^a	90%	90% - 16% - 12% = 62%	3.08
			α_1^a	80%	80% - 35% = 45%	

This table shows the efficacy and coverage values of each innovative intervention, applied to the current values of the statistical parameters in humans and mosquitoes. We note that, which is the infection rate of susceptible humans, is estimated at 94% (probability that a susceptible human becomes exposed >90%). From this rate, the products of efficacy and coverage of the vaccine (16%) and IPTi (12%) were respectively subtracted and applied to the R_0 formula in Python, yielding a value of 4.55 for the vaccine and 4.66 for IPTi (PMC and SMC). The same approach was applied to the probability that a susceptible mosquito becomes exposed, which is 90%.

The ITN, with an efficacy of 50% combined with a coverage of 69%, gives a real efficacy of 35%, which was subtracted from the survival rate of susceptible adult Anopheles, =80%, thereby reducing R_0 to 3.71. Finally, a combination of the real efficacy of different innovative interventions (mix intervention) was subtracted from the infection rate of susceptible mosquitoes (λ^a), reducing R_0 to 3.08. It should be noted that the different coverage values were drawn from the Demographic and Health Survey DHS-DRC III 2023-24 [7].

4.1.2. Effective predictive model for reducing incidence in children under 5 years (80% coverage)

Table VI. Variation of R0 under optimal conditions

Intervention	Efficacy	Coverage	Parameter	Current value	Value after intervention	New R0
Vaccination	75%	80%	λ^h	94%	94% - 60% = 34%	2.90
			λ^a	90%	90% - 60% = 30%	2.90
IPTi	30,3% (PMC) and 88,3% (SMC)	80% (PMC) and 80% (SMC)	λ^h	94%	94% - 28% = 66%	4.16
			λ^a	90%	90% - 28% = 62%	4.16
ITN	50%	80%	α_1^a	80%	80% - 40% = 40%	3.22
Mix-intervention			λ^h	94%	94% - 60% - 28% = 6%	
			λ^a	90%	90% - 60% - 28% = 2%	0.48
			α_1^a	80%	80% - 40% = 40%	

This table shows the same situation as the previous one (Table 5), but under the target coverage level of 80% for all interventions. Under this scenario, the mix intervention strategy reduces the basic reproduction number to **$R_0 = 0.48$** (which is **<1**), indicating that malaria transmission could theoretically be interrupted. Figure 4 illustrates the relationship between the human infection rate and the basic reproduction number (R_0), highlighting the threshold below which transmission is no longer sustained.

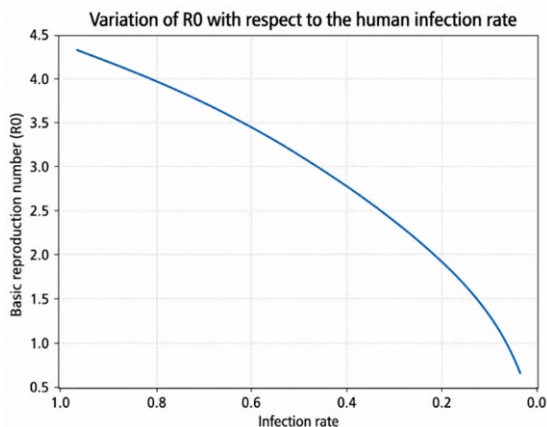


Figure 4: Variation in the basic reproduction number R_0 as a function of the human infection rate

This graph shows the variation of R_0 when the human infection rate varies from 1 to 99%. We observe that the increase in the human infection rate is directly proportional to the increase in R_0 , and that if one were to consider the individual modification of the infection rate, this rate would need to be maintained below 10% to hope to definitively extinguish the disease soon.

5. DISCUSSION

This discussion puts into perspective the results obtained in this study on the dynamics of malaria transmission among children under five in the DRC, by comparing them with similar work conducted in other contexts. The objective was to model the impact of high-impact innovative interventions from the NSP NMCP 2024-2028 on malaria morbidity among children under 5 years in the DRC.

5.1. Impact of innovative interventions

Innovative interventions such as the R21/Matrix-M vaccine, SMC, and PMC present considerable potential to reduce the incidence and mortality due to malaria. The data show still limited implementation, with restricted targeted areas. This contrasts with the successes reported in other countries such as Ghana and Burkina Faso, where the R21 vaccine demonstrated a 77% reduction in clinical malaria cases [26].

Rapid and strategic expansion of interventions is necessary to maximize their impact. Furthermore, the integration of next-generation ITN could play a key role in high-transmission regions, as shown by the study of Protopopoff and al. (2018) [19].

5.2. Predictive modeling

The predictive model developed in this study represents an important advance for estimating the impact of future interventions. The forecasts show a significant reduction in incidence in the event of intervention intensification, confirming the results of similar studies in Tanzania and Kenya by Bhatt and al. in 2015 [20]. However, the precision of the model remains dependent on the quality of input data, underscoring the importance of strengthened surveillance systems.

The results obtained with current parameters confirm the importance of innovative interventions in the fight against malaria in the DRC. The results show a significant evolution of the basic reproduction number (R_0) according to different combinations of interventions.

5.2.1. Reduction of the infection rate in susceptible humans (λ^h):

From a high initial infection rate ($\lambda^h=94\%$), interventions such as the vaccine (16% efficacy) and IPTi (12% efficacy) respectively reduced R_0 to 4.55 and 4.66. These results corroborate those of Duffy and al. (2020), who showed that the introduction of the RTS,S/AS01E vaccine in high-transmission areas can significantly reduce the incidence of clinical malaria in children under 5 years [36]. Similarly, the work of Aponte and al. (2009) demonstrated the efficacy of IPTi in areas with moderate to high transmission [21].

5.2.2. Impact on the mosquito population

ITNs, with a real combined efficacy of 35%, reduced R_0 to 3.71 by lowering the survival rate of adult mosquitoes (α_1^a). The studies by Bhatt and al. (2015) have already emphasized that ITNs contribute to a significant reduction in malaria mortality, particularly when they achieve high coverage (>80%) [20].

5.3. Combination of interventions

A mix intervention (vaccine, IPTi, and ITNs) brought R_0 to 3.08 under current coverage conditions. This confirms the conclusions of the NMCP [1], according to which integrated strategies allow synergistic reductions in transmission, exceeding the individual impact of each intervention. Under optimal intervention coverage conditions (80%, expected target), this combination reduces R_0 to 0.48, a value below 1. This reduction is crucial, as it means that transmission is theoretically interrupted (i.e., two infected individuals infect one other person on average).

5.3.1. Comparison with other studies

The results obtained in this study are consistent with data published in other contexts. Regarding the RTS, S/AS01 vaccine: A study by Olotu and al. conducted in East Africa showed that widespread vaccine use can reduce malaria incidence by 40% over three years, although its efficacy strongly depends on vaccination coverage and duration of protection [23]. Regarding ITNs: Meta-analyses conducted by Lengeler (2004) demonstrated that ITNs can reduce infant mortality by 20%. However, real efficacy depends on effective use, which remains a limitation in many contexts [24].

5.3.2. Intermittent preventive treatments

The systematic review by Meremikwu and al. (2008) emphasized that IPTi, although effective in infants and pregnant women, requires broader adoption to achieve a significant impact on disease dynamics [25].

Strengths of the study

These results were particularly relevant for the NSP of the NMCP-DRC 2024-2028, which aims to reduce malaria-related morbidity and mortality. Achieving 80% coverage for all innovative interventions would not only reduce disease spread but also approach elimination goals in certain areas. The efficacy of combined interventions confirms the conclusions of Winskill and al. (2017), who demonstrated that the integration of ITNs, vaccines, and preventive treatments can maximize impact, particularly in high-transmission areas.

Limitations of the study

Although robust, this model has several limitations:

- Exclusion of the adult population, which acts as a transmission reservoir.
- Non-integration of genotypic resistance of the parasite and physiological resistance of the vector to pyrethroids.
- Use of national average parameters that obscure epidemiological disparities between high- and low-transmission health zones.

Perspectives and implications

Under current conditions, R_0 remains above 1, meaning that malaria transmission persists. However, 80% coverage for all interventions reduces R_0 to 0.48. These results underscore the need to intensify efforts to achieve the coverage targets recommended by the WHO (World Health Organization, 2022).

CONCLUSION

The eradication of malaria among children under five in the DRC is not a biological impossibility, but rather a challenge of vaccination and prophylactic coverage. Mathematical evidence establishes that the transmission breakpoint ($R_0 < 1$) is only achievable through massive and simultaneous scale-up of all innovative interventions.

Declarations

- a. Abbreviations:** DRC: Democratic Republic of the Congo; NMCP: National Malaria Control Program; MV: Malaria Vaccine; SMC: Seasonal Malaria Chemoprevention; IPTi: Intermittent Preventive Treatment in infants; PMC: Perennial Malaria Chemoprevention; ITN: Insecticide-Treated Net; DHIS2: District Health Information System 2.
- b. Ethical approval and consent to participate:** The study protocol was reviewed and approved by the Ethics Committee of the Kinshasa School of Public Health (KSPH), University of Kinshasa, DRC (Approval No. ESP/CE/248/2024). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and all applicable national regulations governing research involving human participants and human data. This study used secondary, anonymized routine malaria surveillance data extracted from DHIS2 of the DRC. Because no participants were directly recruited or contacted and no identifiable personal information was collected, the requirement for informed consent to participate, including parental or legal guardian consent for minors, was waived by the Ethics Committee of the KSPH, University of Kinshasa.
- c. Consent for publication:** Not applicable.
- d. Availability of data and materials:** The datasets analyzed during the current study were extracted from DHIS2 of the DRC. Access to the DHIS2 database was granted by the National Health Information System Division (Division du Système National d'Information Sanitaire, DSNIS) through an authorized user account ("Packy_Mbayo"). The datasets are not publicly available because they are owned by the Ministry of Public Health, Hygiene and Social Security of the DRC. They are available from the corresponding author upon reasonable request and with permission from DSNIS.
- e. Authors' contributions:** Packy Mukanya Mbayo conceived the study, developed the mathematical model, performed the statistical analyses, interpreted the results, and drafted the manuscript. André Ngombe Kaseba enriched the discussion by providing scientific interpretation and critical review of the findings. Jonathan Mubenga Mubenga adapted the mathematical model and performed the Python-based computational analyses. Kennedy Lobukulu contributed to improving the structure and scientific presentation of the manuscript. Wilfried Nlandu Tembele critically reviewed the manuscript and contributed to improving its scientific quality. Michel Kabamba Nzanji contributed to the revision and improvement of the manuscript structure. Joris Losimba

Likwela provided the documentation and literature synthesis on innovative malaria control interventions used in the study. Éric Mukomena Sompwe designed the study and contributed to the methodological framework. Thérèse Mambu Nyangi supervised all stages of the research, from study conception to the approval of the final manuscript. All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for all aspects of the work. All other authors reviewed and approved the final manuscript.

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- h. Clinical trial number:** not applicable.
- i. Clinical trial number:** not applicable
- j. Funding disclosure:** No funding.

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