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Agent-based simulation of seasonal malaria chemoprevention strategy in Southern Tanzania: comparing dihydroartemisinin-piperaquine with or without primaquine

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Abstract

Background The effect of seasonal malaria chemoprevention (SMC) strategy on malaria transmission using a single low dose of primaquine (SLDPQ) added to artemisinin-based combination therapy has not been established in Africa. An agent-based model and simulation (ABMS) was used to assess SMC effectiveness using dihydroartemisinin-piperaquine (DP) with and without SLDPQ in Masasi and Nanyumbu Districts, Tanzania.

Methods ABMS was developed in AnyLogic platform using secondary data from a cluster-randomized DP-based SMC study conducted in the districts, to assess the effectiveness of DP with and without SLDPQ for control of malaria in under-five children. The model incorporated human, mosquito, transmission, intervention, and environment sub-models, and simulated three monthly rounds of SMC over a 180-day period. Environment temperature, an important factor in mosquito breeding was simulated in three scenarios, first using average field temperature, and then when it was increased or decreased by 1^0C from the average. Model outputs were compared with field results to evaluate external validity.

Results Overall, 2275 participants, 1135 in the intervention and 1140 in the control arm were involved in the model. At baseline, malaria prevalence was 11.5% (130/1135) and 16.3% (186/1140) in the intervention and control arm, respectively. At the end of 125-day simulation period malaria prevalence declined to 4.1% (47/1135), and it rebounded to 7.1% (80/1135) at the end of 180-day simulation period after three rounds of DP alone administration. Addition of SLDPQ to DP led to a further declined of the prevalence to 1.4% (16/1135) and 3.9% (44/1135) at the end of 125-day and 180-day, respectively. In the DP alone, the increase in average temperature by 1˚C further decreased malaria prevalence to 2.6% (30/1135) and 5.0% (57/1135) at the end of 125-day and 180-day, respectively, whereas the decrease of temperature by 1 ˚C decreased the malaria prevalence to 3.2% (36/1135) and 4.2% (48/1135) at the end of 125-day and 180-day, respectively.

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Conclusions The ABMS has demonstrated that addition of SLDPQ to DP reduced malaria transmission significantly regardless of the increase or decrease of the average temperature by 1 ˚C. SLDPQ can be added to DP-SMC and scaled-out for the control of malaria in Tanzania.

Keywords Agent-based modelling, Effectiveness, Seasonal malaria chemoprevention, Dihydroartemisinin-piperaquine, Primaquine, Under-five children

Background

Despite recent decline in its prevalence, malaria remains a major global public health concern, especially in sub-Saharan Africa [1]. Tanzania is one of the ten countries with the highest prevalence of malaria, and in 2023 it accounted for the 3.3% and 4.3% of the cases and malaria related deaths globally, respectively [2]. Malaria affects all age groups, however, children under five years of age are the most vulnerable to the infection [1].

Vector control using insecticides-treated bed nets (ITNs), indoor residual spraying, prompt diagnosis and management of cases using effective antimalarial drugs are the major malaria control measures in Tanzania [3]. In 2012, the World Health Organization (WHO) recommended seasonal malaria chemoprevention (SMC) to children under the age of 5 years using sulfadoxine-pyrimethamine (SP) in combination with amodiaquine (AQ) [4]. SMC entails treating the targeted population regardless of its infection status, during the peak malaria transmission season in a region where the transmission of the infection is highly seasonal, to protect them from new infections and clear the existing infections [5]. In the Sahel region, the strategy has significantly reduced the burden of malaria in the under five children [6]. The SMC strategy can be adopted in Southern regions of Tanzania where malaria transmission is highly seasonal, with 60% of the transmission occurring during the rainy season. However, *Plasmodium falciparum* parasite resistance against SP and AQ is common in East Africa [7], therefore, the two drugs cannot be used for SMC. Artemisinin-based combination therapies (ACT) particularly those not in use as first-line treatment for uncomplicated malaria can be used for SMC in the region [7, 8]. Dihydroartemisinin-piperaquine (DP) is an efficacious ACT, and its long-acting partner drug piperaquine has a long prophylactic effect that can prevent reinfection for more than 30 days in adult and about 3 weeks in children after the intake [7–9]. SMC using DP has shown to significantly reduce malaria burden in children in Tanzania and other malaria endemic settings [7, 10, 11]. DP however, is not potent against mature *P. falciparum* gametocytes; therefore, it cannot interrupt the transmission of the infection from humans to the female *Anopheles* mosquitos. On the other hand, primaquine is the only readily antimalarial drug that can kill the mature *P. falciparum* gametocytes, therefore, block the transmission [12]. It is expected that when primaquine is added to DP for SMC it can significantly reduce the burden of the infection not only to the target population, but also to the whole population. The WHO recommends adding a single low-dose of primaquine (0.25 mg/kg) to ACTs to contain the spread of artemisinin resistance, and eliminate malaria in low transmission settings [13, 14]. Primaquine can also be employed to reduce malaria transmission in high-malaria endemic areas and for SMC [15]. Controlled trials have shown SLDPQ to be safe and sufficient to block the transmission of the *P. falciparum* gametocytes [12, 14, 16–18]. However, many African countries are reluctant to adopt SLDPQ because of lack of effectiveness data at the community level in African population [12, 19]. For instance, in 2020, Tanzania adopted SLDPQ for malaria treatment in low to very low transmission areas, however, to date the drug has not been rolled out due to lack of evidence of its effectiveness at the population level [20].

Computational modelling is one of the tools that have been used to predict the effect of interventions against infections [21–23]. The tool can probably be used to understand the effect of SLDPQ when added to DP and used as SMC for the control of malaria in Tanzania. Agent-based modelling and simulation (ABMS) is a powerful computational tool and flexible that can be used to simulate complex interactions between various agents of malaria transmission [24, 25]. ABMS has the potential to capture the dynamics of transmission of the infection as well as the heterogeneous mixing and social networks of agents, incorporate geographical data and physical space, and hence aid in allocation of resources, and targeted control measures [21]. Furthermore, ABMS makes use of the artificial intelligence (AI) for modelling and simulation, thus allowing agents to learn as they interact with one another, and their surroundings, leading to new behaviours as they gain experience [26]. AnyLogic is one of the modelling software, and it offers a versatile modelling framework that enables the integration of diverse components, including spatial heterogeneity and individual-level behaviours essential for capturing the complexity of malaria dynamics [27]. Therefore, using ABMS techniques implemented in the Anylogic simulation platform, this study aimed to evaluate the effectiveness of DP with and without SLDPQ when used for SMC in children

less than five years old in Masasi and Nanyumbu Districts, Tanzania.

Materials and methods

Study design and area

This study utilized secondary data from a two arms (interventional and control) clusters randomized study conducted in Masasi and Nanyumbu Districts, Tanzania [7]. Secondary data were accessed on 5th February 2025, and it included demographic characteristics of the recruited children, their malaria rapid diagnostic test (mRDT)-based infection status before and seven weeks after the intervention, uptake of DP in the targeted population during the three rounds of SMC, and ITNs coverage in the catchment population. One author (ROM) was involved in the collection of data in the field, therefore, he had the information that could identify individual participants. However, ROM was not directly involved in the development of the model and simulation. Additional data including the efficacy and prophylactic effect of DP and SLDPQ, and the incubation period of the *P. falciparum* parasite in female *Anopheles* mosquito and human were obtained from the published literature [12, 28, 29]. The collected data were simulated using ABMS in AnyLogic platform, run for 180 days, and with 10 simulation runs for all parameters to reduce bias owing to the stochasticity of some parameters. The effectiveness of the interventions was checked on days 125 (125th day represents 7 weeks after third round of SMC) and 180 (180th day represent 12 weeks after third round of SMC).

Masasi and Nanyumbu Districts are in Mtwara Region, Southern Tanzania, with Masasi located between 10.72724˚latitude and 38.8101˚longitude, and Nanyumbu between 11.06667˚latitude and 38.32975˚ longitudes as illustrated in Fig. 1, which was generated using the free, open-source Quantum Geographic Information System (QGIS) software. The average annual rainfall in both districts is 939 mm, and the temperature ranges between 15.6 ˚C and 32.2 ˚C. More than 60% of malaria cases occur during the rainy season between March and July in both Districts [30]. The use of ITNs, prompt diagnosis followed by treatment with ACTs, intermittent preventive treatment in pregnancy using SP, and recently SMC are the major malaria control measures in the Districts [31].

Procedures

Model development

The ABMS to assess the effectiveness of DP with and without SLDPQ was developed in AnyLogic platform as previously described in the ITNs effectiveness model [32]. Briefly, the model was developed using human

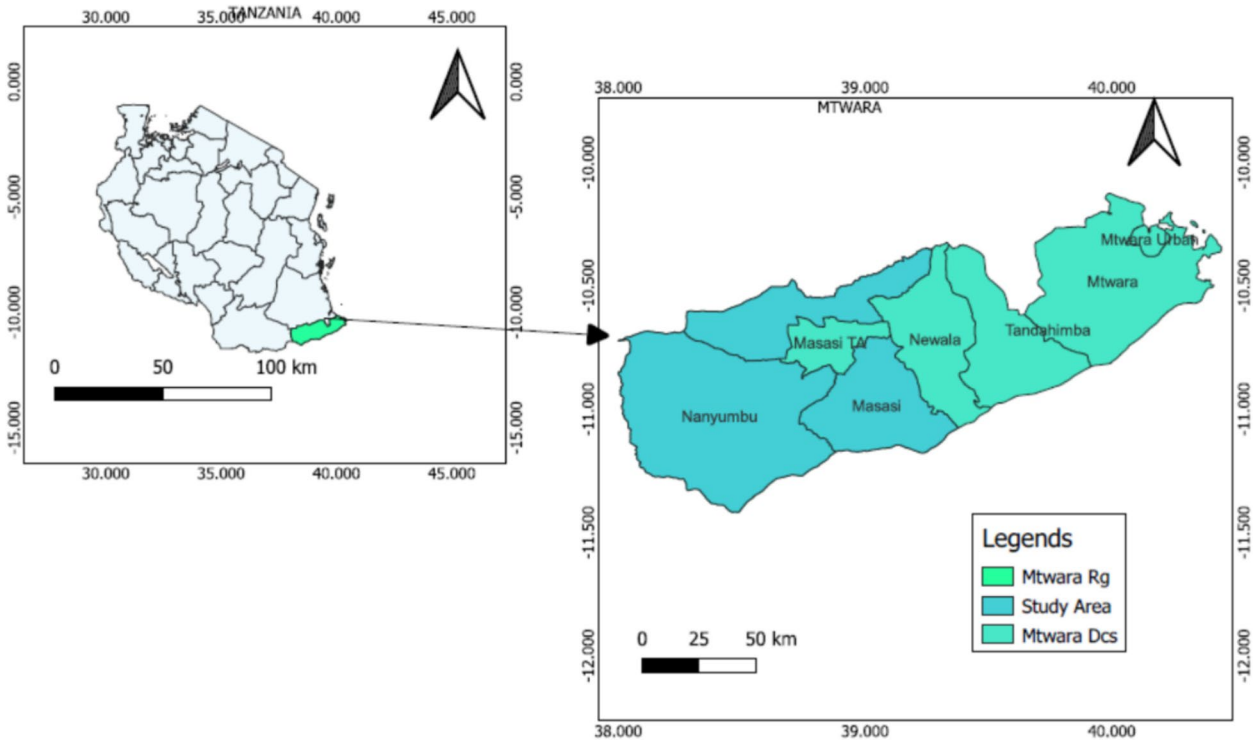

Fig. 1 Map showing the study area

sub-model, mosquito sub-model, transmission sub-model, intervention sub-model, and an environment sub-model. Slight modifications were done to the model to accommodate the simulation for the effectiveness of DP alone or plus SLDPQ by modifying the transmission and intervention sub-model.

Malaria transmission sub-model

Malaria infection begins when an infectious female Anopheles mosquito bites the human [5, 33]. The infectious mosquito releases the malaria parasites (sporozoites) into the human bloodstream in the process of taking blood, and the human become infected after completing the incubation period of 10–14 days [33]. Likewise, when the mosquito bites a malaria-infected human, it takes gametocytes in the blood, an infectious parasite stage to the mosquito, which in turn restarts the transmission cycle [5].

In simulating the malaria transmission, the Susceptible-Exposed-Infected-Recovered (SEIR) model framework was used and it accounted for the incubation period of the parasite in both the human and mosquito hosts [21, 34]. Malaria transmission occurs when the mosquito takes a blood meal from human, thus during the blood meal stage the human and mosquito exposure status was checked to determine whether the infection had been transmitted or not. In the model, the transmission was triggered by a message passing either from human to mosquito agent or from mosquito to human agent, as previously described [32]. The human agent was at any time-point being either susceptible, exposed, infected, or recovered. After being bitten by the infectious mosquito, the susceptible human had a 4% probability of becoming exposed. Thereafter, the exposed human agent would transit into the infected state after completing the incubation period of 10–14 days [21, 28, 33]. On the other hand, susceptible mosquito could contract the infection once it had come into contact with the infected human agent. The human would return to the recovery state after receiving a full dose of DP. The probability of humans in the study population to be cured was set at 0.95–0.99 based on the DP cure rate of 95%–99% [7, 35, 36]. Furthermore, DP has a prophylactic effect of 14–21 days in children [8, 9], therefore, the human agent had the probability of returning to the susceptible state after this prophylactic period.

Similarly, at any time-point the mosquito agent would be in any of the following states: susceptible, exposed, or infected. After it had bitten the infected or recovered human agent, the susceptible mosquito had a 2% probability of becoming exposed. An exposed mosquito becomes infectious after an incubation period of 9–11 days, depending on ambient temperature, and remains infectious for the rest of its life [33, 37]. On the other hand, if the mosquito had taken a blood meal from a recovered human agent who had used SLDPQ, the probability of becoming exposed was only 7% to 16% [12, 38]. This is because SLDPQ has the efficacy ranging from 84 -93% [12, 16, 17].

Malaria interventions sub-model

SMC temporarily prevents new infections by providing prophylactic effects and also clears the existing infections in the targeted population [39]. The schizontocidal antimalarial drugs target asexual parasites responsible for the malaria symptoms, and young gametocytes, which, if allowed to mature, would lead to the transmission of the infection [7, 40]. This leads to a reduced disease burden and transmission in the targeted population [41, 42]. In modelling SMC, variables such as the number of rounds for medication, treatment time, time lapse between rounds, and prophylactic effect of drugs were taken into consideration (Table 1). Three rounds of SMC were administered for three consecutive months. In each round, a full course of DP was administered once a day for three consecutive days. DP was administered to all eligible participants in the intervention clusters regardless of their infection status. Furthermore, SLDPQ was simulated to be administered once in each round, together with the first dose of DP.

The SMC involved only children under the age of five years; however, under the real condition in the field, older children and adults acted as a source of infection to the under -fives. Therefore, in the ABMS, the rate at which the adult population contributed as a source of infection to the under- fives was estimated at 10% per month, whereas death due to malaria was not considered in this study. Like in the field, in the ABMS the prevalence of malaria was checked at the seventh week after the third

Table 1 Summary of model parameters, assigned values, and supporting references

Parameter	Value	Source
Number of rounds	3	[7]
Interval between rounds	30 days	[7]
Population size	2275 children	[7]
House quality	Closed, open, and partially closed eaves	[7, 43, 44]
Prophylactic effect period in days	14–21 days	[35, 45, 46]
Simulation time in months	6	Current study
Treatment clusters	Intervention and control	[7]
DP efficacy	0.95–0.99	[7, 29]
PQ efficacy	0.84 -0.93	[12, 14, 16]

round of SMC to evaluate the effect of DP alone, or DP plus SLDPQ. To further analyse the effect of SMC over time, the model was ran for 180 days (three months after the third round of SMC administration).

Scenarios tested

It was assumed that there was a 0.3 probability that agents in the control clusters would seek medical attention during the simulation period. Three scenarios were tested, the first two were used to check the effectiveness of the drugs, that is first when DP was administered alone and second when DP and SLDPQ were administered together, and the third scenario was used to check the effect of temperature variation on the effectiveness of SMC when the average environment temperature is increased or decreased by 1 ˚C.

DP alone scenario In the first simulation scenario, it was assumed that, 95 to 99% of the treated human agents would be cured of the malaria infection and move to recovery [7, 36, 47]. On the other hand, the remaining 1%–5% of the treated humans who were infectious would move from treated to infected due to the failure rate of DP. However, DP does not protect humans from new mosquito bites, and hence, infection might occur at any time throughout its prophylactic window of 14–21 days [7, 35, 45, 46]. Therefore, human agents bitten by the infectious mosquito from day 20 after the intake of DP would transit to the exposed state and hence develop new infections [36].

DP plus SLDPQ scenario The second simulation was performed by applying both DP and SLDPQ, and its effect on reducing malaria infection was analysed. Since PQ can clear the liver-stage infections, then all of the recovered human agents returned to the susceptible state after 14–21 days of prophylaxis [7, 35, 45, 46] Furthermore, when the susceptible mosquito bites, the recovered human agent who had taken PQ would have had the probability of transiting to the exposed status of only 7% to 16% [12, 15, 16]. In this model, the primary objective was to assess the transmission-blocking activity of primaquine (PQ); therefore, it was assumed that gametocytes were either cleared or rendered non-infectious following treatment.

Temperature variation scenario The first and second simulations were performed using the average field temperature of 24 ˚C to 27˚C. The third simulation was performed by varying the average field temperature by increasing or reducing 1˚C from the average temperature. Temperature is a major component in the lifecycle of the malaria infection, affecting the mosquito breeding rate when the temperature has deviated from the average minimum and maximum temperature required for the optimal breeding of the vector [37, 48, 49]. Incorporating it in the model would help to understand the impact of the intervention in relation to temperature change for instance due to global warming.

Model validation

To validate the model, the obtained simulation results were compared with the field results to assess how closely the model reproduced observed malaria trends. The prevalence of malaria infection at baseline and after the three rounds DP alone was compared between the field and the ABMS results. *Chi*-square, or fisher's exact test, and confidence interval for risk difference (RD) and risk ratio (RR) was used to assess how much the model results aligns with the field results.

Study endpoints

The primary study endpoint was the prevalence of malaria infection after the three rounds of the SMC using DP plus SLDPQ compared to the DP alone. Secondary endpoints included: (i) prevalence of malaria infection after the three rounds of DP alone, (ii) prevalence of malaria infection after the three rounds of DP plus SLDPQ, and (iii) the ABMS prevalence of malaria after the three rounds of DP alone or plus SLDPQ compared to the prevalence in the field after the three rounds of DP alone, and (iv) prevalence of malaria infection after three rounds of DP in relation to variation in the average environment temperature by increase or decrease by 1 ˚C.

Ethical considerations

The study was approved by the Kibong'oto Infectious Diseases Hospital- Nelson Mandela African Institution of Science and Technology—Centre for Educational Development in Health, Arusha, with reference number KNCHREC00067/09/2022.

Results

A total of 2275 male and female children under the age of five years were included in the model, 1135 (49.9%) in the intervention and 1140 (50.1%) in the control arm. Of the children 52.1% were females.

Effectiveness of DP alone or plus SLDPQ on malaria prevalence

Before the administration of DP the prevalence of malaria in the intervention arm was 11.5% (130/1135), and in the control arm it was 16.3% (186/1140). At the end of the 125-day simulation period, malaria prevalence in the intervention arm decreased significantly to 4.1% (47/1135) after the administration of the three

rounds of DP alone. In the control arm, the malaria prevalence decreased to 10.0% (114/1140). At the end of 180- day simulation, malaria prevalence in the intervention arm decreased significantly to 7.1% (80/1135) after the administration of the three rounds of DP alone. In the control arm, the malaria prevalence decreased to 13.4% (153/1140). Malaria prevalence at the end of the simulation period for both arms is presented in Table 2. The model also indicated that, malaria prevalence in the intervention arm declined by 63.8% (83/130) and 38.5% (50/130) following the three rounds of DP, at the end of the 125-day and 180-day simulation period, respectively, whereas there was a decline of malaria prevalence by 40.8% (76/186) and 17.7% (33/186) in the control arm at 125-day and 180-day simulation period, respectively.

The effect of adding SLDPQ to DP is presented in Table 3. Following the addition of SLDPQ to DP, malaria prevalence declined to 1.4% (16/1135), and then 3.7% (42/1135) at the end of 125-day and 180-day simulation period, respectively. In the control arm, the malaria prevalence declined to 7.6% (87/1140), and then 7.0% (80/1140) at the end of 125-day and 180-day simulation period, respectively. On the other hand, malaria prevalence declined by 87.7% (114/130), 67.7% (88/130) following the addition of SLDPQ to DP in the intervention arm, and in the control arm malaria prevalence declined only by 53.2% (99/186) and 57.0% (106/186) for 125-day and 180-day simulation period, respectively.

Table 3 Malaria prevalence following the addition of SLDPQ to the DP regimen

Day	Intervention	Reduction	Control	Reduction
Baseline	11.5% (130/1135)		16.3% (186/1140)	
30	0.5% (6/1135)	95.2%	19.9% (227/1140)	– 22%
60	0.3% (3/1135)	98%	14.6% (166/1140)	10.8%
90	0.1% (1/1135)	99%	10.4% (118/1140)	36.6%
120	1.2% (14/1135)	89.2%	8.0% (91/1140)	51.1%
125	1.4% (16/1135)	87.6%	7.6% (87/1140)	53.2%
150	2.5% (28/1135)	78.4%	7.1% (82/1140)	55.9%
180	3.7% (42/1135)	67.7%	7.0% (80/1140)	57.0%

Effectiveness of DP on malaria prevalence in relation to variation in average environmental temperature

Figure 2 depict the effect of varying the average daily temperature by increasing or reducing the average baseline temperature by 1 °C on the effectiveness of SMC. At the baseline and with the average daily temperature ranging from 24˚C to 27 ˚C, the DP-SMC implementation led to a reduction in malaria prevalence by 63.8% (83/130) and 38.5% (50/130) at the end of 125-day and 180-day simulation period, respectively. When the temperature was increased by 1 °C, the malaria prevalence declined by 76.9% (100/130) ($x^2 = 3.44$, $p = 0.06$) and 56.2% (73/130) ($x^2 = 3.76$, $p = 0.05$) at the end of 125-day and 180-day simulation period, respectively, whereas when the temperature was decreased by 1 °C the prevalence was reduced by 72.3%% (94/130) ($x^2 = 1.25$, $p = 0.26$) and 63.1% (82/130) ($x^2 = 7.96$, $p = 0.01$) at the end of 125-day and 180-day simulation period, respectively, in the intervention arm. In the control arm, malaria prevalence was reduced to 38.7% (72/186) and 17.7% (33/186) at the end of the 125-day and 180-day simulation period, respectively, using the baseline average temperature. When the temperature was increased by 1˚C the prevalence was reduced by 52.6% (98/186) ($x^2 = 3.39$, $p = 0.06$) and 38.7% (72/186) ($x^2 = 6.13$, $p = 0.01$) at the end of the 125-day and 180-day simulation period, respectively, whereas, the malaria prevalence was reduced by 43.5% (101/186) ($x^2 = 4.36$, $p = 0.04$) and 44.6% (83/186) ($x^2 = 10.56$, $p = 0.001$) at the end of the 125-day and 180-day simulation period, respectively, when the average temperature was reduced by 1 °C.

Table 2 Malaria prevalence when DP alone was used

Day	Intervention	Reduction	Control	Reduction
Baseline	11.5% (130/1135)		16.3% (186/1140)	
30	1.1% (13/1135)	90.0%	16.8% (191/1140)	– 2.7% (-5/186)
60	0.5% (6/1135)	95.4%	12.3% (140/1140)	24.7% (46/186)
90	0.3% (3/1135)	97.7%	10.0% (114/1140)	38.7% (72/186)
120	3.7% (42/1135)	67.7% (88/130)	9.6% (110/1140)	40.8% (76/186)
125	4.1% (47/1135)	63.8% (83/130)	10.0% (114/1140)	38.7% (72/186)
150	5.2% (59/1135)	54.6% (71/130)	10.9% (125/1140)	32.8% (61/186)
180	7.1% (80/1135)	38.5% (50/130)	13.4% (153/1140)	17.7% (33/186)

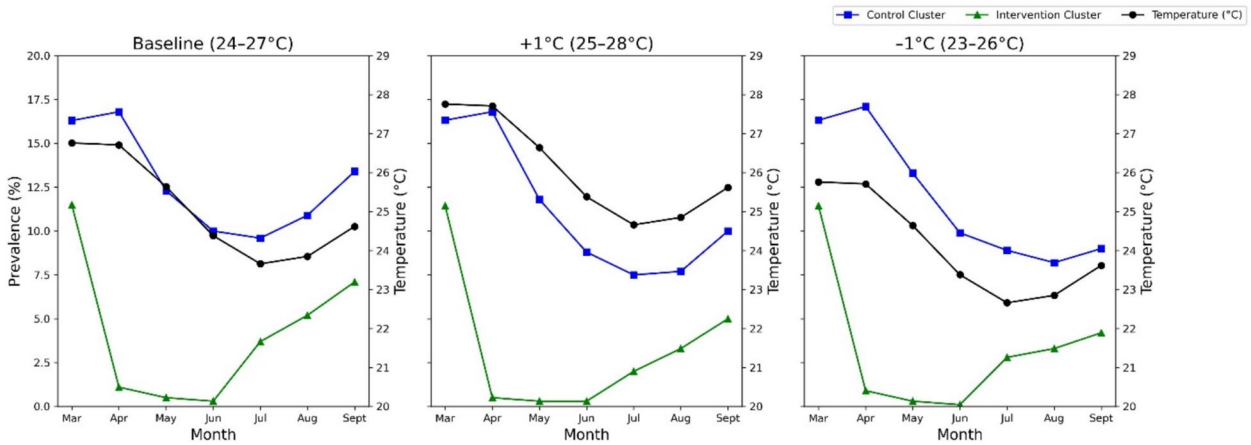

Fig. 2 Effect of Temperature variation on malaria prevalence

Comparison of malaria prevalence by ABMS and field observations after the interventions

Figure 3 depicts the prevalence of malaria before and after treatment in both the field and by ABMS. In the field, the baseline malaria prevalence was 13.8% (161/1171) in the intervention arm and 18.1% (212/1169) in the control arm [7]. The prevalence declined to 5.8% (60/1036) in the intervention arm seven weeks after the third round of SMC, and in the control clusters it dropped to 9.26% (97/1048) [7]. In the model, the baseline malaria prevalence was 11.5% (130/1135) in the intervention and 16.3% (186/1140) in the control arm. At the end of 125-day simulation period, the prevalence dropped to 4.1% (47/1135) in the intervention arm, and 10.0% (114/1140) in the control arm. Across both arms and time points, the results showed that there were no

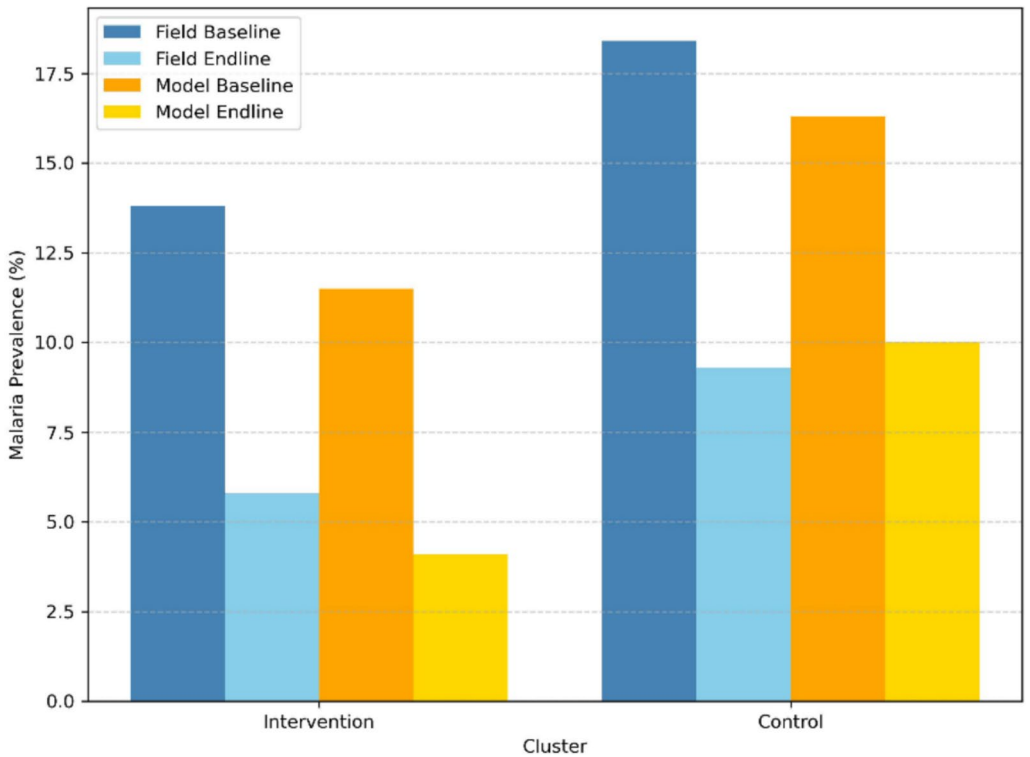

Fig. 3 Comparison of malaria prevalence between field observations and ABMS results

statistically significant differences between the model and the field results, Table 4.

Discussion

The SMC is advocated for control of malaria in children aged less than five years in endemic settings where malaria transmission is highly seasonal [7, 50, 51]. The southern region of Tanzania qualifies for the SMC, and recently the Ministry of Health recommended SMC using the available ACTs to control malaria in the region. However, the effectiveness of ACTs is reduced by its inability to kill mature *P. falciparum* gametocytes, a parasite stage responsible for transmitting the infection from man to the female *Anopheles* mosquito. Primaquine, in contrast, is effective against mature *P. falciparum* gametocytes; yet no community-based studies have been conducted in African population to ascertain the effectiveness of adding primaquine to ACTs. This study used ABMS in AnyLogic platform to assess the effect of adding SLDPQ to DP when used as SMC for control of malaria in children aged less than five years in Masasi and Nanyumbu Districts, Tanzania. The model findings indicated that, at the end of 125-day simulation period and the administration of three rounds of DP alone, malaria prevalence declined by 63.8% whereas in the control arm, the prevalence declined only by 41.9%. Similar findings have been reported in the field in Masasi and Nanyumbu Districts, Tanzania [7], and in other countries following the administration of ACT-based or non-ACT SMC without primaquine [7, 8, 52]. Furthermore, the addition of SLDPQ to DP led to a further decline of the malaria prevalence by approximately 87.6%, whereas in the control arm it declined by 53.2%. Similar findings have been reported in clinical trials conducted in other countries [15, 16, 53]. Primaquine can act both by killing and sterilizing the *P. falciparum* gametocytes, preventing the transmission of the infection from man to mosquito [12, 18, 54]. The additional effect observed in the model following the addition of SLDPQ to DP is attributed to the ability of primaquine to act against the mature gametocytes. Thus, the ABMS indicates that addition of SLDPQ to ACTs for SMC may probably lead to a significant decrease in malaria prevalence in the targeted population in Masasi and Nanyumbu Districts, and in other malaria-endemic settings where the transmission of the infection is highly seasonal.

Furthermore, temperature plays a crucial role in shaping malaria transmission by affecting mosquito development and breeding rates, and the extrinsic incubation period of *Plasmodium* with optimal transmission occurring at the range of 25 ˚C to 27 ˚C [55]. A small deviation from the average optimal temperature can cause a fluctuation in the transmission [56]. Compared with the percentage decline of malaria at the average field temperature, the percentage decline was higher when the temperature was increased or decreased by 1 ˚C from the average temperature at the end of 125-day simulation period. However, at the end of 180-day simulation period the percentage decline in malaria was statistically significantly higher after the increase in temperature by 1 ˚C. The findings signify the importance of time lapse after the interventions administration. At 125-day after SMC administration the intervention maintained its ability to control the infection, however, as the time goes the ability declined as indicated at the end of 180-day period. Conversely, the increase in average temperature by 1 ˚C had a slightly higher percentage of decline of malaria prevalence than the decrease in the average temperature by 1 ˚C. Furthermore, the high malaria prevalence at baseline indicated that the temperature was optimal for mosquito activities compared to when the temperature was reduced or increased by 1 ˚C. The baseline average temperature was also optimal for the parasite development in the mosquito. Malaria prevalence normally drops when the temperature falls below 24 °C or increases above 28 °C attributed by slower parasite development at cooler temperatures or increased mosquito mortality rate at hotter temperatures [55].

On the other hand, whereas randomized clinical trials play a significant role in assessing the efficacy new interventions, they are however relatively expensive and labour intensive [57], making modelling an important complementary tool. Mathematical and computational models have been widely used to study infectious diseases dynamics including malaria as well as the impact of various interventions strategies [21, 58–60]. Several

Table 4 Summary of statistical test results, including RD, RR, and significance measures

Cluster	Time point	Prevalence		P-values			
		Field	Model	Chi-square	Fisher's test	RR	RD
Intervention	Baseline	13.8	11.5	0.11035		0.833 (95% CI 0.671, 1.034)	− 0.0230 (95% CI − 0.0501, 0.0042)
Intervention	End line	5.8	4.1		0.09115	0.715 (95% CI 0.493, 1.038)	− 0.0165 (95% CI − 0.0354, 0.0018
Control	Baseline	18.1	16.3	0.27041		0.900 (95% CI 0.752, 1.076)	− 0.0182 (95% CI − 0.0490, 0.0127)
Control	End line	9.2	10.1	0.55866		1.080 (95% CI 0.835, 1.398)	0.0074 (95% CI − 0.0175, 0.0322)

studies have reported a strong agreement between modelling outputs and clinical trials findings [21, 58, 60, 61]. In this study, the ABMS findings were compared with the field findings from the same site where the data used in the model were collected. Both the ABMS and the field findings indicated a trend of decline of malaria prevalence after the three rounds of DP administration, supporting its external validity [62]. There was also no statistically significant difference in the prevalence of malaria at the end of 125-day simulation period in the model and at 7 weeks after DP administration in the field.

Despite its strength, the study had limitations: First, the ABMS relied on assumptions regarding coverage, adherence, and treatment completion, which were modelled as constant across all SMC rounds. In real-world settings, participation varies due to absenteeism, refusal, concurrent illness, or incomplete adherence, potentially affecting intervention impact. Second, the model incorporated simplified representations of human behaviour, mosquito ecology, and transmission dynamics, which may not fully capture the complexity of malaria epidemiology in diverse communities. Third, the model did not account for potential drug resistance, pharmacokinetic variability, or differences in host immunity, all of which could influence the effectiveness of DP or SLDPQ in practice. Nonetheless, it is unlikely that these limitations might have reduced the model's validity. Future study will explore the integration of malaria vaccination with SMC by building up on the modelling insights from Tchoumi et al., who demonstrated potential gains of combining vaccination with existing interventions [63].

Conclusion

The ABMS findings showed that the addition of SLDPQ to DP for SMC significantly reduced the prevalence of malaria in children under the age of five years in Nanyumbu and Masasi Districts. Therefore, SMC using DP plus SLDPQ can be implemented in the settings to control the infection. The strong agreement in findings between the field and model results indicates that ABMS can be employed to study the effectiveness of new interventions against different infections before they are deployed in the population.

List of abbreviations

ABMS	Agent based modelling and simulation
ACT	Artemisinin-based combination therapies
DP	Dihydroartemisinin-piperaquine
ITNs	Insecticides-treated bed nets
SLDPQ	Single Low-Dose of Primaquine
SMC	Seasonal malaria chemoprevention
RD	Risk difference
RR	Risk ratio

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Author contributions

CTM, DGN, ROM, JT, and TC conceptualized the study, CTM performed data curation, developed the model and drafted the original manuscript. DGN, JT, and TC, supervised the student, DGN, ROM, JT, and TC reviewed and edited the manuscript.

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Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The study was approved by the Kibong'oto Infectious Diseases Hospital-Nelson Mandela African Institution of Science and Technology—Centre for Educational Development in Health, Arusha, with reference number KNCHREC00067/09/2022.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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