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Projected impact of integrated malaria intervention packages on under-five *Plasmodium falciparum* prevalence and clinical incidence in Ghana's Guinea Savannah zone, 2023–2028: a modelling study.

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Abstract

Background: Malaria remains endemic in Ghana's northern Savannah zone, which experiences highly seasonal transmission and disproportionate child burden. Within Ghana's High-Burden-to-High-Impact framework, optimizing intervention mixes at the subnational level is critical for informing evidence-based, tailored intervention packages under resource constraints. This study simulated and compared the projected impacts of different scenarios of key malaria preventive and

control tools on under-five *Plasmodium falciparum* Prevalence Rate and clinical incidence between 2023 and 2028.

Methods: We parameterised the Epidemiological MODeling software (EMOD v2.20) agent-based model of Plasmodium falciparum transmission and calibrated it to under-five parasite prevalence from the Ghana Demographic and Health Surveys and Multiple Indicator Cluster Surveys (2011–2022) using a beta-binomial likelihood. We projected under-five outcomes for 2023–2028 under business-as-usual (BAU) and 11 alternative scenarios that scaled insecticide-treated nets (ITN), indoor residual spraying (IRS), seasonal malaria chemoprevention (SMC), the RTS,S/AS01E vaccine and case management (CM), singly and in combination, in line with the National Malaria Elimination Programme strategy. Outcomes were annualised clinical incidence, annual-mean PfPR and survey-comparable PfPR (September–December mean, matching DHS/MIS fieldwork). Reductions relative to BAU were estimated by paired bootstrap across nine stochastic replicates, and the contribution of each tool by Shapley decomposition.

Results: Under BAU, under-five clinical incidence did not decline (1,284 episodes per 1,000 child-years in 2023; 1,372 in 2028) and annual-mean PfPR was 15.8% in 2028. Scenarios including scaled IRS produced the largest gains: in 2028, incidence was 49% (95% CI 39–59) lower than BAU with the full package (Scenario 14), 48% (38–58) with ITN + CM + IRS + SMC (Scenario 11) and 45% (36–53) with ITN + CM + IRS (Scenario 8), averting 3,810, 4,037 and 3,874 clinical episodes per 1,000 children over 2023–2028, respectively. Scaling ITN, SMC or RTS,S alone reduced incidence by 2–5%. IRS scale-up accounted for 84% and ITN scale-up for 17% of the full package's benefit, with synergy between the two ($p = 0.02$). All scenarios with SMC at 95% reduced survey-comparable PfPR by 82–90%, but their incidence reductions ranged from 4% to 49% because the survey window overlaps the SMC campaign. No scenario reached the national target of halving incidence by 2028 (best 45%, 95% CI 36–55, relative to 2023).

Conclusion: Maintaining current coverage will not reduce under-five malaria in Ghana's Guinea Savannah zone. Packages that intensify vector control IRS together with high ITN use and improved case management, alongside SMC and malaria vaccination as recommended by the NMEP and WHO could roughly halve clinical incidence, but even the full package may fall short of the 2028 national target in high-transmission years. Sustained multi-year investment, district-level tailoring and evaluation based on incidence, not survey-season prevalence alone, are needed.

Keywords: Agent-based Modelling; EMOD; *Plasmodium falciparum*; Ghana; Malaria interventions, Under-five Malaria Prevalence.

Background

Malaria continues to pose a significant threat to child health in Ghana. According to the World Health Organization (WHO), the country recorded approximately 6.7 million malaria cases and 11,635 deaths in 2024, per the WHO World Malaria Report 2025 (1), with the disease remaining one of the leading causes of outpatient visits and childhood mortality (2). Historically, malaria has

accounted for up to 40% of all outpatient consultations nationwide, disproportionately affecting children under five years of age, who bear the highest malaria burden across sub-Saharan Africa (3,4). Despite a decline in parasite prevalence, from around 27% among children aged 6–59 months in 2014 to approximately 14% in 2019 (5,6), Malaria remains endemic in every region of Ghana with transmission and burden varying widely across the country (2). The transmission intensity and burden, however, vary widely across the country's ecological zones, requiring tailored strategies for effective malaria control (7). Ghana's geography comprises of three primary ecological zones, the northern Guinea savannah, the central transitional forest-wooded savannah and the southern coastal savannah belt (3). Each zone has distinct rainfall patterns and malaria transmission dynamics (8).

Reflecting the zone's single rainy season, the Guinea savannah experiences a sharp annual peak in malaria cases (3). In contrast, the transitional forest-wooded savannah and coastal savannah zones experience bimodal rainfall patterns each year, with two peaks, the first from April to August and the second from September to November, producing two smaller malaria peaks (3,9). Routine case data indicated an average monthly malaria incidence in the Guinea savannah going up to approximately 915 cases per 100,000 persons during the peak season (3). This ecological heterogeneity translates into uneven malaria burden. A 2016 Multiple Indicator Cluster Surveys (MICS) survey in 2016 found an overall parasite prevalence of 20.6% among children under five years of age, with the highest rates observed in the transitional forest-wooded savannah zone (middle belt of Ghana) compared to the northern and southern zones (3,10). More recently, the 2022 Ghana Demographic and Health Survey (GDHS) recorded a national under-five parasite prevalence of 8.6% by microscopy, down from around 27% in 2014, though burden remains disproportionately concentrated in the northern zones at 15 % in 2022 GDHS. Recent geospatial analyses have further identified persistent "hotspots" in northern and central Ghana, where certain districts report disproportionately high malaria incidence while others report considerably lower levels (11). These spatial differences support the shift from uniform strategies to targeted control approaches (12). In line with this, Ghana's National Malaria Strategic Plan has adopted a stratified framework that emphasizes zone- and region-specific planning (13).

Intervention coverage across the country also varies: Insecticide-treated nets (ITNs) are widely distributed, but actual usage remains suboptimal (14). The 2019 MICS reported that about 74% of households owned at least one ITN and 67% of the population had access to one, yet only 54% of children under five years of age had slept under an ITN the previous night (6). Regional disparities are particularly stark. While ITN ownership was as high as 88% in the Upper East Region, just 56% owned ITNs in the Greater Accra Region (6). Indoor residual spraying (IRS) coverage remains limited, only about 6% of households reported IRS in the year 2018, mostly in selected high-transmission rural districts (6). Combining ITN and IRS, approximately 75% of households benefit from at least one preventive intervention (6). For treatment, about 69% of febrile children under five years of age were taken for health facility care, but about half (34%) of these were tested for malaria as per national diagnostic guidelines prior to treatment(15). Of those treated, nearly

85% received WHO-recommended artemisinin-based combination therapies (ACTs), indicating relatively good adherence to drug malaria treatment policy but highlighting gaps in diagnostic coverage and prompt treatment (15).

In response to the highly seasonal transmission in the northern regions, Ghana introduced Seasonal Malaria Chemoprevention (SMC) in 2019, targeting children under five years old (16). This intervention involves administering monthly antimalarial drugs (typically sulfadoxine-pyrimethamine and amodiaquine) during the peak transmission season to prevent malaria episodes (17). Seasonal Malaria Chemoprevention implementation began in selected districts of the Guinea Savannah and Upper West Regions, but this has since expanded (18). A significant development in Ghana's malaria control is the introduction of the RTS,S/AS01$_E$ malaria vaccine. Following pilot deployments between 2019 and 2021 in high-transmission districts in Northern Region, over one million doses have been administered (19). After WHO recommended the vaccine for routine use in 2021, Ghana became one of the first countries to have incorporated it into its Expanded Programme on Immunization (EPI) (20). The vaccine is now being rolled out in moderate-to-high-transmission areas as part of an integrated strategy to reduce childhood malaria burden. This is used as an additional tool in support of routine ones such as ITNs, IRS and effective case management (CM) (16).

Given the scale of the malaria burden, coupled with constrained financial resources, optimizing the combined tools and targeting of interventions is critical. Mathematical transmission models provide an evidence-based approach for such optimization (12). The Epidemiological MODeling (EMOD) software developed by the Institute for Disease Modelling (IDM) simulate malaria dynamics under various intervention scenarios and have proven useful in strategic decision-making (12,21,22). Modelling enables public health planners to compare different intervention mixes under local ecological and epidemiological conditions (12). In Ghana, the impacts of individual malaria interventions are widely documented through clinical trials; however, the impact of combined intervention packages cannot be estimated through randomized controlled trials alone. Mathematical models can help estimate this combined impact to inform decision-making, yet their application to project malaria intervention impacts in Ghana remains limited. Only a few exist, for instance, the effectiveness of malaria interventions at the regional level in Ghana using a mathematical modelling application has been assessed (23). Yet, none has specifically focused on the Guinea Savannah zone, where malaria transmission remains highly seasonal and persistent despite several routine ongoing interventions.

This study contributes to filling that gap by applying the EMOD modelling framework to simulate and compare the projected impacts of key malaria control strategies between 2023 and 2028 in the Guinea Savannah zone. By focusing on this ecological belt, the study offers context-specific evidence that informs not only national malaria control efforts but also subnational planning and prioritization, especially under Ghana's High Burden to High Impact (HBHI) agenda (24). With that in mind, this study aimed to determine the individual and combined effects of ITNs, IRS, SMC and RTS,S/AS01$_E$ on malaria prevalence among children under five years of age in Ghana's

Guinea Savannah zone. The findings provide practical guidance for the National Malaria Elimination Programme (NMEP) strategic planning as part of Ghana Health Service (GHS) and its regional health directorates in targeting limited resources efficiently. Moreover, this analysis enriches the global literature on agent-based modelling in malaria control and reinforces the relevance of zone-specific analysis in driving high-impact interventions.

Methods and Materials

Study Setting

Data used for this study was sourced from the Guinea Savannah zone of Ghana, covering the northern part of the country. The zone lies approximately between latitudes 8°N and 11°N and longitudes 0°W and 1.5°W (25). The zone includes administrative regions such as the Northern, NorthEast, Upper East, Upper West and Savannah Regions of Ghana (Figure 1). The zone borders with Burkina Faso to the north and the transitional forest-wooded savannah zone to the south. The zone falls within the Guinea savannah ecological belt. It has a single rainy season that lasts from May to October each year, followed by a long dry season dominated by harmattan winds from November to March (26). Average temperatures range from 25°C to 35°C, with the hottest months occurring between March and April of every year. Annual rainfall typically ranges between 900 mm and 1,100 mm, with the peak rainfall occurring usually in August (27). Relative humidity is generally lower than in the forest-wooded savannah and coastal zones, averaging 60–70% during the wet season and dropping to around 40–50% in the dry season (22).

The zone is mostly rural, with limited access to health infrastructure in some districts. Malaria transmission in the Guinea Savannah zone is highly seasonal, peaking during the rainy season due to increased mosquito breeding (28). The dominant malaria parasite in the zone is Plasmodium falciparum, transmitted by three primary Anopheles vector species (*An. gambiae s.s., An. arabiensis* and *An. funestus*). In a six-year entomological survey in northern Ghana, *Anopheles gambiae* sensu lato accounted for 95.3% of adult female Anopheles collected and *Anopheles funestus* for 1.7%, with abundance varying by month and peaking around the rainy season (28). Consistent with the epidemiology of the zone, the EMOD model represented *An. gambiae s.s., An. arabiensis* and An. *funestus* as the principal vector taxa (24). The rainfall pattern, temperature and vegetation significantly influence mosquito density and the risk of malaria, making this zone a key focus for seasonal intervention strategies such as SMC and targeted distribution of IRS and ITNs.

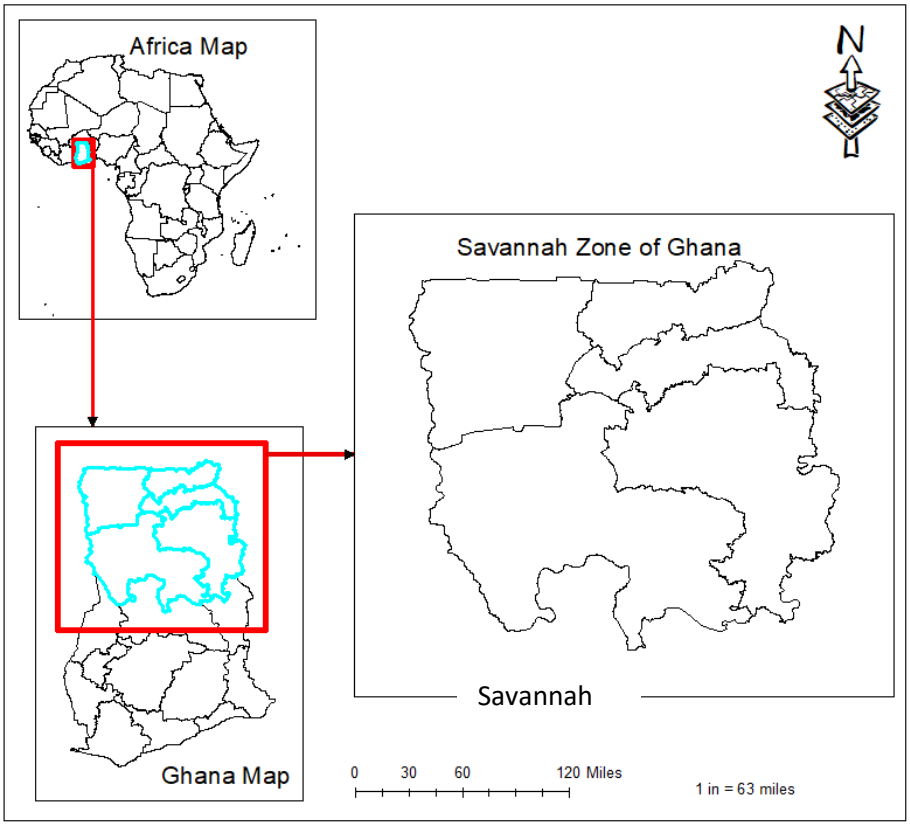
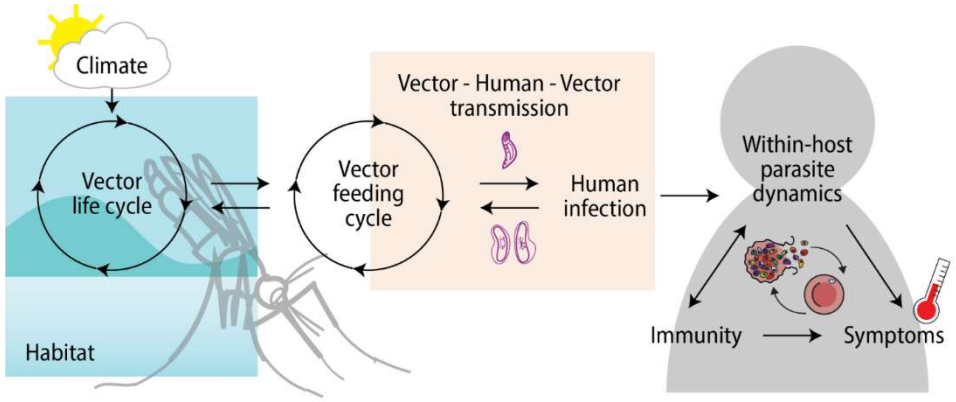


Figure 1: Savannah zone of Ghana, Source: Authors own construct, 2024

The EMOD malaria transmission model

The malaria model is complex, with numerous configurable parameters. Figure 2 illustrates the structural components of the EMOD malaria model used in this study. The model simulates climate-driven vector life cycles, vector feeding behaviour and bidirectional human–vector transmission processes. It incorporates within-host parasite dynamics, host immunity acquisition and symptom development, which together determine infection prevalence and clinical incidence. In this analysis, the EMOD framework was parameterised using epidemiological and intervention coverage data relevant to the Savannah zone of Ghana and used to project the impact of national malaria control interventions from 2023 to 2028. Interventions were modelled by modifying transmission parameters, vector survival, biting rates and treatment access within the simulated

population. This structure allows estimation of changes in infection prevalence, clinical cases and transmission intensity under alternative intervention scale-up scenarios.



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Figure 2: Schematic of malaria transmission and disease components in EMOD

Source: (IDM documentation, 2022)

Also, Figure 3 presents the technical architecture of EMOD and the associated toolkits used to configure, execute and analyse simulations. Human-readable inputs, including demographic, climate and intervention campaign files, are converted into EMOD-readable configuration files using emodpy and idmtools. Simulations are executed on high-performance computing infrastructure, allowing multiple stochastic runs and scenario comparisons.

Model outputs include time-series indicators, age-stratified infection metrics and disease-related events, which are processed using the EMOD Analyzer toolkit to generate CSV files, summary tables and plots.

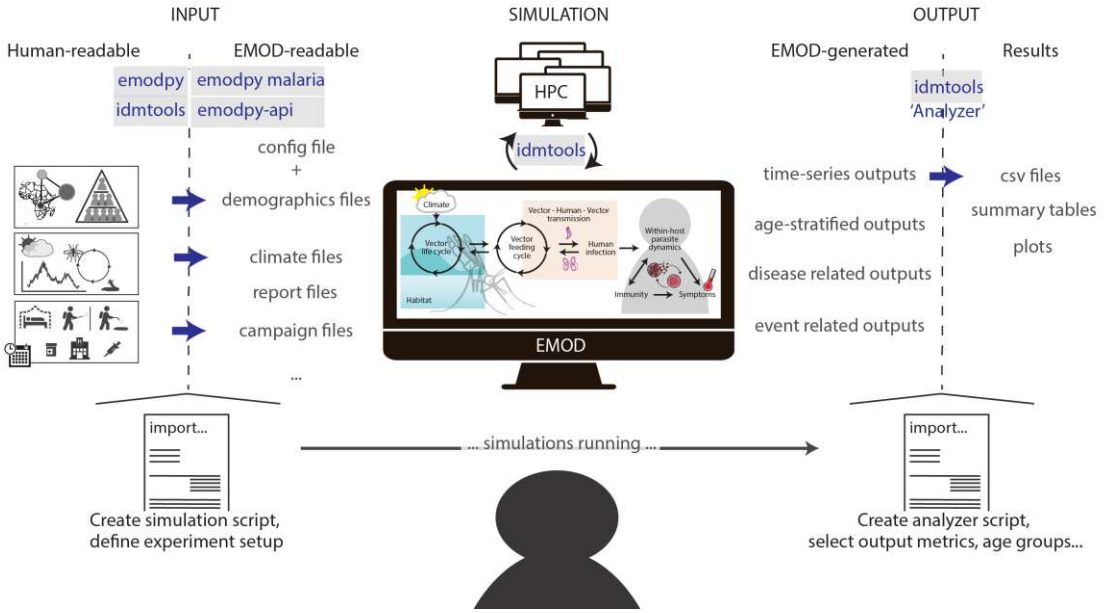


Figure 3: EMOD - technical overview and toolkits

Source: (IDM, 2022)

In this study, malaria transmission and the effects of interventions were simulated using EMOD version 2.20, an agent-based model specifically designed for *Plasmodium falciparum*. The model includes a temperature-sensitive mosquito life cycle, mosquito population dynamics, human infection and immunity processes and the effects of different malaria control tools. The patterns of parasite growth, immune response and malaria illness by age were previously adjusted to match real-world data from nine locations across sub-Saharan Africa. Daily air temperatures for the Guinea Savannah zone were estimated using the zone's geographic coordinates and weather data from the Global Surface Summary of the Day. Three mosquito species common in the area, *Anopheles gambiae* s.s, *Anopheles arabiensis* and *Anopheles funestus*, were modelled separately, each with specific behaviours related to human biting and indoor feeding (29).

To reflect differences in malaria exposure among individuals, mosquito biting risk was modelled using an exponential distribution that varied by age and body surface area. The total population for the zone was scaled down to 1,000 people in the simulation to reduce computing time, and the results were adjusted afterward to represent the full population (Figure 3). All simulation inputs, model scripts, and instructions for running and analyzing the results are publicly available (Data Availability section). The modelling scripts were written using Python version 3.6.0 and R version 4.0.2.

Modelling overview

To project malaria prevalence in Ghana's Savannah zone from 2023 to 2028, we followed a four-step simulation process using the EMOD modelling framework (Figure *2*). The model was first

run without interventions over 50 years (1960–2009). This phase, often called "burn-in" or equilibration, helps the simulation stabilize and develop realistic levels of population immunity under natural malaria transmission conditions (30). For this step, 50 different larval habitat scale values were tested to capture variation in environmental conditions across the zone. This process allowed the model to reflect the zone's baseline malaria transmission potential before any large-scale control activities were introduced. In the second phase, real-world intervention data from 2010 to 2022 were added to the baseline model. These included records of ITN use, IRS coverage, and treatment-seeking behaviours. The model was then adjusted (calibrated) to match observed malaria prevalence from national surveys such as the Ghana Demographic and Household Surveys (GDHS) and the MICS. Calibration ensured that the model outputs reflected the actual malaria trends recorded during this period (31). Once the model was calibrated, we re-ran it from 1960 to 2022 using the selected larval habitat scaling and the known intervention history. This allowed us to reconstruct how malaria dynamics may have evolved over time under observed conditions (32).

In the final phase, we introduced different intervention strategies into the model, including ITNs, IRS, SMC, and the RTS, S/AS01E malaria vaccine and simulated their impact from 2023 to 2028. The results from these forward-looking simulations were used to assess how various strategies could influence malaria prevalence in the Guinea Savannah zone. The overall simulation workflow is summarised in Figure 4.

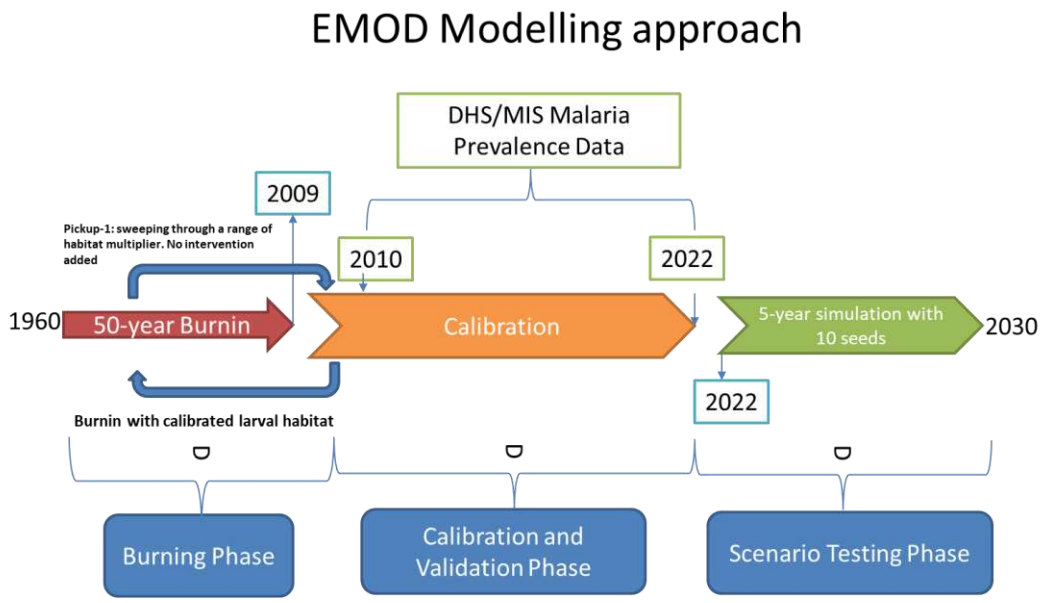


Figure 4:The Agent-based Model: EMOD Modelling approach

Model calibration

Setting baseline transmission intensity

To set baseline malaria transmission level for the Savannah zone, we used Plasmodium falciparum Prevalence Rate (PfPR) detected by microscopy, assuming a detection threshold of 50 parasites per microliter (33). To match observed parasite prevalence among children under five years of age from national surveys GDHS and MICS for 2011, 2014, 2016, 2019, and 2022), we adjusted the larval habitat availability in the model using a scaling factor (27). This adjustment helped the model reproduce observed PfPR values under real-world intervention coverage, including ITN ownership and use, case management and IRS during those years. Data for SMC and RTS,S/AS01$_E$ malaria vaccine coverage were obtained from reports by the SMC Alliance Ghana, NMEP and the WHO, respectively (34,35). (Figure 8).

Because GDHS and MICS surveys are conducted for two to four months, we calculated average monthly PfPR values for each survey year based on the months when data were collected. A total of 50 different larval habitat scale values were tested. For each value, the model was run for 50 years (1960–2009) without interventions to build up population immunity. Then, real-world levels of ITN, IRS, case management, SMC, and RTSS/AS01$_E$ were applied to these partially immune populations. The model then simulated under-five PfPR for each of the selected years (2011–2019) during the exact survey months. This produced a range of simulated PfPR outcomes across the different larval habitat scale factors. These model outputs were then compared to the observed GDHS and MICS values using a beta-binomial likelihood approach (36). The scale factor that gave the best fit that is, the highest log-likelihood, was selected as the final larval habitat setting for the zone (Figure 5). This calibrated setting was used to run all future simulations from 2023 to 2030.

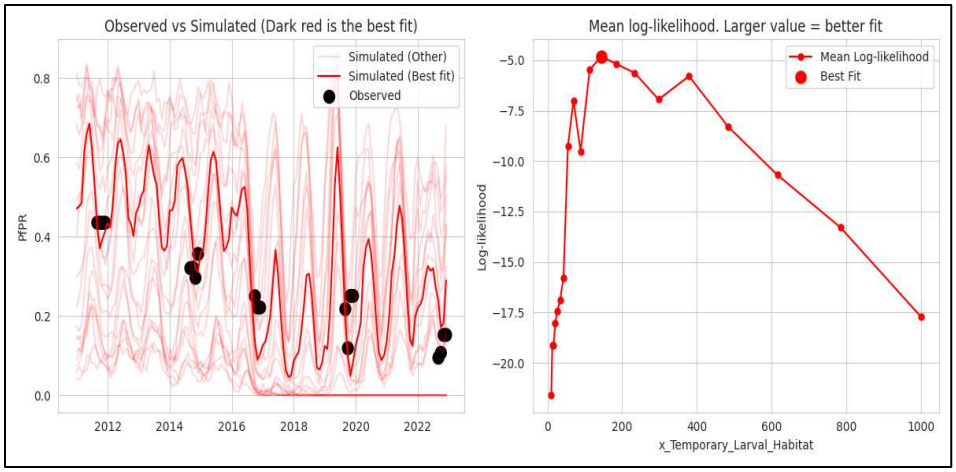


Figure 5: Transmission calibration for the Savannah Zone of Ghana. The left panels show the right panels depict the transmission calibration, showing simulated monthly PfPR in children under 5 years compared to empirical estimates (black dots) from GDHS, MIS, and MICS surveys between 2011 and 2022. Light red curves represent outputs from multiple simulations using varying larval habitat scaling factors, while the solid red line indicates the best-fit simulation. These calibrations help capture long-term transmission dynamics specific the region.

Parameterizing historical interventions [2010–2022]

From 2010 to 2022, several malaria control interventions were expanded across the Savannah zone. This period of intensive implementation was used to set the historical intervention parameters in the model as shown in Figure 6. For each intervention, the model included details on the type of intervention, when it was introduced, how much coverage it achieved, and the expected impact. The specific interventions simulated during this period included case management for both uncomplicated and severe malaria, ITNs, IRS, SMC, and the RTSS/AS01$_E$ malaria vaccine.

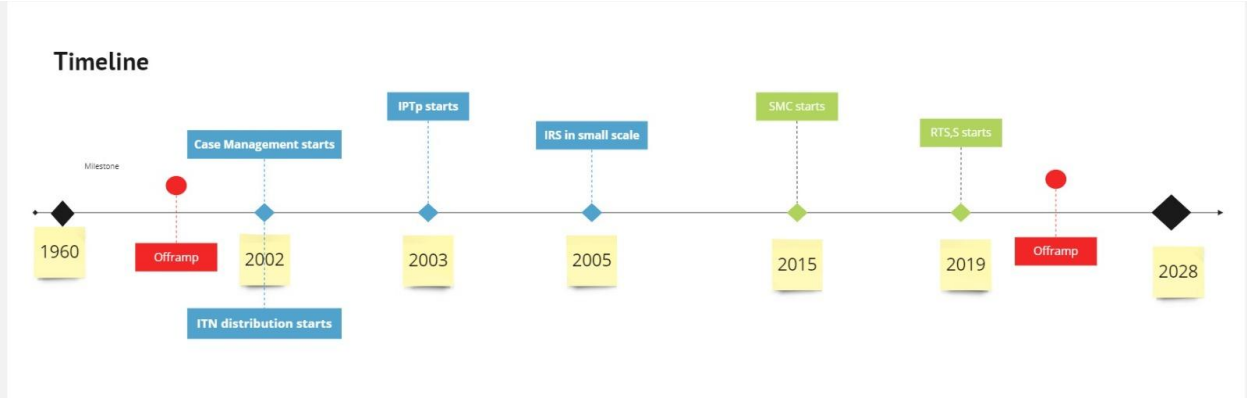


Figure 6: Historical interventions 2000–2022

Case management

Data from the 2011, 2014, 2016, 2019, and 2022 GDHS and MICS surveys were used to estimate how case management coverage for uncomplicated malaria changed over time (Figure 7). Coverage was defined as the proportion of children under five with fever in the two weeks before the survey who received treatment with an ACT. Since adult treatment data were not available in the GDHS, adult coverage was assumed to be the same as for children, based on a study showing similar treatment behaviour by medicine vendors for both groups (12). Estimates were weighted using the cluster-level weights provided in the GDHS datasets. For years without a survey, CM coverage was assumed to remain at the most recent available value.

$$\Pr(\text{Treat}_i = 1 \mid e_i, y_i) = \begin{cases} c_{y_i}, & e_i = \text{clinical} \\ 0.49, & e_i = \text{severe} \end{cases} \quad t_{\text{treat},i} = t_{e,i} + d(e_i), d(e_i) = \begin{cases} 5, & e_i = \text{clinical} \\ 3, & e_i = \text{severe} \end{cases}$$

In this formulation, Treat_i is an indicator that individual i receives antimalarial treatment following an episode, e_i denotes episode type (uncomplicated clinical malaria or severe malaria), and y_i is the calendar year. The parameter c_y is the year-specific case management coverage for uncomplicated malaria, estimated from the GDHS and MICS as the weighted proportion of febrile children under five who received an ACT in the two weeks preceding the survey. Adult uncomplicated coverage was assumed equal to c_y due to lack of adult GDHS treatment data. For years without surveys, c_y was held constant at the most recent observed value. Severe malaria treatment coverage was fixed at 0.49 across the zone. Treatment timing is represented by $t_{\text{treat},i}$, which occurs after a fixed

delay $d(e)$ from episode onset t_e, set to 5 days for uncomplicated cases and 3 days for severe cases. Treated cases received artemether–lumefantrine as the ACT regimen.

Insecticide-treated nets

ITNs coverage by age group for each mass distribution year (2011, 2014, 2016, 2019, and 2022) was estimated using data from the GDHS and MICS surveys, focusing on children under five. Usage was defined as the percentage of individuals who reported sleeping under a treated net the night before the survey (Figure 6). Coverage levels for each campaign year were adjusted in the model using net retention patterns and loss rates, modelled with a Weibull distribution to reflect an average net lifespan of about 2.5 years. This allowed the model to capture how ITN coverage declines over time after distribution.

The simulation followed Ghana's national distribution schedule, which typically includes mass campaigns every three years. Historical distributions primarily involved pyrethroid-only nets. The model also incorporated demographic coverage adjustments to age group and assigned effectiveness values such as killing and blocking effects based on parameters available in the EMOD software. These values were updated for each distribution year to reflect evolving ITN types and levels of insecticide resistance. Initial killing and blocking effects, along with their decay over time, were aligned with available data and experimental findings to ensure the simulations reflected realistic ITN performance.

To mathematically represent the joint influence of ITN coverage, retention, usage, and decay in effectiveness, the intervention was modelled as.

$$\lambda(t,a) = \lambda_0(t)[1 - C_r(a)\, S(t - t_r)\, U(a)\, B_0\, e^{(-\frac{t-t_r}{\tau_B})}]$$

In this formulation, $\lambda(t,a)$ is the force of infection at time t for age group a, and $\lambda_0(t)$ is the baseline force of infection in the absence of ITNs.

$C_r\ (a)$ represents age-specific ITN coverage at distribution round r, with t_r denoting the campaign year 2011, 2014, 2016, 2019, or 2022. In your model, coverage for each campaign was informed by GDHS and MICS data for children under five and then adjusted across age groups according to demographic structure.

$S(t - t_r)$ represents net survival over time following distribution. You modelled net retention using a Weibull survival function to reflect an average lifespan of approximately 2.5 years. Formally, this can be written as:

$$S(\Delta) = e^{[-(\frac{\Delta}{\eta})^k]}$$

where $\Delta = t - t_r$, η is the scale parameter corresponding to a mean lifespan of about 2.5 years, and k is the shape parameter governing the rate of net loss.

$U(a)$is the reported usage probability, defined as the proportion of individuals who slept under a treated net the previous night, derived from GDHS/MICS survey responses.

$B_0$is the initial blocking effect of the net, and $\tau_B$is the constant decay governing the reduction in blocking effectiveness over time. These parameters were assigned based on EMOD defaults and updated across campaign years to reflect differences in net type and insecticide resistance. Killing effects are incorporated similarly within the EMOD vector mortality structure but are not explicitly shown in this reduced form.

The combined effect of coverage, retention, usage, and time-varying net efficacy was modelled as a multiplicative reduction in the force of infection, as shown above.

Indoor Residual Spraying

Indoor residual spraying (IRS) interventions were modelled using data from the GDHS for the years 2011, 2014, 2016, 2019 and 2022. Each IRS round in the simulation was scheduled to match the actual year of implementation. To do this, the simulation timeline was aligned so that the start date for each IRS campaign reflected its correct timing.

Standard values from field studies and similar modelling work were used to define IRS effectiveness. The initial killing effect was set at 1, representing full efficacy immediately after spraying. The duration of peak effectiveness was set at 180 days, based on data from PMI Burkina Faso, while the rate of decline in effectiveness (decay time constant) was set at 90 days, based on studies in Benin. The repelling effect followed the same pattern, with an initial value of 1, a 180-day box duration, and a 90-day decay period. These IRS processes were incorporated into the transmission model using the following functional form.

$$\mu_v(t) = \mu_{v0}(t) + C_y K_0 h(t - t_y)$$

Where

$$h(\Delta) = \begin{cases} 1, & 0 \le \Delta \le 180 \\ \exp\left(-\dfrac{\Delta - 180}{90}\right), & \Delta > 180 \end{cases}$$

Here, $\mu_v(t)$ represents the effective mosquito mortality rate at time t, and $\mu_{v0}(t)$is the baseline mortality in the absence of IRS. $C_y$denotes IRS coverage in implementation year y, with spraying occurring at time t_y. $K_0 = 1$ represents the initial killing effect immediately after spraying. The function $h(\Delta)$captures residual insecticidal activity over time since spraying. For the first 180 days, efficacy remains at full strength, consistent with the box duration derived from PMI Burkina Faso data. After 180 days, effectiveness declines exponentially with a decay time constant of 90 days, consistent with findings from Benin. The repelling effect follows the same functional structure and parameter values.

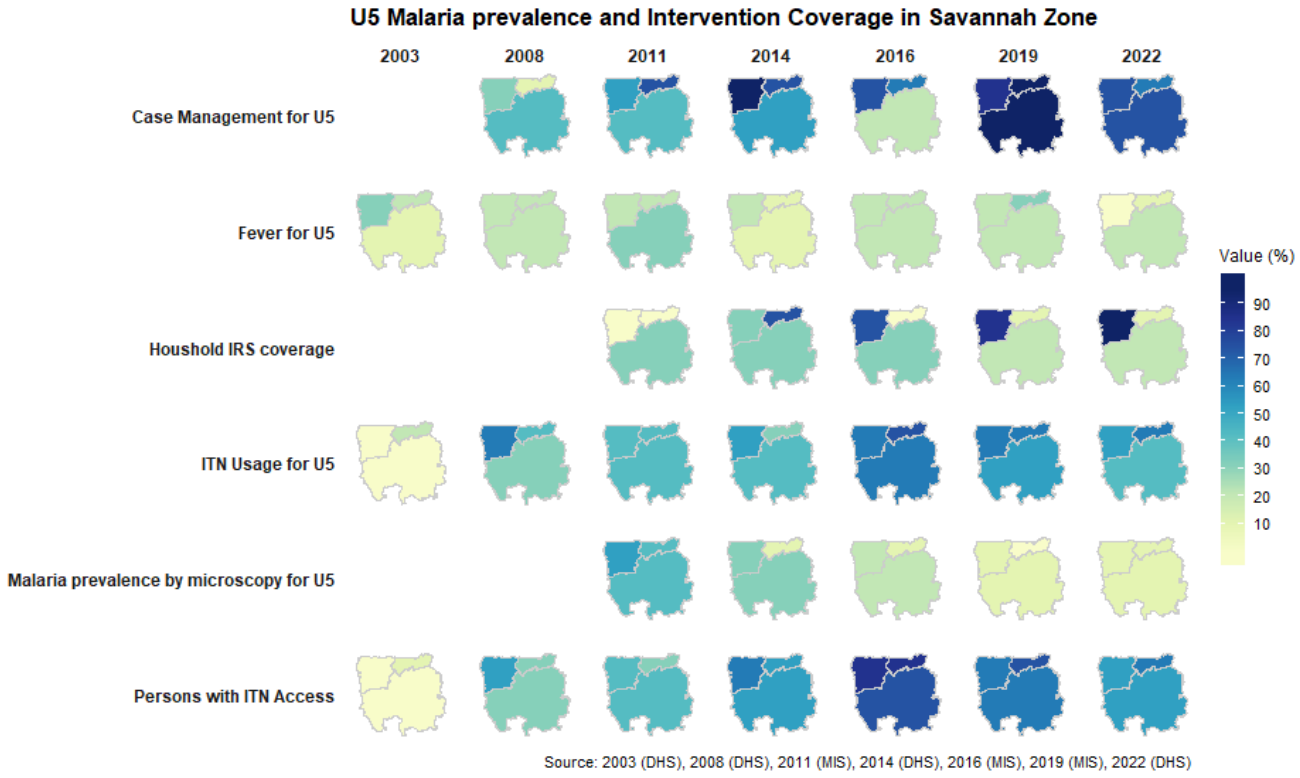


Figure 7: U5 fever, malaria prevalence and intervention coverages

Seasonal malaria chemoprevention

Seasonal malaria chemoprevention (SMC) in Ghana follows WHO guidance, which recommends SMC in areas where over 60% of malaria transmission occurs within four months and the annual PfPR exceeds 5%. In these high-transmission seasonal zones, SMC campaigns have achieved very high coverage Figure 6. However, due to the lack of a reliable population denominator, it was not possible to recalculate coverage using dose using data alone. Instead, post-campaign survey results were used to estimate SMC coverage. Seasonal malaria chemoprevention was implemented as a repeated mass drug administration campaign targeting children aged 3 to 59 months. In each round, 80 percent of eligible children were assumed to receive treatment. SMC was delivered in four monthly rounds per transmission season from 2016 to 2022. Each round was modelled independently, with no assumption of correlation between rounds beyond age eligibility. Protection following SMC administration was represented using a time dependent efficacy function. The initial protective efficacy was set at 82.6 percent. Protection remained constant for 10.4 days after administration and then declined exponentially with a mean decay duration of 20.3 days. Thus, for a child treated at time t_0, protective efficacy at time t was defined as:

$$E_{\mathrm{SMC}}(t) = \mathbf{1}(t \geq t_r)\, c_{\mathrm{SMC}}\, E_0 \begin{cases} 1, & 0 \leq t - t_r \leq d_{\mathrm{box}} \\ \exp\left(-\dfrac{t - t_r - d_{\mathrm{box}}}{d_{\mathrm{decay}}}\right), & t - t_r > d_{\mathrm{box}} \end{cases}$$

This equation defines the time-varying protective effect of SMC after each round r at time t_r, implemented using the vaccdrug mechanism in EMOD. You targeted children aged 0.25 to 5 years with coverage $c_{\text{SMC}} = 0.8$. The initial protective effect is $E_0 = 0.826$, with a box duration $d_{\text{box}} = 10.42$ days followed by exponential waning over $d_{\text{decay}} = 20.34$ days. In interpretation, $E_{\text{SMC}}(t)$ can be used as a modifier that reduces infection risk or clinical risk for eligible children during and after each SMC round.

Drug parameters for sulfadoxine-pyrimethamine plus amodiaquine were taken from published pharmacokinetic studies (37), while pharmacodynamic properties were adjusted by calibrating the model against clinical trial data from Ghana and Tanzania(38,39). The effectiveness of SMC in reducing clinical malaria cases was also validated using rollout data from Mali (40). For the simulation, it was assumed that all children completed the full three-day course of treatment.

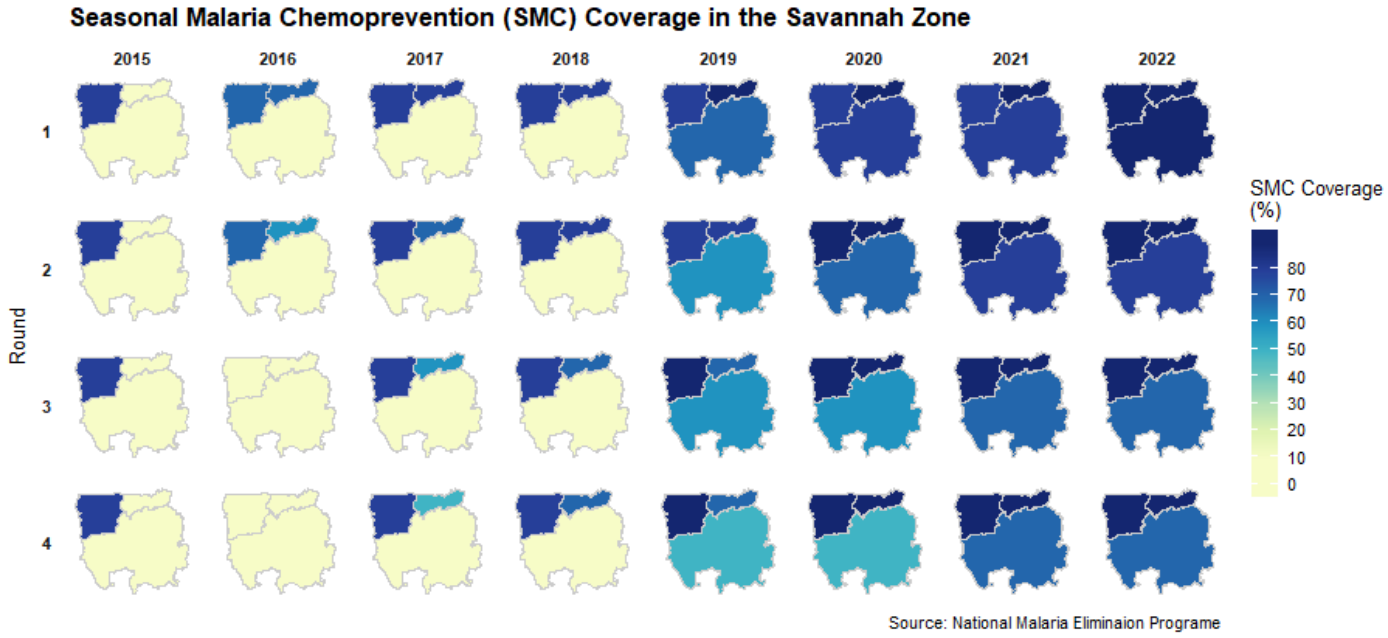


Figure 8: SMC Coverage in Ghana from 2015-2022

Malaria Vaccine [RTS,S/AS01$_E$]

The RTS, S malaria vaccine was modelled by updating individual characteristics and scheduling vaccination rounds to reflect real-world rollout between 2019 and 2022. When a child received the third dose of the vaccine, their vaccination status in the model was changed from "None" to "GotVaccine," indicating they had completed the core vaccination series. This status change triggered the vaccine's protective effect in the simulation. To ensure that children could receive all scheduled doses, no blackout period was applied between doses. The model included both the

third dose and the first booster dose, with specific timing and coverage levels based on available rollout data on Ghana from the WHO (41).

The RTS,S/AS01$_E$ vaccine was implemented as an age-targeted routine immunisation programme delivered to newborn cohorts. Vaccination was modelled as a staged process in which eligible children entered the vaccination schedule shortly after birth and subsequently received sequential doses at fixed delays, conditional on receiving the previous dose.

Let $t_b$denote the time of birth and $t$the current time. Entry into the vaccination programme occurred at time $t_0 = t_b + \delta$, where δ represents a short delay after birth. Children were then eligible to receive three sequential doses at delays $\Delta_1 = 150\ days$, $\Delta_2 = 180\ days$, and $\Delta_3 = 270$ days following entry into the programme. Dose-specific receipt was probabilistic with coverage:

$$c_1 = \text{RTS,S rollout coverage}, c_2 = 0.95c_1, c_3 = 0.95c_1.$$

A child received dose d only if the previous dose had been received and the child remained within the target age window.

Vaccine efficacy was modelled as acquisition-blocking protection that reduces susceptibility to infection. For a dose administered at time t_d, the protective efficacy $E_d(t)$ followed a box-plus-waning profile:

$$E_d(t) = \begin{cases} E_0, & 0 \le t - t_d \le B, \\ E_0 \exp\left(-\dfrac{t - t_d - B}{\tau}\right), & t - t_d > B, \end{cases}$$

where $E_0 = 0.8$ is the initial protection, $B = 365$ days is the period of constant protection, and $\tau = 592.4$ days is the exponential waning time constant.

The overall vaccine protection acting on an individual i at time t was defined as the sum of contributions from each received dose:

$$\Phi_i(t) = \sum_{d=1}^{3} R_{i,d}\ E_d(t),$$

where $R_{i,d}$is an indicator equal to 1 if child i received dose d, and 0 otherwise.

This protection modifies the force of infection multiplicatively:

$$\lambda_{\text{vacc}}(t) = \lambda(t)\,[1 - \Phi_i(t)],$$

where $\lambda(t)$is the baseline force of infection.

In this formulation, E_0 represents the initial efficacy of RTS, S/AS01 vaccine against infection immediately after vaccination. The parameter B represents the duration of sustained protection following each dose, and τ governs the gradual loss of immunity over time. The dose indicators $R_{i,d}$ capture programme coverage and adherence to the dosing schedule. The coverage parameter $c_1$defines the rollout scenario, while reduced coverage for later doses reflects drop-off between scheduled visits. By linking vaccine protection to the force of infection, the model allows vaccination to reduce malaria acquisition risk in vaccinated children and to alter transmission dynamics at the population level.

Model validation

After establishing the baseline transmission level in the pre-2010 model, simulations were run using historical intervention data from 2010 to 2022. However, the resulting U5 PfPR could not be independently validated, as there were no additional survey data available beyond the GDHS and MICS from this same period. Therefore, model calibration for transmission intensity relied solely on the available GDHS and MICS data collected between 2010 and 2022. Independent validation against routine District Health Information Management System (DHIMS-2) incidence data or against clinical trial and cohort data from sites in the zone was not performed; this is acknowledged as a limitation.

Intervention scenario setup

Fourteen intervention scenarios were defined in line with the NMEP strategic plan and WHO guidance for areas of high, seasonal transmission (Table 1). Scenario 1 represented business-as-usual (BAU), using 2022 coverage: pyrethroid-only ITN use among children under five 71.3%, IRS 34.0%, SMC 85.0%, RTS,S/AS01E third-dose coverage 70.0% and case management (CM) 60.0%. Single-intervention scenarios (Scenarios 2–6) scaled one tool to its target coverage (ITN 95%, CM 80%, IRS 50%, SMC 95% or RTS,S/AS01E 95%) while all other tools remained at BAU coverage; no tool was removed. Combined scenarios (Scenarios 7–14) scaled ITN to 95% and CM to 80% together with the listed tools, with unlisted tools at BAU coverage. Single-intervention scenarios were included to quantify the marginal value of scaling each tool, information needed to prioritise investment under constrained or declining funding, and, together with the combined scenarios, to estimate synergies between tools that cannot be measured in randomized controlled trials.

The selection and timing of interventions followed the NMEP guidelines for the zone. With additional mass distributions scheduled for 2024 and 2027, ITNs were simulated at usage levels of 95 compared to the counterfactual which was 71.3% among under five as observed in GDHS-2022. CM coverage was modelled at a coverage of 80% compared to counterfactual coverage of 60.0% for under five in the year 2022 from GDHS, capturing region-specific treatment-seeking behaviour and the effective use of ACTs. SMC was modelled for under-fives. Baseline coverage

in 2022 was set at 85% as an average for the zone, based on historical NMEP reports and field studies conducted in Ghana and Chad (42,43). SMC coverage rate was modelled at 95% from 2023 to 2028, reflecting anticipated scale-up efforts and improved treatment access in alignment with the NMEP. The malaria vaccine 3rd round coverage was modelled at 95% compared two 2022 baseline coverage of 70% by WHO (41).

The model was initialized from a calibrated burn-in simulation and ran forward over a six-year projection period. Baseline transmission dynamics incorporated vector species composition, climate forcing, calibrated larval habitat scaling, and equilibrium demography. Interventions were layered onto this baseline to construct alternative policy scenarios. Scenarios were defined by systematically varying coverage levels of key interventions through a parameter sweep framework. The following intervention parameters were varied: ITN use among children under five (0.713 and 0.95), IRS coverage (0.34 and 0.50), SMC coverage (0.85 and 0.95), and RTS,S/AS01$_E$ third-dose coverage (0.70 and 0.95), while case management for uncomplicated malaria in children under five was held at 0.60 and increased to 80%. Each unique combination of these coverage levels constituted a distinct intervention scenario. This factorial structure enabled evaluation of single-intervention effects as well as combined strategies under moderate and high coverage conditions (see details in Table 1).

Outcomes were extracted for the under-five age group. For comparison with household surveys, prevalence was summarised as the mean of monthly PfPR over September–December, the months of GDHS and MIS/MICS fieldwork used for calibration (DHS/MIS survey-window PfPR). Because this window overlaps the July–October SMC campaign, annual-mean PfPR (mean of 12 monthly values) and annualised clinical incidence (EMOD clinical cases per person-year, expressed per 1,000 child-years) were also reported, together with new infections, severe malaria incidence, gametocyte prevalence and an anaemia indicator. Each scenario was simulated with three stochastic runs across three simulated sub-populations (nine replicates) sharing random-number seeds with BAU; comparisons with BAU were therefore paired by replicate, and percent reductions and clinical episodes averted were estimated with 95% confidence intervals (CI) from 4,000 paired bootstrap resamples. Progress towards the National Malaria Elimination Strategic Plan (NMESP) 2024–2028 goal of halving case incidence from 2022 was assessed against BAU in 2023, the closest simulated year to the baseline. The contribution of each tool was estimated by Shapley decomposition of cumulative 2023–2028 episodes averted using all simulated tool combinations, and by log-linear models with pairwise interactions and replicate fixed effects. Robustness was examined across the three simulated sub-populations, across alternative survey months, and by the number of replicates (Supplementary Figures S6, S9 and S10). Parametric sensitivity analysis of model inputs was not performed (see Limitations).

517 Table 1:Prediction Scenarios and Intervention Coverage Levels in the Savannah Zone

Scenario Type	**Scenario Description**	**p-ITN**	**IRS**	**SMC**	**RTS, S/AS01$_E$**	**CM**
Impact of Single Interventions						
1. Business-as-Usual (BAU)	Baseline coverage levels aggregated from 2022; pyrethroid-only ITNs	71.3%	34.0%	85.0%	70.0%	60.0%
2. ITN Only	p-ITN scaled to 95%	95.0%	34.0%*	85.0%*	70.0%*	60.0%*
3. CM Only	Case management scaled to 80%	71.3%*	34.0%*	85.0%*	70.0%*	80.0%
4. IRS Only	IRS implemented at 50% coverage	71.3%*	50.0%	85.0%*	70.0%*	60.0%*
5. SMC Only	SMC scaled to 95%	71.3%*	34.0%*	95.0%	70.0%*	60.0%*
6. RTS,S/AS01$_E$ Only	RTS,S/AS01$_E$ scaled to 95%	71.3%*	34.0%*	85.0%*	95.0%	60.0%*
Impact of Combined Interventions						
7. ITN + CM	p-ITN at 95%; CM at 80%	95.0%	34.0%*	85.0%*	70.0%*	80.0%
8. ITN + CM + IRS	p-ITN at 95%; CM at 80%; IRS at 50%	95.0%	50.0%	85.0%*	70.0%*	80.0%
9. ITN + CM + SMC	p-ITN at 95%; SMC at 95%; CM at 80%	95.0%	34.0%*	95.0%	70.0%*	80.0%
10. ITN + CM + RTS,S/AS01$_E$	p-ITN, RTS,S/AS01$_E$ at 95%; CM at 80%	95.0%	34.0%*	85.0%*	95.0%	80.0%
11. ITN + CM + IRS + SMC	p-ITN at 95%; IRS 50%; SMC 95%; CM 80%	95.0%	50.0%	95.0%	70.0%*	80.0%
12. ITN + CM + IRS + RTS,S/AS01$_E$	p-ITN at 95%; IRS 50%; RTS,S/AS01$_E$ 95%; CM 80%	95.0%	50.0%	85.0%*	95.0%	80.0%
13. ITN + CM + SMC + RTS,S/AS01$_E$	p-ITN 95%; SMC 95%; RTS,S/AS01$_E$ 95%; CM 80%	95.0%	34.0%*	95.0%	95.0%	80.0%
14. Full Package: ITN + CM + IRS + SMC + RTS, S/AS01 vaccine	p-ITN 95%; IRS 50%; SMC 95%; RTS, S 95%; CM 80%	95.0%	50.0%	95.0%	95.0%	80.0%

ITN: Standard insecticide-treated nets/pyrethroid-only nets, IRS: Indoor Residual Spraying, SMC: Seasonal malaria chemoprevention, RTS,S/AS01$_E$ vaccine: Malaria Vaccine, CM: Case Management. * BAU coverage retained in the scenario. Scenario numbers follow this table throughout.

Results

Burden under business-as-usual

Under BAU (Scenario 1), under-five malaria burden did not decline over the projection period (Figure 9). Annual clinical incidence was 1,284 episodes per 1,000 child-years in 2023 and 1,372 (95% CI 1,296–1,447) in 2028, and annual-mean PfPR was 14.7% and 15.8% (14.3–17.4), respectively. All outcomes were strongly seasonal: monthly PfPR rose from about 17% in January–March to 27% in July and fell to 2–5% in September–November, coinciding with SMC rounds, whereas clinical incidence and new infections peaked earlier, in May (about 1,880 clinical episodes and 8,980 infections per 1,000 child-years). Gametocyte prevalence and the anaemia indicator followed the same seasonal pattern. Year-to-year variation was substantial, with higher burden in 2026 and 2028 than in 2025 and 2027.

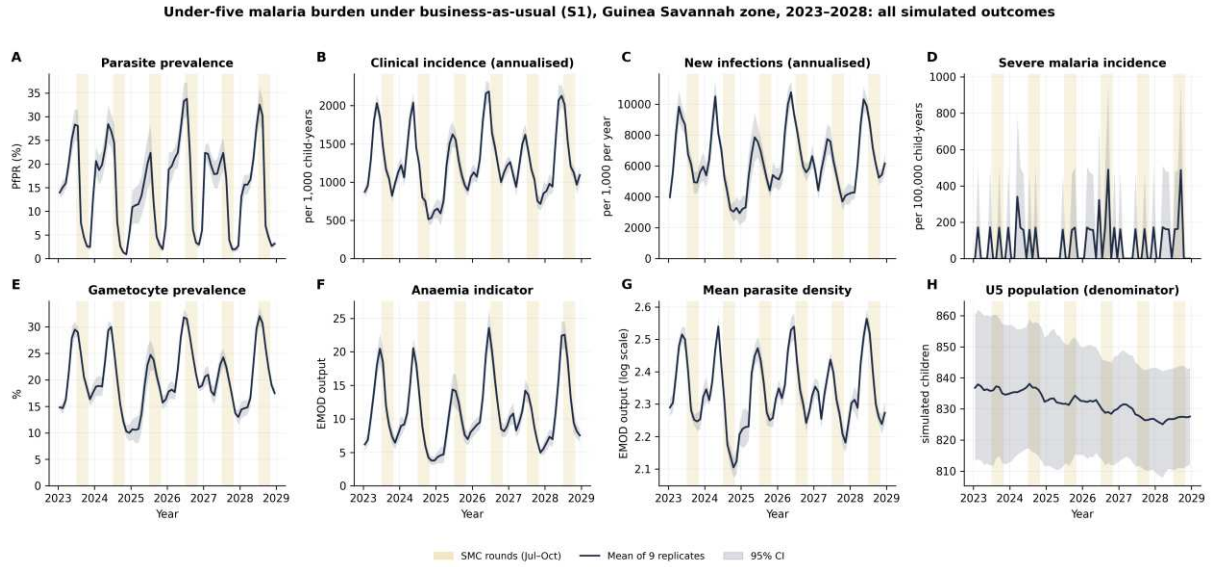


Figure 9: Under-five malaria burden under business-as-usual (Scenario 1), Guinea Savannah zone, 2023–2028. Monthly (A) parasite prevalence (PfPR, %), (B) annualised clinical incidence per 1,000 child-years, (C) annualised new infections per 1,000, (D) severe malaria incidence per 100,000 child-years, (E) gametocyte prevalence, (F) EMOD anaemia indicator, (G) mean parasite density (EMOD output, log scale) and (H) simulated under-five population. Lines are means of nine stochastic replicates with 95% confidence intervals; beige bands mark SMC rounds (July–October).

Impact of intervention scenarios

Scenarios that scaled IRS lowered PfPR in every month, whereas scaling ITN, SMC or RTS,S/AS01E alone produced trajectories close to BAU outside the SMC window (Figure 10). The corresponding monthly clinical-incidence trajectories are shown in Supplementary Figure S1. In

2028, clinical incidence was 704 per 1,000 child-years under the full package (Scenario 14; 49% below BAU, 95% CI 39–59), 715 under Scenario 11 (48%, 38–58), 761 under Scenario 8 (45%, 36–53), 841 under Scenario 12 (39%, 33–46) and 856 under Scenario 4, IRS only (38%, 30–46) (Table 2; Figure 11; Supplementary Table S2). Scenarios without scaled IRS reduced incidence by 2–13%: ITN only by 5% (0–11), SMC only by 4% (−5 to 12), RTS,S/AS01E only by 2% (−2 to 5), and the best combination without IRS, Scenario 13, by 13% (6–20). Scenario rankings by annual clinical incidence are shown in Supplementary Figure S11.

The choice of outcome measure altered the apparent ranking of scenarios. Every scenario with SMC at 95% reduced DHS/MIS survey-window PfPR by 82–90%, whereas the corresponding reductions in clinical incidence ranged from 4% (Scenario 5) to 49% (Scenario 14) (Figure 11; Supplementary Table S1). For SMC only, the estimated reduction in PfPR was 59% when measured in September, 98% in October and 82% for the September–December mean, compared with 20% for annual-mean PfPR (Supplementary Figure S6; Supplementary Table S4), indicating that survey-season prevalence captures the temporary clearance of infections during SMC rounds rather than a sustained reduction in burden.

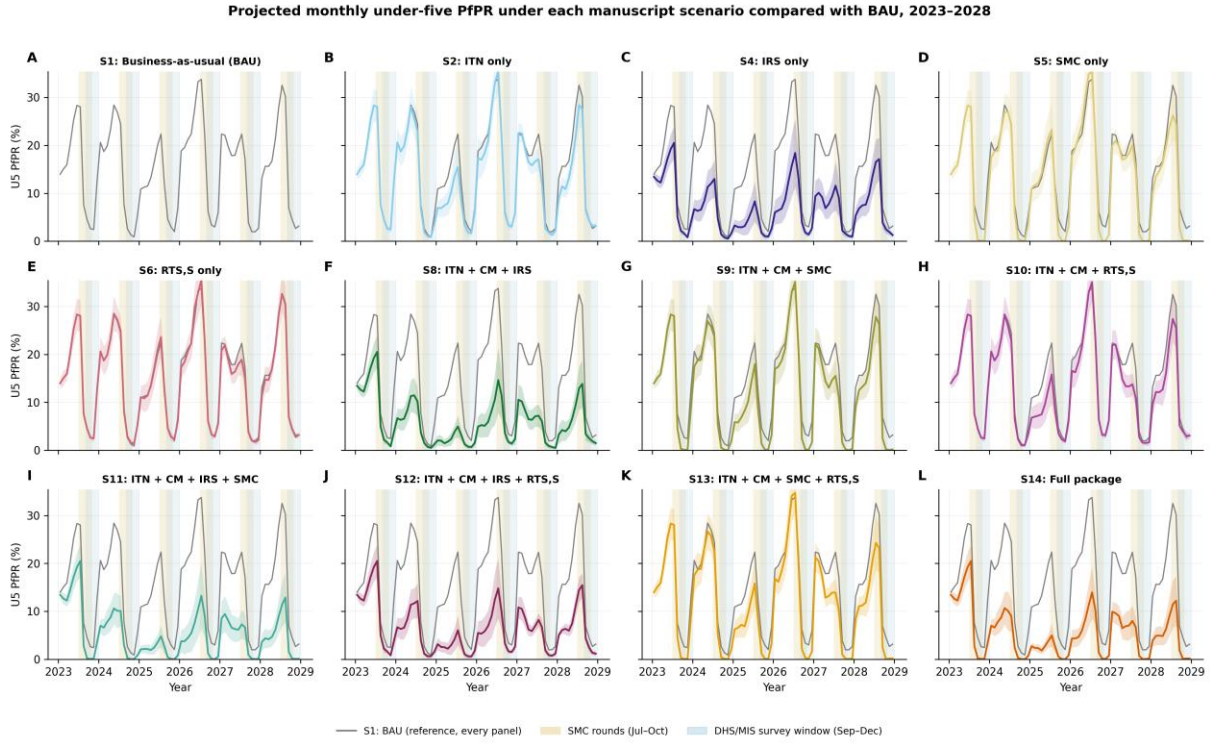


Figure 10: Projected monthly under-five PfPR (%) under each scenario (coloured line with 95% confidence interval) compared with BAU (grey line in every panel), 2023–2028. Panels follow Table 1 order: (A) Scenario 1, BAU; (B–E) single-intervention Scenarios 2, 4, 5 and 6, each scaling one tool with others at BAU coverage; (F–L) combined Scenarios 8–14 with ITN 95% and CM 80%. Beige bands mark SMC rounds (July–October); blue bands mark the DHS/MIS survey window (September–December).

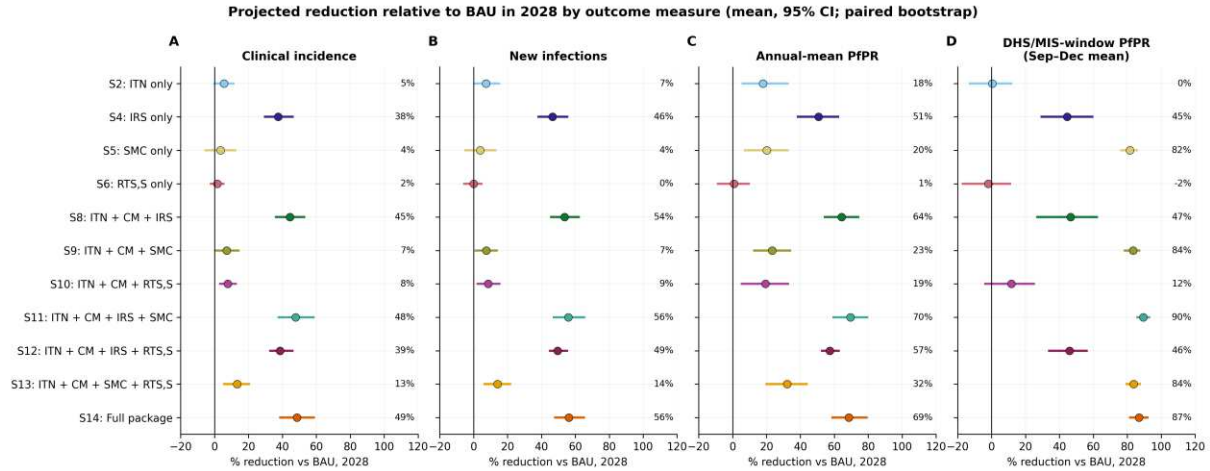


Figure 11: Percent reduction relative to BAU in 2028 in (A) annualised clinical incidence, (B) new infections, (C) annual-mean PfPR and (D) DHS/MIS survey-window PfPR (September–December mean), by scenario. Points are means and lines 95% confidence intervals from 4,000 paired bootstrap resamples of nine stochastic replicates.

Table 2: Projected under-five outcomes in 2028, cumulative clinical episodes averted over 2023–2028 and progress towards the NMESP incidence target, by scenario. Values are means (95% CI) across nine paired stochastic replicates.

Scenario	Survey-window PfPR, % (Sep–Dec)	Annual-mean PfPR, %	Clinical incidence per 1,000 child-years	Incidence reduction vs BAU, %	Episodes averted per 1,000 children, 2023–2028	Reduction vs 2023 baseline, %†
1. Business-as-usual (BAU)	4.28 (3.60–4.97)	15.8 (14.3–17.4)	1372 (1296–1447)	Reference	Reference	-7 (-13 to -1)
2. ITN only	4.27 (3.84–4.70)	13.0 (11.0–14.9)	1296 (1237–1356)	5 (0–11)	614 (418–809)	-1 (-5 to 3)
4. IRS only	2.38 (1.64–3.11)	7.8 (5.6–10.0)	856 (726–986)	38 (30–46)	3381 (2805–3950)	33 (23–44)
5. SMC only	0.79 (0.61–0.97)	12.7 (10.3–15.0)	1323 (1245–1401)	4 (-5 to 12)	94 (-120 to 321)	-3 (-9 to 4)
6. RTS,S only	4.37 (3.97–4.77)	15.7 (14.0–17.4)	1349 (1301–1396)	2 (-2 to 5)	45 (-73 to 153)	-5 (-10 to -0)
8. ITN + CM + IRS	2.29 (1.56–3.01)	5.7 (3.7–7.6)	761 (637–885)	45 (36–53)	3874 (3296–4468)	41 (31–51)
9. ITN + CM + SMC	0.71 (0.52–0.89)	12.2 (9.9–14.4)	1274 (1221–1326)	7 (1–14)	622 (427–844)	1 (-3 to 4)
10. ITN + CM + RTS,S	3.78 (3.31–4.25)	12.8 (10.5–15.0)	1265 (1222–1308)	8 (3–13)	640 (529–735)	2 (-3 to 5)
11. ITN + CM + IRS + SMC	0.45 (0.27–0.63)	4.8 (2.9–6.8)	715 (578–852)	48 (38–58)	4037 (3460–4628)	44 (35–55)
12. ITN + CM + IRS + RTS,S	2.31 (1.95–2.68)	6.8 (5.8–7.8)	841 (740–943)	39 (33–46)	3711 (3312–4086)	34 (28–43)
13. ITN + CM + SMC + RTS,S	0.70 (0.50–0.89)	10.8 (8.4–13.2)	1190 (1143–1236)	13 (6–20)	772 (518–1021)	7 (2–13)
14. Full package (ITN + CM + IRS + SMC + RTS,S)	0.56 (0.30–0.82)	5.0 (3.0–7.0)	704 (570–839)	49 (39–59)	3810 (3374–4261)	45 (36–55)

BAU, business-as-usual; CM, case management; IRS, indoor residual spraying; ITN, insecticide-treated nets; SMC, seasonal malaria chemoprevention. † Reduction in 2028 clinical incidence relative to BAU in 2023, the proxy for the NMESP 2022 baseline (target ≥50%). Scenarios 3 and 7 not available in the model output.

Progress towards the national target and cumulative impact

Relative to 2023, BAU incidence was 7% higher in 2028 (95% CI 1–13). No scenario reached the NMESP goal of a 50% reduction in 2028; the closest were Scenario 14 (45%, 95% CI 36–55) and Scenario 11 (44%, 35–55) (Figure 12). IRS-containing combined scenarios (Scenarios 8, 11, 12 and 14) exceeded a 50% reduction in the lower-transmission years 2024, 2025 and 2027, but not in 2026 or 2028, whereas scenarios without scaled IRS never exceeded 33%. Over 2023–2028, BAU produced about 7,450 clinical episodes per 1,000 children; Scenario 11 averted 4,037 (95% CI 3,460–4,628), Scenario 8 3,874 (3,296–4,468), Scenario 14 3,810 (3,374–4,261), Scenario 12 3,711 (3,312–4,086) and Scenario 4 3,381 (2,805–3,950) (Table 2; Supplementary Figure S3).

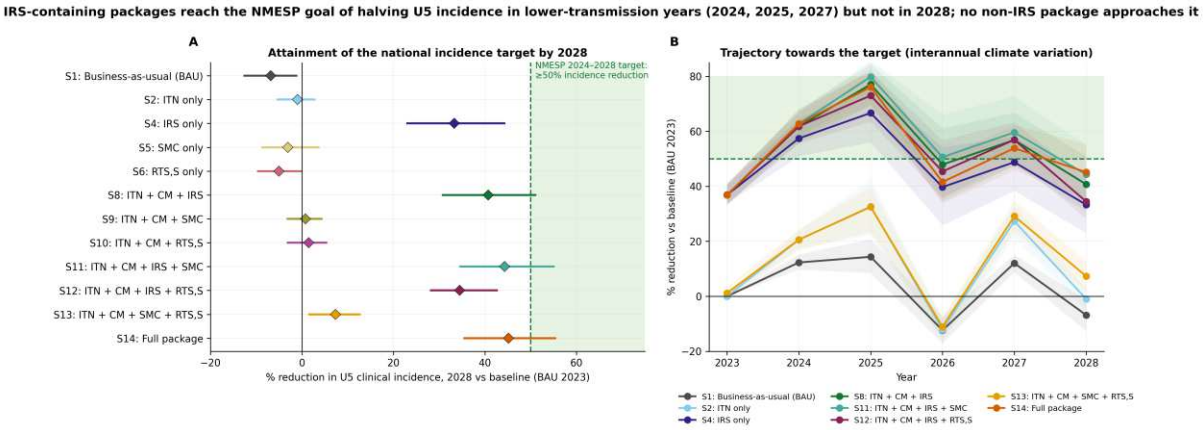


Figure 12: Progress towards the NMESP 2024–2028 goal of halving malaria case incidence. (A) Reduction in 2028 under-five clinical incidence relative to BAU in 2023 (proxy for the 2022 baseline) with 95% confidence intervals; the shaded zone marks attainment of ≥50%. (B) Annual trajectory of the same measure for BAU and selected scenarios; the dashed line marks the 50% target

Contribution of individual interventions

Shapley decomposition attributed 3,185 (95% CI 2,830–3,550) of the 3,810 clinical episodes per 1,000 children averted by the full package to IRS scale-up (84%) and 636 (542–741) to ITN scale-up (17%); the contributions of increasing SMC from 85% to 95% (47; −100 to 184) and RTS,S/AS01E from 70% to 95% (−58; −158 to 44) did not differ from zero (Figure 13; Table 3). The same pattern held in every combined scenario. The broader factorial comparison of all 16 simulated tool combinations showed the same dominance of IRS-containing packages (Supplementary Figure S12). The independent effect of IRS was immediate and sustained, whereas the effect of ITN scale-up emerged after the 2024 mass distribution campaign; ITN and IRS were synergistic, with a joint effect on cumulative incidence 8.9% (95% CI 1.5–15.7) larger than the product of their separate effects (p = 0.02) (Supplementary Figure S8).

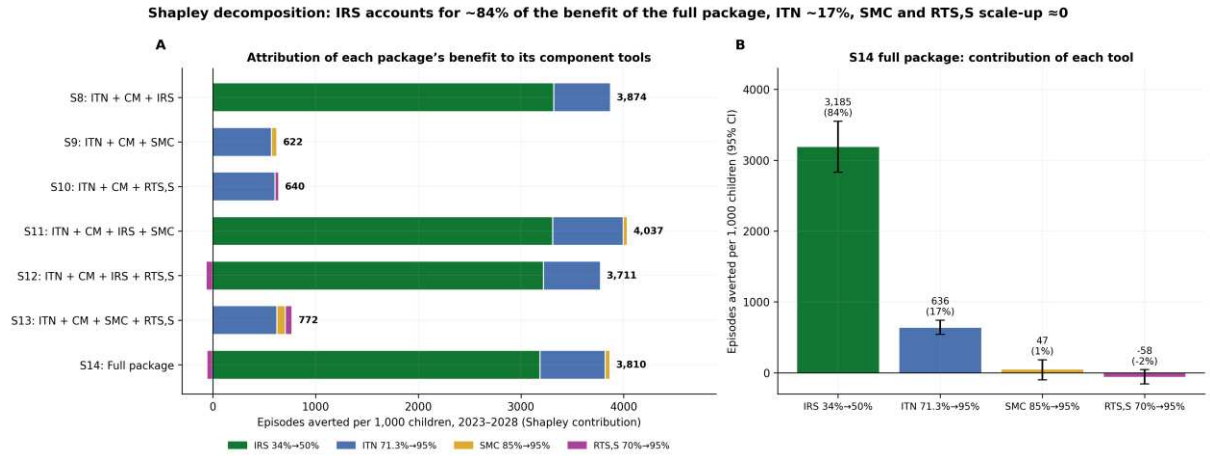


Figure 13: Shapley decomposition of cumulative 2023–2028 clinical episodes averted per 1,000 children into the contributions of each scaled tool. (A) Contributions within each combined scenario (bold numbers are totals). (B) Contributions for the full package (Scenario 14) with 95% confidence intervals from paired bootstrap and share of the total. CM 80% is common to all combined scenarios and is not separately attributable.

Table 3: Shapley contribution of each scaled tool to cumulative 2023–2028 clinical episodes averted per 1,000 children, by combined scenario (95% CI from paired bootstrap).

Scenario	Tool scaled	Episodes averted attributable (95% CI)	Share of total	Total averted
8. ITN + CM + IRS	ITN	554 (376 to 737)	14%	3,874
8. ITN + CM + IRS	IRS	3,320 (2,783 to 3,895)	86%	3,874
9. ITN + CM + SMC	ITN	571 (477 to 685)	92%	622
9. ITN + CM + SMC	SMC	51 (-62 to 174)	8%	622
10. ITN + CM + RTS,S	ITN	605 (504 to 699)	94%	640
10. ITN + CM + RTS,S	RTS,S	36 (-61 to 140)	6%	640
11. ITN + CM + IRS + SMC	ITN	687 (538 to 848)	17%	4,037
11. ITN + CM + IRS + SMC	IRS	3,309 (2,888 to 3,732)	82%	4,037
11. ITN + CM + IRS + SMC	SMC	40 (-233 to 235)	1%	4,037
12. ITN + CM + IRS + RTS,S	ITN	557 (472 to 642)	15%	3,711
12. ITN + CM + IRS + RTS,S	IRS	3,219 (2,775 to 3,678)	87%	3,711
12. ITN + CM + IRS + RTS,S	RTS,S	-65 (-208 to 46)	-2%	3,711
13. ITN + CM + SMC + RTS,S	ITN	623 (543 to 714)	81%	772
13. ITN + CM + SMC + RTS,S	SMC	82 (-77 to 241)	11%	772
13. ITN + CM + SMC + RTS,S	RTS,S	67 (-36 to 172)	9%	772
14. Full package (ITN + CM + IRS + SMC + RTS,S)	ITN	636 (542 to 741)	17%	3,810
14. Full package (ITN + CM + IRS + SMC + RTS,S)	IRS	3,185 (2,830 to 3,550)	84%	3,810
14. Full package (ITN + CM + IRS + SMC + RTS,S)	SMC	47 (-100 to 184)	1%	3,810
14. Full package (ITN + CM + IRS + SMC + RTS,S)	RTS,S	-58 (-158 to 44)	-2%	3,810

Effects on other outcomes and epidemiological indicators

IRS-containing scenarios reduced new infections by 46–56%, peak PfPR by 46–62%, gametocyte prevalence by 42–54% and the anaemia indicator by 31–45% in 2028, while mean parasite density changed by less than 2% (Figure 14; Supplementary Figures S2 and S5; Supplementary Table S3). Across monthly outputs, clinical incidence was strongly correlated with new infections, anaemia and gametocyte prevalence (Spearman $\rho = 0.91$, 0.91 and 0.87, respectively; Supplementary Figure S7). Two indicators increased as exposure fell: clinical episodes per new infection rose from 0.20 under BAU to 0.24–0.25, and the share of annual clinical cases occurring in July–October rose from 36% to 42–49% (Supplementary Figure S4). Scenario rankings were consistent across the three simulated sub-populations, but reductions were smallest in the sub-population with the highest baseline prevalence (for example, 37–43% for Scenarios 4, 8, 11 and 14, compared with 43–60% for the same scenarios in the other sub-populations) (Supplementary Figure S9; Supplementary Table S5). Between-replicate variability and the gain in precision with additional stochastic replicates are shown in Supplementary Figure S10. Severe malaria events were too few in the simulated population for reliable comparisons between scenarios.

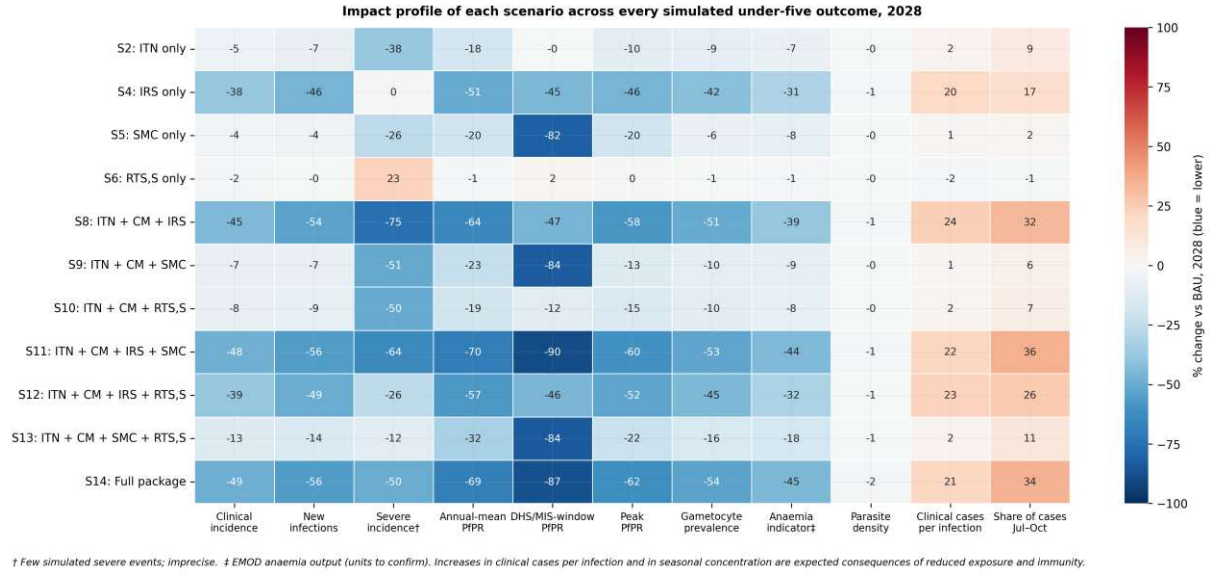


Figure 14: Percent change relative to BAU in 2028 for every simulated under-five outcome and derived indicator, by scenario (blue, lower; red, higher). Increases in clinical episodes per infection and in the share of cases in July–October reflects reduced exposure

Discussions

This study projected the impact of 12 intervention scenarios on under-five malaria in Ghana's Guinea Savannah zone between 2023 and 2028. Three findings stand out. First, maintaining current coverage will not reduce burden: under BAU, clinical incidence and prevalence remained at or above 2023 levels. Second, the benefit of any package was determined mainly by vector control intensification: IRS scale-up accounted for more than 80% of the episodes averted by every IRS-containing package, with a smaller, synergistic contribution from ITN scale-up, and packages

combining ITN, CM and IRS roughly halved incidence. Third, further increments in SMC and RTS,S/AS01E coverage added little to the reduction in clinical incidence, and no package reached the NMESP target of halving incidence by 2028 in a high-transmission year.

The dominant effect of IRS is consistent with observational evidence from the Sahelian belt of northern Ghana, where IRS with non-pyrethroid insecticides substantially reduced parasite prevalence [new reference: Bongo District IRS and SMC study, PLoS Negl Trop Dis 2026], and with modelling showing that vector control drives much of the achievable reduction in high-transmission settings (46,47). However, WHO guidance generally does not recommend deploying IRS in addition to ITNs where ITN coverage is high, except for specific purposes such as insecticide-resistance management [new reference: WHO Guidelines for malaria]. The strong IRS effect and the ITN × IRS synergy in our model may partly reflect assumptions about pyrethroid resistance reducing ITN efficacy and about the efficacy and residual duration of IRS; they should be interpreted as conditional on these assumptions and considered alongside local entomological data when prioritising IRS in the zone.

The small marginal effects of SMC and RTS,S/AS01E require careful interpretation. Both tools were already at high BAU coverage (85% and 70%), so scenarios measured the effect of increasing coverage to 95%, not the value of the tools themselves; single-intervention scenarios, including Scenario 5 (SMC only), scaled one tool on top of BAU coverage of all other tools rather than deploying it in isolation. RTS,S/AS01E is delivered to successive birth cohorts, so by 2028 only part of the under-five population had received the higher coverage, and the vaccine was modelled as partial, waning protection against infection. The principal intended benefits of SMC and vaccination, prevention of severe disease and death in young children, which trial evidence shows are enhanced when the two are combined (48), could not be estimated reliably in a simulated population of about 830 children. These results therefore do not support withdrawing SMC or vaccination, which the NMEP and WHO recommend for this setting, but indicate that further coverage gains in these tools will not, by themselves, reduce clinical incidence substantially.

The outcome measure strongly influenced conclusions. Prevalence measured in September–December, the period of household-survey fieldwork used for calibration, overlaps the July–October SMC campaign; it therefore reflects the temporary clearance of infections by SMC and overstated the effect of SMC-containing scenarios by up to twenty-fold relative to clinical incidence. Evaluations of intervention packages in SMC areas, including interpretation of future GDHS and MIS results, should report clinical incidence or annual-average prevalence alongside survey-season prevalence.

Reduced exposure also changed the epidemiology of residual malaria. With IRS, a larger share of infections became clinical and a greater proportion of cases occurred in July–October, consistent with lower acquired immunity in young children. As transmission falls, prompt diagnosis and treatment and well-timed SMC therefore become more rather than less important, and interruption of vector control could lead to resurgence among children with reduced immunity.

Progress towards the NMESP target depended strongly on inter-annual transmission conditions: IRS-containing packages exceeded a 50% reduction in lower-transmission years but not in 2026 or 2028, so programme progress should be judged over several years rather than in a single year. Reductions were also smaller in the simulated sub-population with the highest baseline prevalence, supporting the NMESP's sub-national approach, in which the highest-burden districts may require intensified or additional interventions to achieve the same proportional reduction [new reference: NMESP 2024–2028].

The findings support Ghana's ongoing shift toward subnational, data-driven malaria control. Deploying integrated intervention packages such as ITNs, CM, IRS, SMC and RTS,S/AS01$_E$ malaria vaccine offers greatest impact than isolated approaches, especially in high-burden areas like the Savannah zone. Strategic resource allocation should therefore favour combined interventions over single tools, aligning with Ghana's National Malaria Strategic Plan (2021–2025) and WHO's HBHI framework, which both emphasize stratified, high-impact targeting (52,53).

Scaling up such combinations will require coordinated planning across programs particularly between malaria control, immunization, and community health services. Timing campaigns (e.g., ITN distributions, SMC rounds, RTS, S/AS01$_E$ malaria doses) to align operationally can improve efficiency and uptake, as shown in Burkina Faso and Mali (35).

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Limitations

This study has several limitations. First, confidence intervals reflect stochastic variation across nine replicates only; parametric sensitivity analysis of key assumptions, including larval habitat scaling, ITN and IRS efficacy and decay, insecticide resistance, SMC efficacy and adherence, and vaccine efficacy and waning, was not performed, so projections are conditional on these inputs. Second, calibration relied on under-five PfPR from GDHS and MICS surveys, and the model was not independently validated against routine DHIMS-2 incidence or clinical trial data from sites in the zone. Third, the simulated population of about 830 children per replicate was too small to estimate severe malaria and mortality, which are the principal targets of SMC and vaccination. Fourth, coverage was assumed stable with perfect adherence, and the model did not include changes in insecticide or drug resistance, population mobility or climate anomalies beyond the historical forcing. Fifth, the projection horizon ended in 2028, and CM coverage was not varied independently in the available output, so the effects of scaling CM alone (Scenario 3) and with ITNs (Scenario 7) could not be reported. Finally, results represent the Guinea Savannah zone as a whole and do not capture district-level heterogeneity, although consistent rankings across three simulated sub-populations suggest that the main conclusions are robust.

Conclusion and Recommendation

Under current intervention coverage, under-five malaria burden in Ghana's Guinea Savannah zone is projected to remain high through 2028. Packages that intensify vector control, combining IRS with high ITN use and improved case management, are projected to roughly halve clinical incidence and avert three to four clinical episodes per child over six years, whereas scaling single tools achieves little. Within the NMEP and WHO frameworks, the full package (ITN, CM, IRS, SMC and RTS,S/AS01E) is the recommended option for this zone, with ITN + CM + IRS + SMC as the most efficient alternative when resources are constrained. Even these packages may not meet the NMESP 2028 incidence target in high-transmission years, so sustained multi-year investment, district-level tailoring and monitoring based on incidence as well as survey-season prevalence are needed. Future work should integrate routine surveillance data, explicit resistance dynamics and parametric uncertainty, and estimate impacts on severe disease and mortality.

Declarations

Ethics Approval and Confidentiality of Data

Ethical approval for this study was obtained from the University of Health and Allied Sciences Research Ethics Committee (UHAS-REC A.1 [81] 23-24). As the study did not involve the direct participation of human subjects, individual consent was not required. However, all datasets used were anonymized and handled with strict confidentiality, following institutional data protection guidelines.

Consent for publication

Not applicable.

Availability of data and materials

Data availability statement: The GDHS data was acquired through permission sought from GDHS. Additional administrative approvals were granted by the NMEP to access secondary data relevant to the study (https://dhsprogram.com/data/dataset/Ghana_Standard-DHS_2022.cfm?flag=1). The datasets used and analysed in the current study are available from the corresponding author on reasonable request. Also, all scripts used can be accessed from https://github.com/VincentUwumboriyhieGmayinaam/Mathematical-modelling-of-Malaria-Interventions-in-Ghana-from-2022-2030.git for reproducibility

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

VUG and IAA: Conceptualisation, methodology, visualisation, and computational modelling. DA and IAA: Supervision, review and editing. AA: Contribution to methodology. MA, AKM, EM, BM, and SO: Review and editing**.**

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Authors' information (optional)

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Supplementary Materials

S1: Supplementary Figures and Tables

Supplementary Files

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