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RESEARCH ARTICLE

Impact of Control Interventions on Malaria Incidence in the General Population of Mali

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Abstract

Background The increase in malaria incidence and the reduction of funding for malaria control have highlighted the need to step up efforts in the fight against malaria in Mali. To further refine the malaria control strategy implemented in the country, this study aimed to evaluate the impact of control interventions at the health district level on malaria incidence in the general population.

Method Malaria, rainfall, and intervention data were collected for the 75 health districts of Mali for the period from April 2017 to March 2022. The impact of the different control interventions on malaria incidence in the general population was assessed at the health district level with a Generalized Additive Mixed Model considering rainfall.

Results Although coverage rates varied widely between health districts, most interventions showed an improvement in coverage over the study period. Two interventions had a small impact on incidence: long-lasting insecticidal net mass distribution (LLIN), with a reduction rate of 2.2 ‰ for an adjusted coverage rate from 30.0 to 79.0% (odds ratio (OR): 0.998; 95% confidence interval (CI) 0.997–0.999), and seasonal malaria chemoprevention (SMC), with a reduction rate of 1.9 ‰ for an adjusted coverage rate from 30.0 to 80.0% (OR: 0.9979; 95% CI 0.996–0.998).

Conclusion The analysis found a small impact of LLIN and SMC on malaria incidence at the district level. Malaria control should be reinforced by improving coverage and utilization rates in the general population and in the most vulnerable groups and by deploying larger numbers of community health workers where needed.

Keywords Impact · Malaria · Evaluation of interventions · Geo-epidemiology · Mali

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Abbreviations

WHO	World Health Organization
GTS	Global Technical Strategy
iCCM	Integrated community case management
SMC	Seasonal malaria chemoprevention
IPTp	Intermittent preventive treatment in pregnancy
LLIN	Long-lasting insecticidal net
IRS	Indoor residual spraying
NMCP	National Malaria Control Program
RDT	Rapid diagnostic test
ACT	Artemisinin-based combination therapy
SP + AQ	Sulfadoxine pyrimethamine + amodiaquine
SP	Sulfadoxine pyrimethamine
DOT	Directly observed treatment
GPHC	General Population and Housing Census
DHIS2	District Health Information Software version 2
CHIRPS	Climate Hazards Group InfraRed Precipitation with Station Data
DHS	Demographic and Health Survey

GAMM Generalized Additive Mixed Model
OR Odds ratio
CI Confidence interval
NSP Nation strategic plan

1 Introduction

Despite significant progress in the fight against malaria in the first two decades of the century, the global burden of the disease remains high. In 2022, there were an estimated 249 million cases of malaria worldwide, a 5 million increase compared with 2021 [1]. The rise in the global number of malaria cases is largely explained by growing vector resistance to insecticides and by the rise in political and security conflicts in many parts of Africa. In addition, the global economic crisis and the application of austerity programs have led to cuts in funding for malaria control, setting back progress in many endemic countries [1–3]. In 2021, global malaria spending totaled $3.5 billion, far short of the annual funding target of $7.5 billion [1]. Both the rise in malaria incidence and the reduction of funding have prompted malaria endemic countries and their international partners to devise new approaches for improving the allocation of resources in the fight against the disease.

Mali is among the 11 countries where an increase in malaria transmission has been observed in recent years. Between 2021 and 2022, the number of cases in the country rose from 3,204,130 to 3,770,000 and incidence went from 150 to 172 per 1000 person-years [4]. As in neighboring countries, growing vector resistance and political and security conflicts have played a role in this trend [4]. Another key factor is the reduction of funding for malaria control, with only 45% of estimated budget met in 2022 compared to 81% in 2019 [4]. This drop is especially worrisome since the vast majority of the mobilized funds come from international partners, all of which are directed towards priority activities [4].

The World Health Organization (WHO) Global Malaria Program is the cornerstone of efforts to control and eliminate malaria at the global level. This program builds on the Global Technical Strategy (GTS) for Malaria 2016–2030, a framework adopted by the World Health Assembly in 2015 that set the target of reducing global malaria incidence and mortality rates by at least 90% by 2030 [5]. The WHO Guidelines for Malaria (2023) recommend the following interventions [6]: case management through early diagnosis and prompt treatment in health facilities and in community health worker sites as part of integrated community case management (iCCM); prevention through seasonal malaria chemoprevention (SMC) and intermittent preventive treatment in pregnancy (IPTp); vector control through the distribution of long-lasting insecticidal nets (LLIN), indoor residual spraying (IRS), and larval control; and mass drug administration. In addition, the WHO Framework for Malaria Elimination (2017) encourages malaria endemic countries to conduct risk stratifications, as these can help tailor interventions in different health zones according to the level of transmission risk [7].

The malaria control strategy of Mali is in line with the WHO Malaria Guidelines and Framework for Malaria Elimination and is coordinated at different levels by the National Malaria Control Program (NMCP). The following malaria control interventions have been put in place in the country: case management through early diagnosis and prompt treatment in public or private health facilities and in community health worker sites as part of iCCM; SMC; IPTp; LLIN mass distribution; LLIN routine distribution; and IRS [4]. All interventions are funded by international partners (mainly the Global Fund and the U.S. President's Malaria Initiative) and implemented by Malian health personnel.

In Mali, e*arly diagnosis* of all suspected cases is performed free of charge either by rapid diagnostic test (RDT) or by thick blood smear microscopy. Over the 2018–2022 period, 76% (15,390,276) of suspected cases were tested by RDT and 15% (2,951,036) by thick blood smear [4]. *Prompt treatment* consists of the oral administration of artemisinin-based combination therapy (ACT) for uncomplicated malaria cases and the injection of artesunate (or artemether or quinine as second line) for severe malaria cases. Treatment is currently free of charge for children under 5 years and for pregnant women [4]. *Integrated community case management* (iCCM) entails the provision of care by community health workers to households located within a radius of 3 km from a community health worker site and includes the management of uncomplicated malaria cases for all ages. The intervention was introduced in Mali in 2010 [8].

Seasonal malaria chemoprevention (SMC) is the door-to-door administration of sulfadoxine pyrimethamine + amodiaquine (SP + AQ) to children aged 3 to 59 months once a month during the high transmission season (from July to October). The intervention was initiated in Mali in 2012 [9, 10] with a pilot study in the health district of Koutiala (Sikasso region in the south) and was then gradually expanded between 2013 and 2016. After a successful pilot phase in the health district of Kita (Kayes region in the south) in 2017, SMC was extended to children aged 5–10 years in 2018 (as was the case in Senegal) in 3 health districts with high transmission (Sélingué, Koutiala, and Kadiolo) in the southern region of Sikasso [11]. In 2016, the intervention was scaled up to the national level for all children aged 3 to 59 months. Since the malaria stratification of 2020 [12], SMC has been implemented in 3 cycles in districts with low malaria transmission (essentially in the north of the country) and in 4 or 5 cycles in districts with high transmission (mainly in the south and center) [13].

Intermittent preventive treatment in pregnancy (IPTp) consists in the administration of a monthly dose of sulfadoxine pyrimethamine (SP) to pregnant women from the 13th week of amenorrhea, which corresponds to the beginning of fetal movement. The SP dose is administered free of charge during prenatal consultations through directly observed treatment (DOT). This intervention was integrated into the prevention policy for women in 2007 [14, 15].

Long-lasting insecticidal net (LLIN) *mass distribution* is performed in large-scale campaigns with the aim of achieving universal coverage, which is defined as 1 LLIN for 2 people [16, 17]. Since LLINs have a lifespan of about 3 years, mass distribution campaigns target one third of regions each year, such that all regions are covered once every 3 years. The intervention was first conducted in 2011 in the southern region of Sikasso and was scaled up to the national level in 2023 based on the stratification conducted in 2020 [12]. As part of the 2023 campaign [18], the more effective interceptor G2 nets and long-lasting piperonyl butoxide-treated insecticidal nets were distributed in health districts where vector resistance to standard LLINs is confirmed [4]. *Long-lasting insecticidal net routine distribution* consists of the free distribution of LLINs to pregnant women during the first prenatal consultation and to children under 1 year during measles vaccination. This intervention was introduced in 2001 and was intensified in 2007 as part of the Keneya Sugu ("Health Fair" in Bambara) vaccination campaign [19].

Indoor residual spraying (IRS) involves the coating of walls and other surfaces in people's houses with a residual insecticide. This intervention was performed in 8 health districts (all health areas) in 2017 and in 2 health districts (18 out of 85 health areas) in 2020. It was discontinued in 2022 due to its very high operational cost.

As in other endemic countries, the increase in malaria incidence and the reduction of funding have highlighted the need to step up efforts in the fight against malaria in Mali. In 2020, the Mali NMCP conducted a risk stratification [13] and set up a mechanism for the monitoring of data and the evaluation of interventions [20]. To help further refine the malaria control strategy implemented in the country, this study aimed to assess the impact of control interventions at the health district level on malaria incidence in the general population considering rainfall.

2 Methods

2.1 Study Location

The Republic of Mali is a West African country located in the Sahel-Saharan strip. In 2022, Mali had 21,904,768 inhabitants and its population growth rate was estimated at 2.7% (General Population and Housing Census (GPHC) 2009 data updated by the National Statistical Institute).

The Malian health care system is organized as a pyramid with 3 levels: the national level, the regional level, and the health district level. Mali is comprised of 11 regions (including the District of Bamako) and 75 health districts. It is characterized by 3 types of climate: the desert climate of the Sahara in the north (where most of the precipitation occurs between August and September and annual rainfall rarely exceeds 100 mm); the semi-desert climate of the Sahel in the center (where the rainy season lasts from June to September and annual rainfall ranges from 100 to 600 mm), and the tropical savannah climate of the south (which is marked by an intense rainy season lasting from May to October and an annual rainfall of up to 1200 mm).

2.2 Data Collection

Data were collected for the 75 health districts of Mali for the period from April 2017 to March 2022.

2.2.1 Malaria Data

Monthly aggregated data on confirmed malaria cases were collected at the health district level from the District Health Information Software version 2 (DHIS2). No personal data were used.

2.2.2 Population Data

Data on population by health district were collected from the National Population Directorate. These data are updated yearly by multiplying GPHC 2009 population figures by the annual national population growth rate of 2.7% [21].

2.2.3 Rainfall Data

Daily rainfall data were collected at the health district level from the Climate Hazards Group InfraRed Precipitation with Station Data (CHIRPS) via the Google Earth engine interface (0.05° resolution) [22, 23]. Remote sensing rainfall data were used because the 24 observation stations currently in operation in Mali do not cover all 75 health districts.

2.2.4 Intervention Data

Data were collected on the number of recipients at the health district level for the following interventions: testing (by RDT or thick blood smear); malaria treatment (with ACT or injectables); SMC; IPTp; LLIN routine distribution; and LLIN mass distribution. For iCCM, data were collected on the number of community health workers at the health district level.

The above data were collected from the NMCP annual reports for SMC and LLIN mass distribution and from the DHIS2 for all other interventions.

For SMC, data on uptake were collected at the regional level from the 2021–2022 NMCP report on SMC monitoring [24]. For LLIN mass distribution and LLIN routine distribution, data on utilization were collected at the regional level from the 2018 Demographic and Health Survey (DHS).

The source, period, and frequency of the collected data are shown in Table 1.

2.3 Data Analyses

The main indicators used in the analyses below are summarized in Table 2.

2.3.1 Temporal Analysis

In most health districts of Mali, the period of high malaria transmission spans two administrative years. To avoid attributing an epidemic tail to the next epidemic wave, each malaria epidemic year was defined from April to March of the following year. All malaria cases occurring during the same epidemic wave were grouped together in the analyses.

Median annual malaria incidence (per 1000 person-years) was calculated at the health district level.

Monthly malaria incidence (per 1000 person-months) was calculated at the national level for the 5 epidemic years by dividing the monthly number of new confirmed cases by the total population.

Monthly rainfall was calculated at the national level for the 5 epidemic years by summing daily rainfall.

Table 1 Source, period, and frequency of the collected data

Variable	Details	Source	Period	Frequency
Malaria cases	Malaria data is defined as monthly incidence of parasitological-confirmed malaria per 1000 population at the health district level	DHIS2	2018–2022	Monthly
Population data	Population data represent the updated population per health district for each year	GPHC	2018–2022	Yearly
Rainfall data 0.05° resolution	Rainfall data represent total rainfall by health district for each epidemic year	CHIRPS		Daily
Usage rate of LLINs The coverage rate for LLIN mass The coverage rate for LLIN routine	The coverage rate for LLIN mass distribution was calculated for each health district by dividing the number of distributed LLINs by half of the total population The coverage rate for LLIN routine distribution was calculated for each health district by dividing the number of distributed LLINs by the population of pregnant women and children under 1 year	DHS	2018	Every 5 Years
Fever prevalence of children	Fever prevalence of children is the proportion of febrile children who received care in public health facilities	DHS	2018	Every 5 Years
Intervention data Diagnosis rate	The diagnosis rate was calculated for each health district by dividing the number of tests performed using RDT and thick blood smear by the number of suspected malaria cases	DHIS2	2018–2022	Monthly
Treatment rate	The treatment rate was obtained for each health district by dividing the number of patients treated for uncomplicated or severe malaria by the number of confirmed malaria patients	DHIS2	2018–2022	Monthly
SMC rate		Report	2018–2022	Yearly
iCCM rate	The iCCM rate number of community health workers by the population to take account of the absence of CHWs	DHIS2	2018–2022	Yearly
IPTp rate	The IPTp coverage rate was determined for each health district by dividing the number of pregnant women who received at least 3 doses of SP by the total number of pregnant women	DHIS2 Report	2018–2022 2018–2020	Monthly Every 3 years

SMC seasonal malaria chemoprevention, *IPTp* intermittent preventive treatment in pregnancy, *LLIN* long-lasting insecticidal net, *DHIS2* District Health Information Software version 2, *GPHC* General Population and Housing Census, *CHIRPS* Climate Hazards Group InfraRed Precipitation with Station data, *DHS* Demographic and Health Survey

Table 2 Main indicators used in the analyses

Indicators	Definition
Annual malaria incidence (cases per 1000 person-years)	Annual number of confirmed malaria cases per 1000 population
Monthly malaria incidence (cases per 1000 person-months)	Monthly number of confirmed malaria cases per 1000 population
Annual rainfall (mm)	Annual sum of daily rainfall
Monthly rainfall (mm)	Monthly sum of daily rainfall
Intervention Coverage rates Testing (%)	Number of tests performed using RDT or thick blood smear divided by the number of suspected malaria cases
Treatment (%)	Number of patients treated for uncomplicated or severe malaria divided by the number of confirmed malaria patients
iCCM (population per community health worker)	Total population divided by the number of community health workers
SMC (%)	Mean number of children aged 3 to 59 months who received 1 round of SMC divided by the population of children aged 3 to 59 months
IPTp (%)	Number of pregnant women who received at least 3 doses of SP divided by the total number of pregnant women
LLIN mass distribution (%)	Number of LLINs distributed in a mass campaign divided by half the total population, based on the target of one LLIN per every 2 people
LLIN routine distribution (%)	Number of routinely distributed LLINs divided by the population of pregnant women and children under 1 year
LLIN utilization rate in the general population (%)	Proportion of people who slept under an LLIN the day before the survey
LLIN utilization rate in pregnant women and children under 1 year (%)	Proportion of women and children under 1 year who slept under an LLIN the day before the survey
Care-seeking rate (%)	Proportion of febrile children who received care in a public health facility
iCCM inverted ratio (community health workers per person)	Number of community health workers divided by the total population

iCCM integrated community case management, *SMC* seasonal malaria chemoprevention, *IPTp* intermittent preventive treatment in pregnancy, *LLIN* long-lasting insecticidal net, *RDT* rapid diagnostic test

2.3.2 Spatial Analysis

For the spatial analysis, all data were aggregated per epidemic year for each health district.

2.3.2.1 Malaria Incidence To account for variations in health facility utilization between health districts, the number of malaria cases per district was adjusted using the method recommended by the WHO in its 2023 annual report (Method 1) [1]:

$$N1 = \mathrm{a} + \mathrm{b}\,\frac{\mathrm{a}}{c} \quad (1)$$

$$N2 = \frac{\mathrm{N1}}{d} \quad (2)$$

$$N3 = \mathrm{N2} \times \frac{\mathrm{f}}{e} + \frac{\mathrm{g}}{e} \quad (3)$$

N1 is the number of cases adjusted by the positivity rate; ***N2*** is the number of cases adjusted by the testing and reporting rates; ***N3*** is the number of cases adjusted by the testing, reporting, and care-seeking rates; ***a*** is the number of confirmed malaria cases reported by public health facilities; ***b*** is the number of presumptive malaria cases (i.e., untested cases treated as malaria); ***c*** is the number of confirmed malaria cases; ***d*** is the reporting rate (number of reports received / number of expected reports) adjusted according to the type of health facility that did not report cases at a given time; ***e*** is the proportion of febrile children who received care in public health facilities; ***f*** is the proportion of febrile children who received care in private health facilities; and ***g*** is the proportion of febrile children who did not seek care. Data for variables *e*, *f*, and *g* were collected at the regional level from the 2018 DHS.

$$adjusted\,malaria\,incidence = \frac{N3}{population \times time} \times 1,000 \quad (4)$$

Malaria incidence was classified into 4 categories: high (> 450 cases per 1000 person-years); moderate (450–250 cases per 1,000 person-years); low (249–100 cases per 1000 person-years); and very low (< 100 cases per 1000 person-years), in accordance with the WHO Framework for Malaria Elimination [7].

A district-level map of annual malaria incidence was built for each of the 5 epidemic years.

2.3.2.2 Rainfall Cumulative annual rainfall was calculated at the health district level for the 5 epidemic years by summing daily rainfall.

A district-level map of annual rainfall was built for each of the 5 epidemic years.

2.3.2.3 Interventions The testing rate was calculated for each health district by dividing the number of tests performed using RDT or thick blood smear by the number of suspected malaria cases.

The treatment rate was obtained for each health district by dividing the number of patients treated for uncomplicated malaria (with ACT) or severe malaria (with injectables) by the number of confirmed malaria patients.

The iCCM coverage rate was calculated for each health district by dividing the total population by the number of community health workers. This rate is written as the population per community health worker.

Given that SMC rounds are distributed in 3 to 5 cycles in Mali, the SMC coverage rate was calculated for each health district by dividing the mean number of children aged 3 to 59 months who received 1 round of SMC by the population of children aged 3 to 59 months.

The IPTp coverage rate was determined for each health district by dividing the number of pregnant women who received at least 3 doses of SP by the total number of pregnant women.

The coverage rate for LLIN mass distribution was calculated for each health district by dividing the number of distributed LLINs by half the total population, based on the target of one LLIN per every 2 people [17]. To account for the fact that health districts are covered by LLIN distribution campaigns only once every 3 years, the coverage rates for the second and third years after distribution were calculated by applying a reduction factor of 25.0% and 50.0%, respectively, to the coverage rate calculated for the first year after distribution [25].

The coverage rate for LLIN routine distribution was calculated for each health district by dividing the number of distributed LLINs by the population of pregnant women and children under 1 year.

For each intervention, coverage rates were mapped at the health district level for the 5 epidemic years.

2.3.3 Modeling Analysis

A modeling analysis of the effects of control interventions on malaria incidence considering rainfall was performed using a spatio-temporal Generalized Additive Mixed Model (GAMM) [26, 27].

All data used in the model were aggregated per epidemic year at the health district level.

For some indicators, coverage rates were adjusted before being entered in the model to account for the gap between administrative coverage and uptake/utilization of inputs. Adjustments were performed as follows:

- For SMC, the adjusted coverage rate was calculated by weighting the administrative coverage rate by the rate of uptake of SP + AQ in children aged 3 to 59 months during each cycle for each health district. The latter rate was calculated based on regional rates of uptake provided in the 2021–2022 NMCP report on SMC monitoring [24].
- For LLIN mass distribution, the adjusted coverage rate was calculated by weighting the administrative coverage rate by the utilization rate of LLINs in the general population for each health district. The latter rate was calculated based on regional utilization rates provided in the 2018 DHS of Mali [28].
- For LLIN routine distribution, the adjusted coverage rate was calculated by weighting the administrative coverage rate by the utilization rate of LLINs in pregnant women and children under 1 year for each health district. The latter rate was calculated based on regional utilization rates provided in the 2018 DHS of Mali [28].

The iCCM indicator used in the modeling analysis (named “iCCM inverted ratio”) was defined as the number of community health workers divided by the total population.

2.3.3.1 Univariate Analysis A univariate analysis of adjusted malaria incidence considering rainfall was conducted to determine the impact of each intervention in the general population. Non-linear relationships between quantitative variables and adjusted incidence were identified using spline smoothing. To account for the spatial structure of the data, a Gaussian field of geographic coordinates was generated. A quasi-Poisson distribution was used due to the overdispersion of dependent variables (Var $(Y_i) = \varphi.\mu_i$). The standardized incidence ratios of interventions were estimated by modeling the log-transformed population as the offset.

The GAMM was built using the following equation:

$$\begin{aligned} log\left(Case_i\right) = offset\left(log\left(Pop_i\right)\right) + f_1\left(Rainfall_i\right) \\ + f_2\left(InterventionCoveragerate_i, bs = cr\right) \\ + f_3(Lat, Lon, bs = \mathrm{gp}, m = 2) \\ + random = list(Year = \sim 1) + \varepsilon \end{aligned} \quad (5)$$

i: health district*; case*: adjusted number of confirmed cases; *Pop*: population; $bs=cr$: cubic regression spline*; lat:* latitude; *lon:* longitude; $bs=gp$*:* gaussian process; *m*: smooth spatial covariance negative power exponential function; *year*: epidemic year.

2.3.3.2 Multivariate Analysis A multivariate analysis of adjusted malaria incidence considering rainfall was performed to determine the overall impact of interventions in the general population. Non-linear relationships between quantitative variables and adjusted incidence were identified using spline smoothing. To account for the spatial structure of the data, a Gaussian field of geographic coordinates was generated. A quasi-Poisson distribution was used due to overdispersion of dependent variables. The standardized incidence ratios of interventions were estimated by modeling the log-transformed population as the offset. Testing and treatment rates were included as interaction terms in the analysis because of their high dependency on malaria incidence.

The multivariate GAMM was performed using the following equation:

$$\begin{aligned} &log\left(Case_i\right) = offset(log(Pop)) + f_i(rainfall) + testing : treatment+ \\ &f_i\left(coverage\ rate\ for\ iCCM_i, bs = cr\right) + f_i\left(adjusted\ coverage\ rate\ for\ SMC_i, bs = cr\right)+ \\ &f_i\left(coverage\ rate\ for\ IPTp_i, bs = cr\right) + f_i\left(adjusted\ coverage\ rate\ for\ LLIN\ routine_i, bs = cr\right)+ \\ &f_i\left(adjusted\ coverage\ rate\ for\ LLIN\ mass\ distribution_i, bs = cr\right) + f_2(lat, lon, bs = \mathrm{gp}, m = 2)+ \\ &random = list(year =\sim 1) + \varepsilon. \end{aligned} \tag{6}$$

i: health district*; case*: adjusted number of confirmed cases; *Pop*: population; $bs=cr$: cubic regression spline*; lat:* latitude; *lon:* longitude; $bs=gp$*:* gaussian process; *m*: smooth spatial covariance negative power exponential function; *year*: epidemic year.

For each intervention, odds ratios was calculated using the estimates from the GAMM model [29].

Statistical significance was set at $p<0.05$.

2.3.3.3 Software Statistical analyses were performed using R software version 4.1.2. (The R Foundation for Statistical Computing Platform 2021) with the packages {mgcv}, {ggplot2} and {plyr}.

3 Results

3.1 Temporal Analysis

3.1.1 Malaria Incidence

At the national level, the number of confirmed malaria cases increased from 2,213,792 (4,536,142 after adjustment) in 2017–2018 to 2,956,964 (6,543,928 after adjustment) in 2021–2022. Median malaria incidence for the 5 epidemic years was 351.06 cases per 1,000 person-years. The median incidence went from 255.5 cases per 1,000 person-years in the first epidemic year (2017–2018) to 325.2 cases per 1,000 person-years in the last epidemic year (2021–2022). A peak in malaria incidence was observed in the years 2019–2020 and 2020–2021.

The evolution of monthly malaria incidence at the national level according to administrative and epidemic years is shown in Fig. 1. Note that all malaria cases occurring during the same epidemic wave were grouped together in the analysis.

Monthly rainfall at the national level for the 5 epidemic years is shown in Fig. S1.

3.2 Spatial Analysis

3.2.1 Malaria Incidence

Adjusted annual malaria incidence was mapped at the health district level for each of the 5 epidemic years (Fig. 2).

Very low incidences were recorded in the northern health districts throughout the study period. The lowest incidence (12.2 cases per 1,000 person-years) was observed in the health district of Al-Ourche (Taoudenni region in the north) in the year 2017–2018. Health districts located in the south and in the Inner Niger River Delta had the highest malaria incidences. The highest incidence (820.6 cases per 1,000 person-years) was recorded in the health district of Yorosso (Sikasso region in the south) in the year 2019–2020.

A district-level map of unadjusted annual malaria incidence for the 5 epidemic years is provided in Fig. S2.

3.2.2 Rainfall

Cumulative annual rainfall was mapped at the health district level for each of the 5 epidemic years (Fig. 3).

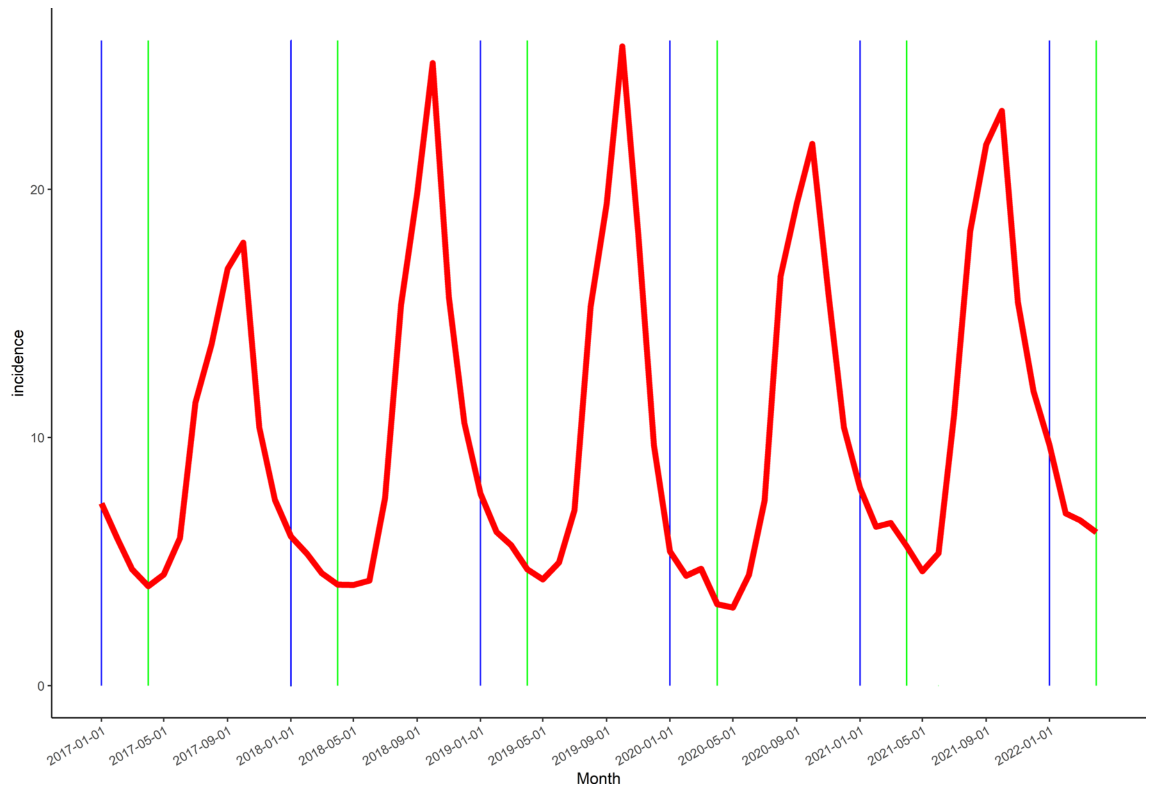

Fig. 1 Unadjusted monthly malaria incidence according to administrative and epidemic years: red line: malaria incidence (cases per 1000 person-months); blue line: start of administrative year; green line: start of epidemic year

The median annual rainfall for the 75 health districts and the 5 epidemic years was 638 mm. The median annual rainfall for the 75 health districts decreased slightly from 591 mm in 2017–2018 to 543 mm in 2021–2022. The lowest annual rainfall (16 mm) was observed in the health district of Taoudenni (Taoudenni region in the north) in the year 2017–2018. The highest annual rainfall (1 355 mm) was observed in the health district of Yanfolila (Sikasso region in the south) in the year 2021–2022.

3.2.3 Interventions

Coverage rates for testing, treatment, iCCM, SMC, IPTp, LLIN mass distribution, and LLIN routine distribution were estimated and mapped at the district level for each of the 5 epidemic years. All maps were built using unadjusted coverage rates.

3.2.3.1 Testing The testing rate was mapped at the health district level for each of the 5 epidemic years (Fig. 4).

The median testing rate for the 75 health districts and the 5 epidemic years was 94.0%. The median annual testing rate increased from 98.3% in 2017–2018 to 100.0% in 2021–2022, with a small drop in 2019–2020 and 2020–2021. The lowest testing rate (42.8%) was observed in the health district of Anderamboukane (Menaka region in the north) in the year 2020–2021. A testing rate of 100.0% was recorded in 43 health districts in 2017–2018, in 8 health districts in 2019–2020, and in 7 health districts in 2021–2022.

3.2.3.2 Treatment The treatment rate was mapped at the health district level for each of the 5 epidemic years (Fig. 5).

The median treatment rate for the 75 health districts and the 5 epidemic years was 90.7%. The median annual rate rose from 71.0% in 2017–2018 to 100.0% in 2021–2022. The lowest treatment rate (14.4%) was observed in the health district of Tidermene (Menaka region in the north) in the year 2021–2022. A treatment rate above 75.0% was recorded in 73 health districts in the year 2021–2022.

3.2.3.3 Integrated Community Case Management (iCCM) The iCCM coverage rate was mapped at the health district level for each of the 5 epidemic years (Fig. 6).

The median iCCM coverage rate for the 75 health districts and the 5 epidemic years was 6,197 population per community health worker. The median annual rate remained stable over the study period. The worst coverage rate (36,962 population per community health worker) was observed in the health district of Nioro (Kayes region in the south) in the year 2021–2022. The best coverage rate (652 population

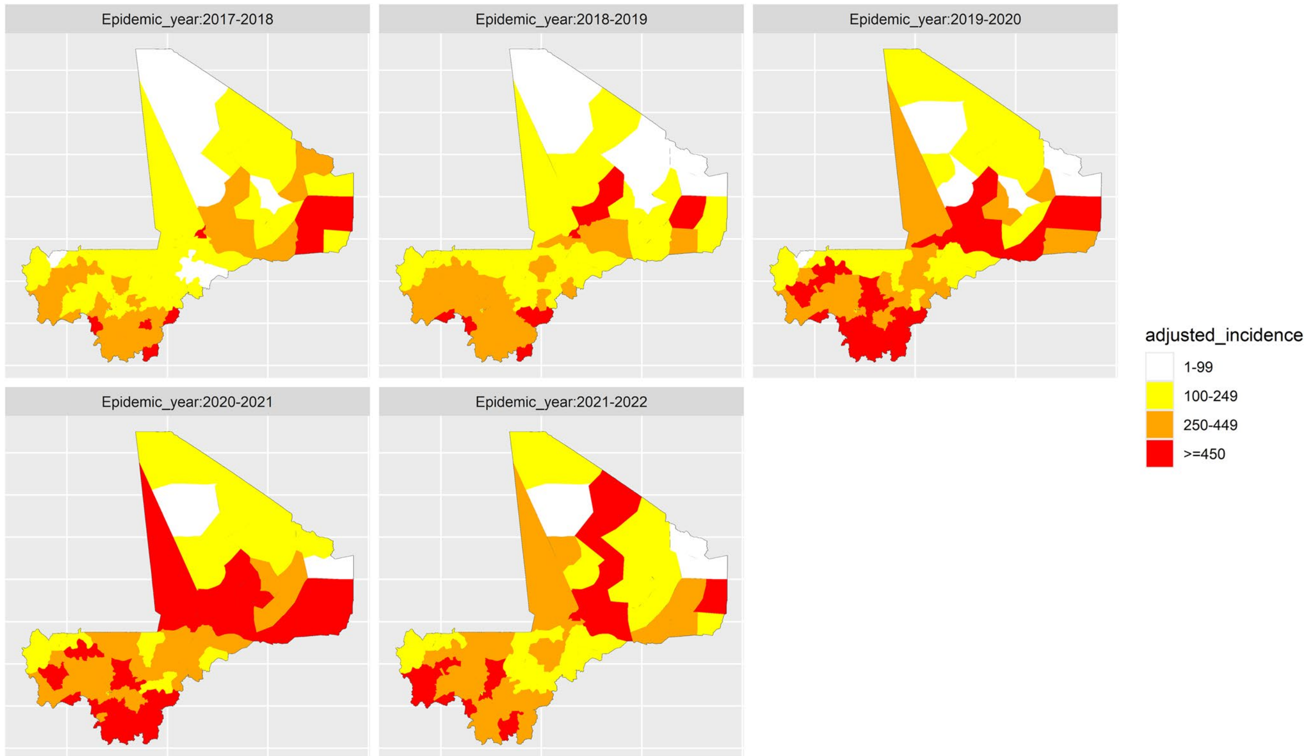

Fig. 2 District-level map of adjusted malaria incidence (cases per person-years)

per community health worker) was observed in the health district of Kidal (Kidal region in the south) in the year 2021–2022.

3.2.3.4 Seasonal Malaria Chemoprevention The SMC coverage rate was mapped at the health district level for each of the 5 epidemic years (Fig. 7).

The median SMC coverage rate for the 75 health districts and the 5 epidemic years was 92.7%. The median annual rate increased from 91.8% in 2017–2018 to 95.0% in 2021–2022. The lowest SMC coverage rate (30.9%) was observed in the health district of Inekar (Menaka region in the north) in the year 2017–2018. The highest SMC coverage rate (175.6%) was observed in the health district of Tidermene (Menaka region in the north) in the year 2019–2020.

A district-level map of adjusted coverage rates for SMC for the 5 epidemic years is provided in Fig. S3.

3.2.3.5 Intermittent Preventive Treatment in Pregnancy The IPTp coverage rate was mapped at the health district level for each of the 5 epidemic years (Fig. 8).

The median IPTp coverage rate for the 75 health districts and the 5 epidemic years was 32.4%. The median annual rate increased from 22.8% in 2017–2018 to 31.9% in 2021–2022. The lowest IPTp coverage rate (8.4%) was observed in the health district of Tin-essako (Menaka region in the north) in the year 2019–2020. The highest IPTp coverage rate (94.5%) was observed in the health district of Kangaba (Koulikoro region in the south) in the year 2021–2022.

3.2.3.6 Long-Lasting Insecticidal Net Mass Distribution The coverage rate for LLIN mass distribution was mapped at the health district level for each of the 5 epidemic years (Fig. 9).

The median coverage rate for LLIN mass distribution for the 75 health districts and the 5 epidemic years was 75.0%. The coverage rate for LLIN mass distribution reached the NMCP target of 80% in all health districts covered by a distribution campaign in the previous 3 years.

A district-level map of adjusted coverage rates for LLIN mass distribution for the 5 epidemic years is provided in Fig. S4.

3.2.3.7 Long-Lasting Insecticidal Net Routine Distribution The coverage rate for LLIN routine distribution was mapped at the health district level for each of the 5 epidemic years (Fig. 10).

The median coverage rate for LLIN routine distribution for the 75 health districts and the 5 epidemic years was 75.0%. The median annual rate increased from 60.9% in

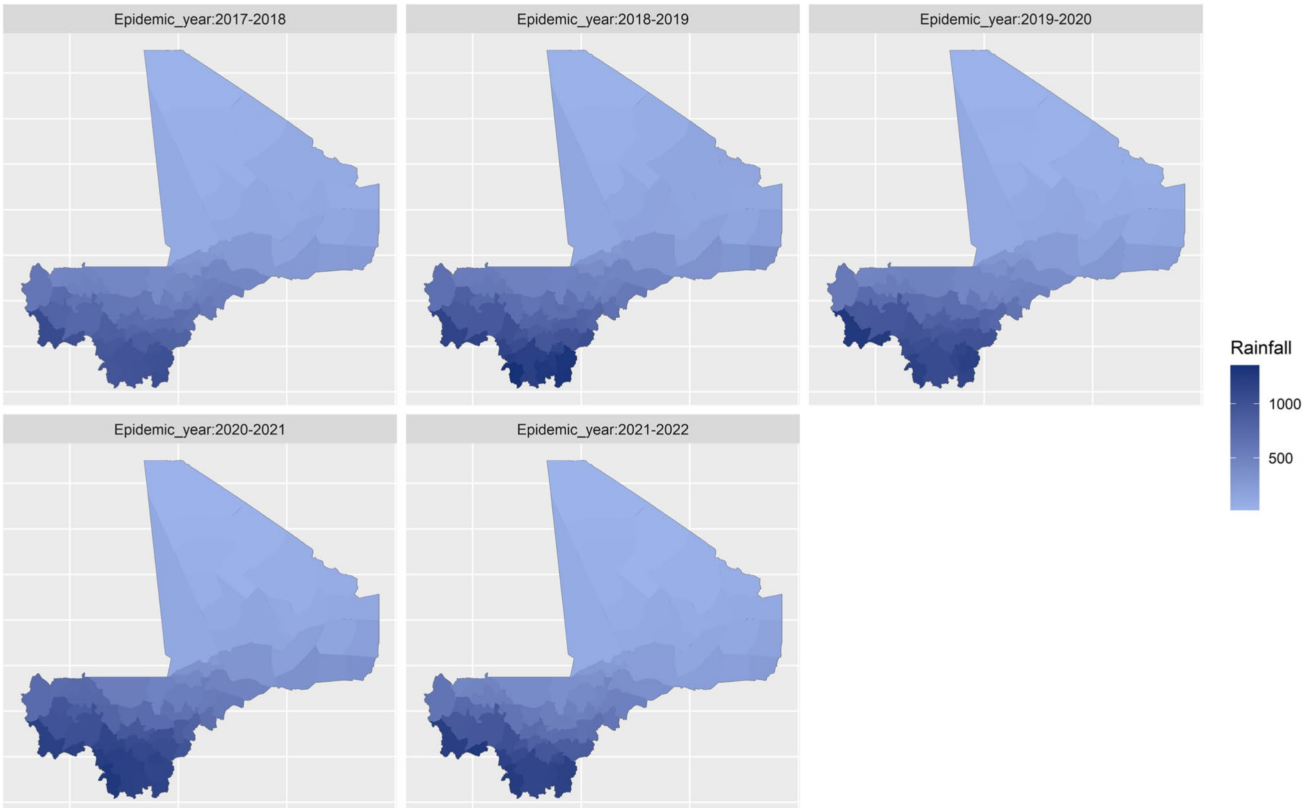

Fig. 3 District-level map of cumulative annual rainfall (mm)

2017–2018 to 66.8% in 2021–2022. The lowest coverage rate (0.9%) was observed in the health district of Tin-essako (Kidal region in the north) in the year 2017–2018. The highest coverage rate (161.0%) was observed in the health district of Kangaba (Koulikoro region in the south) in the year 2021–2022.

A district-level map of adjusted coverage rates for LLIN routine distribution for the 5 epidemic years is provided in Fig. S5.

3.3 Modeling Analysis

3.3.1 Univariate Analysis

In univariate analysis, LLIN mass distribution ($p < 0.001$), LLIN routine distribution ($p < 0.001$), IPTp ($p = 0.006$), iCCM (p = 0.003), and SMC ($p < 0.001$) had a significant negative relationship with malaria incidence in the general population. Significant positive linear relationships were observed between the testing rate and malaria incidence ($p < 0.001$). The iCCM indicator had a non-significant negative relationship with malaria incidence ($p < 0.67$). Incidence increased with the treatment rate but then decreased at higher values ($p < 0.001$). There was a significant positive effect of LLIN routine distribution on malaria incidence.

3.3.2 Multivariate Analysis

In multivariate analysis, LLIN mass distribution ($p < 0.001$) and SMC ($p = 0.009$) had a small reducing effect on malaria incidence in the general population. For LLIN mass distribution, the analysis found a 2.2‰ reduction in malaria incidence in health districts with an adjusted coverage rate from 30.0 to 79.0% (odds ratio (OR): 0.998; 95% confidence interval (CI) 0.997–0.999). For SMC, the reduction in malaria incidence was 1.9‰ in health districts with an adjusted coverage rate from 50.0 to 80.0% (OR: 0.9979; 95% CI 0.996–0.998). There was a statistically significant increasing effect of LLIN routine distribution on malaria incidence for an adjusted coverage rate from 20.0 to 40.0% (OR: 1.109; 95% CI 0.969–1.268) and an adjusted coverage rate from 41.0 to 80.0% (OR: 1.229; 95% CI 1.012–1.494), likely due to a confounding by indication bias. Similarly, IPTp had a statistically significant increasing effect on malaria incidence for an adjusted coverage rate from 41.0 to 60.0% (OR: 1.188; 95% CI 1.021–1.383), also likely due to a confounding by indication bias. The testing and treatment rates increased

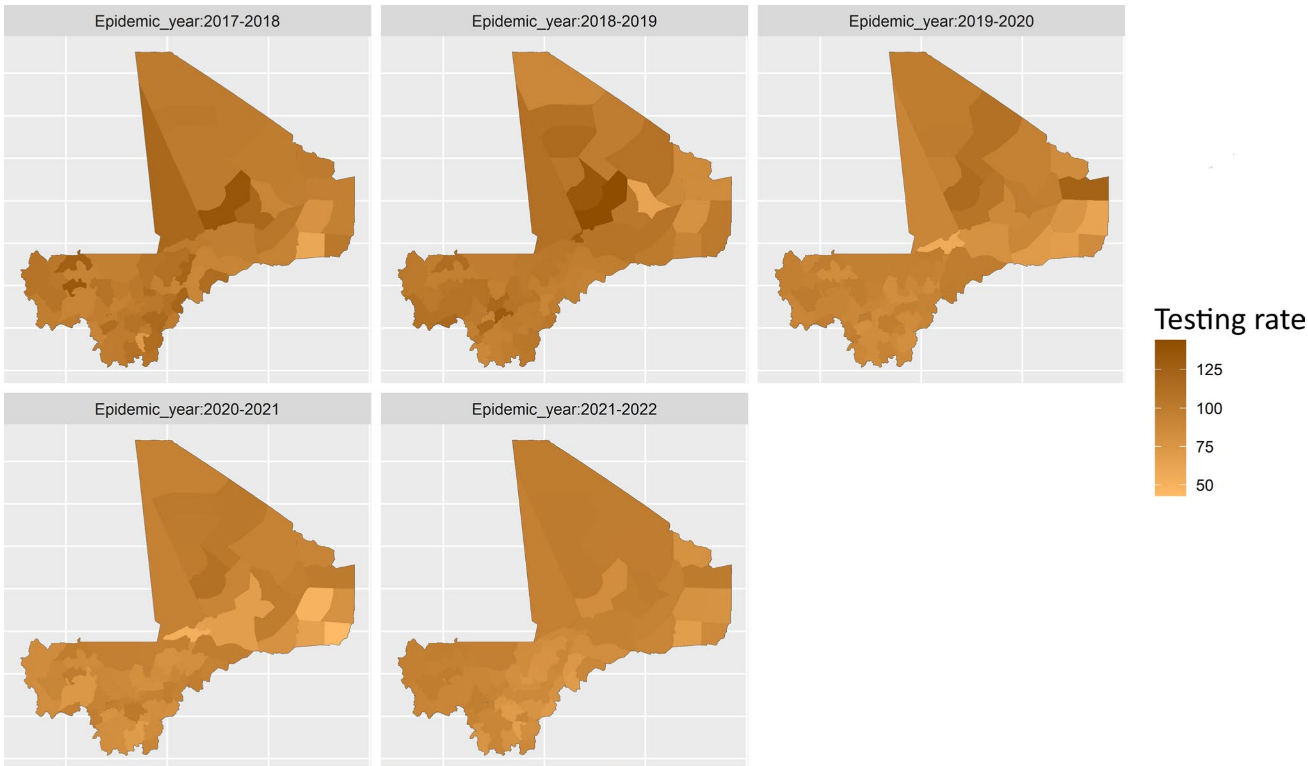

Fig. 4 District-level map of testing rates

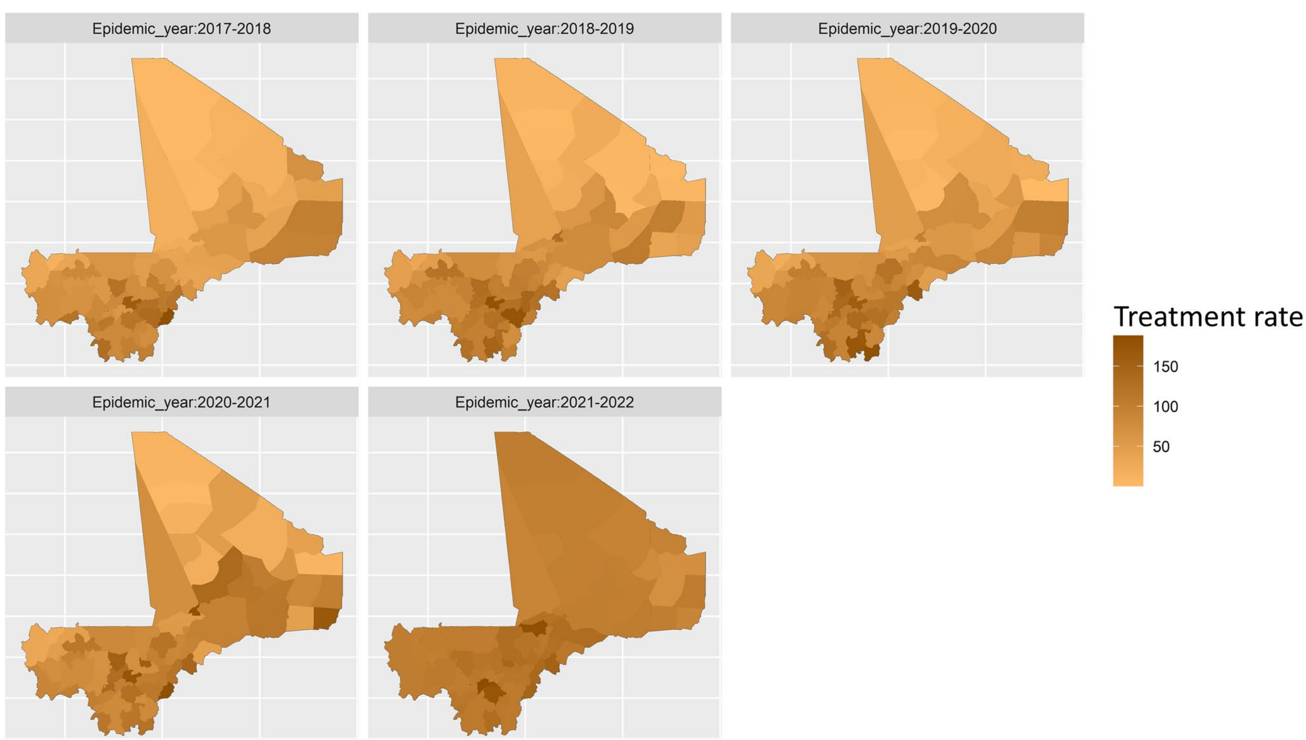

Fig. 5 District-level map of treatment rates

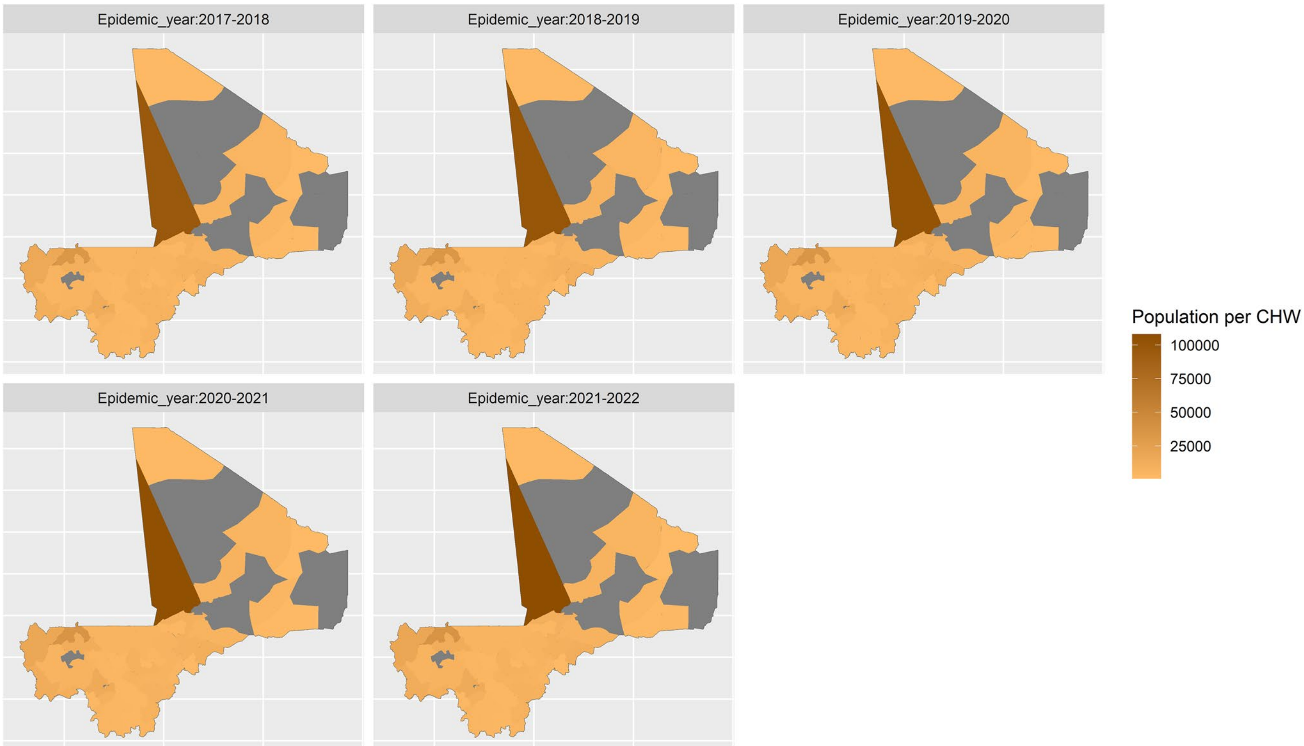

Fig. 6 District-level map of coverage rates for integrated community case management (grey areas have no data)

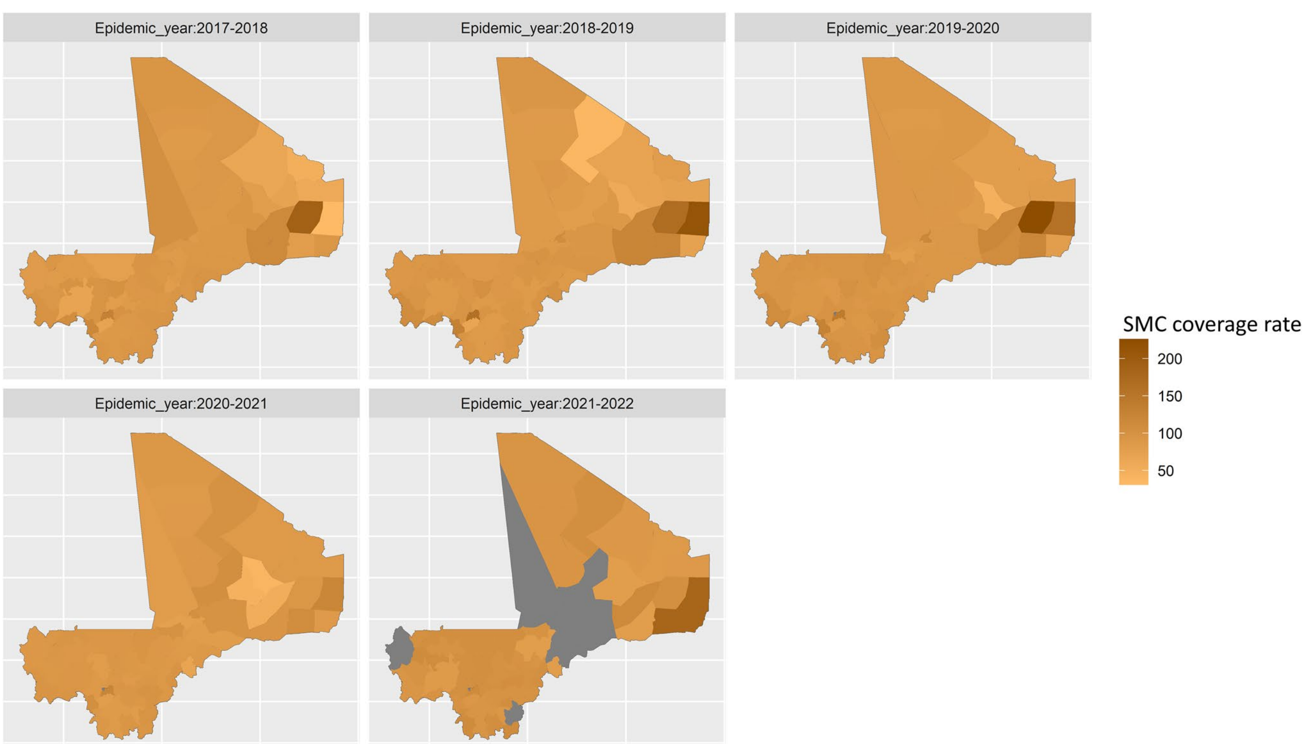

Fig. 7 District-level map of coverage rates for seasonal malaria chemoprevention (grey areas have no data)

Fig. 8 District-level map of coverage rates for intermittent preventive treatment in pregnancy

Fig. 9 District-level map of coverage rates for long-lasting insecticidal net mass distribution (grey areas have no data)

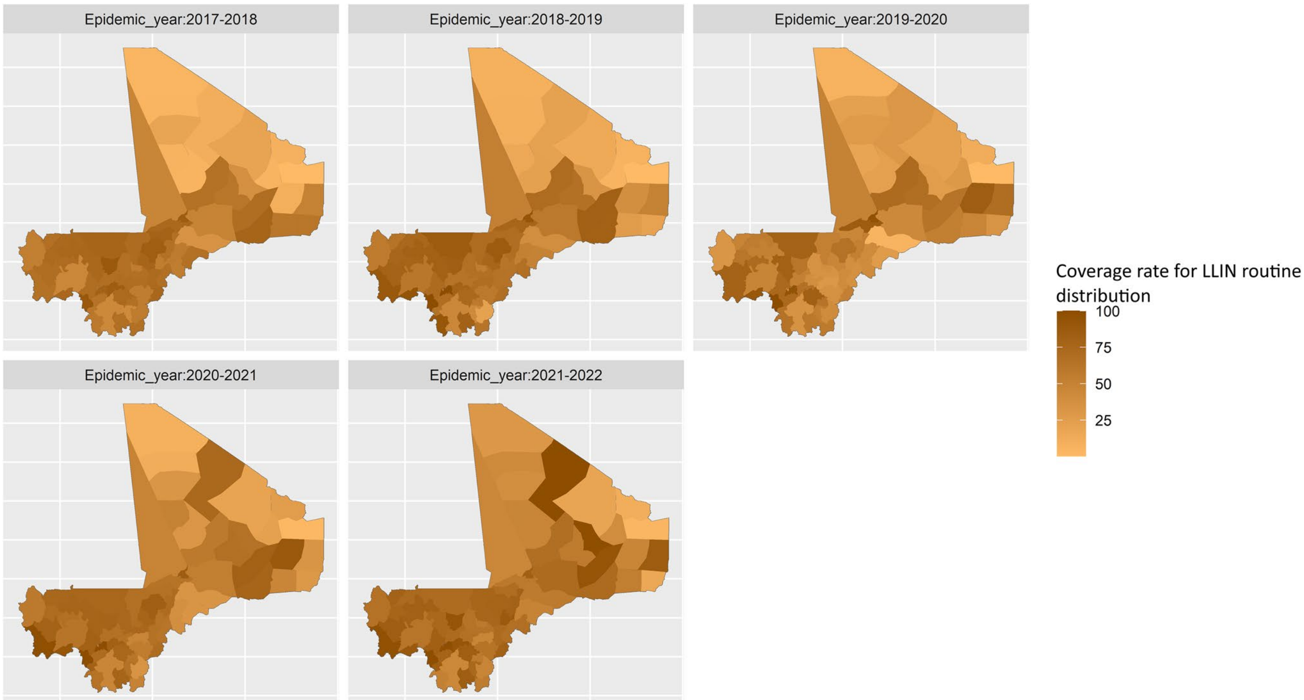

Fig. 10 District-level map of coverage rates for long-lasting insecticidal net routine distribution

significantly with malaria incidence ($p < 0.001$), as expected. The iCCM indicator showed no trend ($p < 0.001$). For rainfall, the OR was 1.416 (95% CI 1.073–1.868) for an annual amount from 200 to 800 mm. The adjusted R-squared of the multivariate model was 77.8%.

The multivariate analysis of the effects of control interventions on malaria incidence in the general population considering rainfall is presented in Fig. 11.

4 Discussion

This study evaluated the impact of control interventions at the health district level on malaria incidence in the general population of Mali considering rainfall. Our results confirm that the incidence of malaria increased slightly in the country between 2017 and 2022 (Fig. 1). An improvement in coverage was observed for 5 of the 7 interventions, namely testing, treatment, SMC, IPTp, and LLIN routine distribution. The intervention with the highest coverage rate was testing, with several health districts reaching the NMCP target of 100% each year (Fig. 4). The intervention with the lowest coverage rate was IPTp, with the NMCP target of 80% being met only once (in 2021–2022) and in only 1 health district (Fig. 8). The interventions that indicate some effect in reducing malaria in the general population were LLIN mass distribution (2.2 ‰) and SMC (1.9 ‰) (Fig. 11).

Our results show that malaria incidence increased over the study period in parallel with improvements in intervention coverage. However, our multivariate analysis did not find strong associations between intervention coverage rates at the health district level and malaria incidence in the general population, which suggests that the increase in incidence is attributable to factors other than the interventions included in the model. One probable factor is growing political instability [30], as hundreds of thousands of people without premunition were displaced over the last ten years from regions with low transmission (Gao, Kidal, Menaka, and Timbuktu in the north) to regions with high transmission (Mopti and Segou in the south), where they were at much greater risk of contamination. The temporary reduction in access to care during the COVID-19 pandemic also likely contributed to the increase in malaria incidence, as suggested by recent studies conducted in malaria-endemic countries [31]. Another likely factor is the excess rainfall observed in 2018–2019 and 2020–2021 in the southern and far northern health districts (Fig. 3).

The median testing rate was 94.0% for the 5 epidemic years, which is the highest coverage rate of all interventions evaluated in our study (Fig. 4). Several health districts reached the NMCP target of 100% each year. The rate of testing decreased slightly in 2019–2020 and 2020–2021, when the border closure linked to the COVID-19 pandemic [31] caused an interruption of RDT imports from China and India. However, RDT imports fully resumed

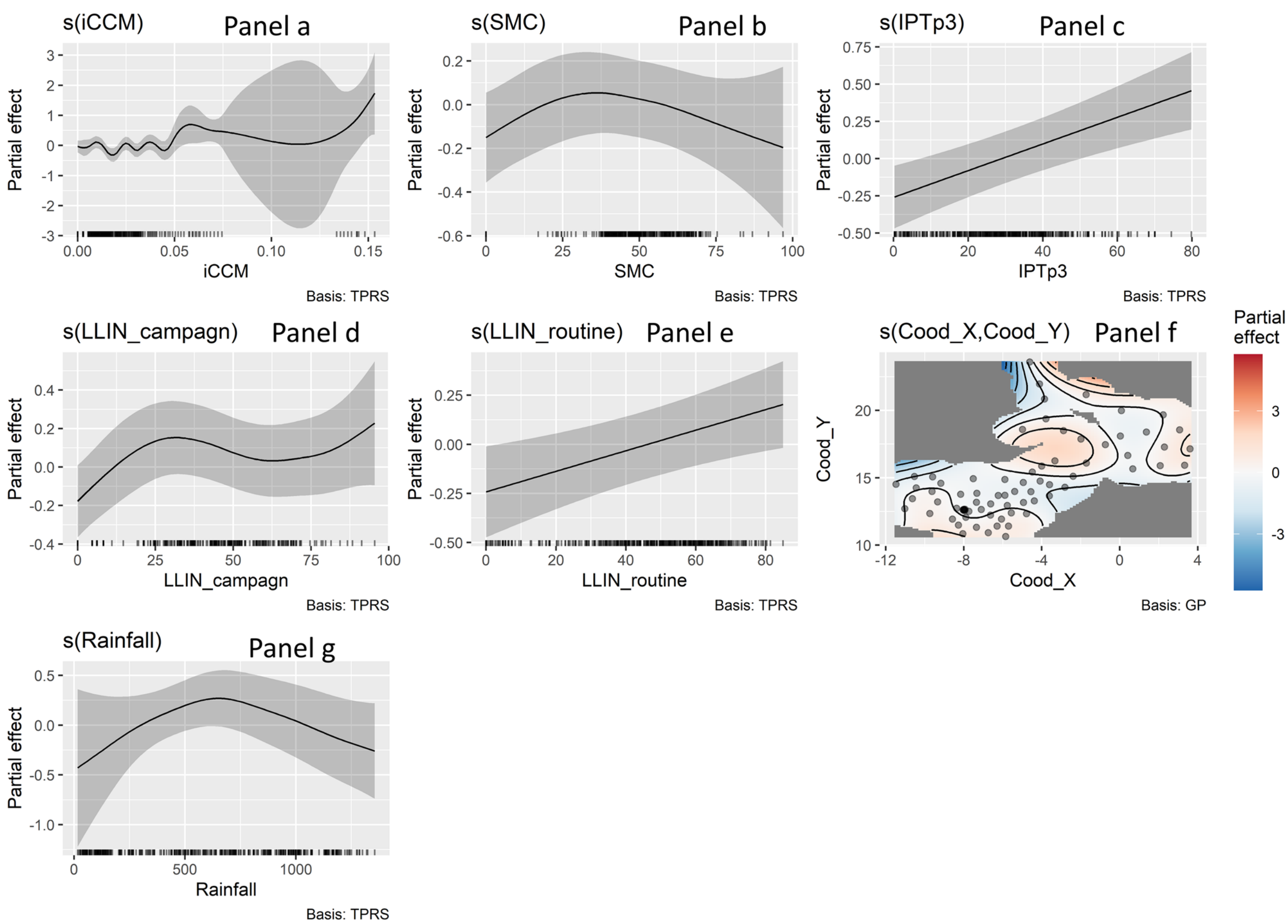

Fig. 11 Multivariate analysis of the effects of control interventions on malaria incidence in the general population considering rainfall: Panel **a** integrated community case management; Panel **b** seasonal malaria chemoprevention; Panel **c** intermittent preventive treatment in pregnancy; Panel **d** long-lasting insecticidal net mass distribution; Panel **e** long-lasting insecticidal net routine distribution; Panel **f** spatial analysis; and Panel **g** rainfall

in 2021–2022, such that there was an improvement in the testing rate over the study period.

The median treatment rate was also high at 90.7%, with several health districts meeting the NMCP target of 100% each year (Fig. 5). The treatment rate increased considerably between 2017 and 2022, which likely explains the slight reduction in the rate of test positivity (from 72.0% in 2017–2018 to 70.0% in 2021–2022) reported by the National Strategic Plan (NSP) for Malaria Elimination 2023–2027 [4]. Although the NMCP purchased only 15,222,664 packets of ACT compared to the required 16,367,834 packets, needs were largely met throughout the study period because patients were able to purchase ACT on the private market [4]. By contrast, there was a major shortage of artesunate, with only 5,251,570 vials purchased over the study period compared to the required 23,807,221 vials [4]. This shortage is explained by the fact that the NMCP purchased vials based on a proportion of severe malaria cases of 10%, when in fact the mean proportion of severe cases reported between 2017 and 2022 was 30% [4].

The good supply of RDTs and ACT packets over the study period was made possible by funding from the President's Malaria Initiative and the Global Fund. To further improve the testing and treatment rates, the NMCP has begun to implement the NSP 2023–2027, which includes the use of pan RDTs to facilitate the detection of other species [32] and the deployment of mobile teams that are better adapted to nomadic populations. However, the NMCP is unlikely to increase the artesunate supply in the near future. Not only are the country's financial resources limited, but the fact that the proportion of severe cases is estimated at 5% in malaria-endemic countries as a whole [33] suggests that severe malaria is overdiagnosed and overreported by Malian health practitioners. Based on this assumption, the NMCP has set up a plan to accompany practitioners in the management of malaria, with a targeted follow-up in health districts that report an excessively high proportion of severe cases.

The iCCM coverage rate was somewhat better in the south than in the north, but it fell short of the target of 1,500 population per community health worker in all health districts, including in urban areas like Bamako and Sikasso (Fig. 6). This rate remained stable over the study period, as the recruitment of new community health workers was insufficient to compensate for population growth. Our study found no impact of iCCM on malaria incidence. Nevertheless, the NMCP recruited and trained 1,000 new community health workers as part of the NSP 2023–2027, all of whom were deployed across the country in 2024. This reinforcement can be expected to show its effect in the long run, since iCCM also helps to facilitate and improve the implementation of other interventions, in particular testing, treatment, SMC, and IPTp [34]. Note that the long-term impact of iCCM on malaria incidence has been demonstrated in studies conducted among children under 5 years in West Africa [34, 35].

The SMC coverage rate reached the NMCP target of 90% in almost all health districts in the first 4 years of the study (Fig. 7). However, in 2021–2022, 10 health districts in the north and south of the country did not receive SMC due to COVID-19-related shortages and the Malian government's inability to mobilize sufficient resources to compensate for the end of World Bank funding. When excluding these 10 health districts, the SMC coverage rate was found to increase slightly over the study period. Our study showed SMC to be one of the interventions that contributed to the reduction of malaria incidence in the general population. Consistent with this finding, the 2022 NMCP report indicates that SMC has a considerable impact on malaria transmission in the target population, as the proportion of children under 5 years in the population of patients with confirmed malaria decreased from 52 to 26% after the intervention was introduced in 2012 [4]. The impact of SMC observed in our study can be explained by the fact that children constitute the main reservoir of parasite carriers. It can also be explained by good uptake of SP + AQ, as reflected in the adjusted coverage rates presented in Fig. S3. In this regard, a recent study has shown that the administration of SP + AQ by community health workers during SMC campaigns improves adherence in the target population [36]. Given the importance of targeting children to reduce malaria incidence in the general population, the NMCP recently established follow-up community visits to ensure the uptake of the last 2 doses of SP + AQ. In the future, SMC coverage could be further improved by setting up routine administration of SP + AQ by health community workers [37].

The IPTp coverage rate remained below the NMCP target of 80% in all but 1 health district (Fig. 8). However, it did increase over the study period, thanks to the generalization of prenatal consultations and the acquisition of sufficient numbers of SP tablets by the NMCP [4]. Our results show no impact of the intervention on malaria incidence. Nevertheless, the reinforcement of IPTp in pregnant women seems essential both because it is one of the key interventions recommended in the WHO Malaria Guidelines [6] and because its impact on malaria transmission has been demonstrated in a number of studies conducted in Mali [38–40]. To improve IPTp coverage, the NMCP has recently allowed community health workers to administer SP to pregnant women starting with the second dose [41], with pilot studies currently underway in Mali to assess the impact of this strategy on malaria incidence. The intervention could be further reinforced by making prenatal consultations free of charge, improving the quality of care offered to pregnant women in health facilities, and reinforcing DOT.

The coverage rate for LLIN mass distribution reached the NMCP target of 80% in all health districts covered by a distribution campaign in the previous 3 years (Fig. 9). The rate was especially high in 2019–2020, 2020–2021, and 2021–2022, as large numbers of health districts were covered in the campaigns of 2019 and 2020. This good coverage is corroborated by the results of the 2021 Malaria Indicator Survey, according to which 70% of LLINs are distributed through mass campaigns in Mali [42]. Our results show a contribution of LLIN mass distribution to the reduction of malaria incidence in the general population, even though effect sizes are very small. The impact of the intervention may have been limited by unsatisfactory utilization, as reflected in the adjusted coverage rates shown in Fig. S4. Indeed, although studies suggest that LLINs are well accepted in Mali [43], LLIN utilization in the general population falls short of the 100% target (1 LLIN per 2 people), with the 2018 DHS reporting a utilization rate of 73% at the national level [28]. To improve the utilization of LLINs in the general population, the NMCP has recently devised a communication plan that entails messaging in local radio stations and on television as well as awareness raising by community health workers [37]. This plan will be implemented in 2025 to pave the way for the distribution campaign of 2026. Note that the 2026 campaign will also involve the distribution of the more effective interceptor G2 nets and long-lasting piperonyl butoxide-treated insecticidal nets in all health districts to compensate for growing vector resistance to standard LLINs [4].

The coverage rate for LLIN routine distribution remained below the NMCP target of 80% in the majority of health districts (Fig. 10). However, it increased slightly over the study period, largely thanks to funding from the President's Malaria Initiative. Unlike for LLIN mass distribution, our modeling analysis found no reducing effect of LLIN routine distribution on malaria incidence in the general population. The fact that only 5,571,582 of the 8,675,552 units acquired by the NMCP over the study period were distributed to pregnant women and children under 1 year suggests that the low coverage rate is due to poor access to care, the rate of care-seeking in the Malian population being estimated at

51% [4]. Occasional LLIN shortages in health facilities may also have played a part in this. Compounding the problem of unsatisfactory coverage is the insufficient utilization of LLINs (as reflected in the adjusted coverage rates shown in Fig. S5), with the 2018 DHS reporting a rate of utilization of 84% in pregnant women and 79% in children under 1 year [28]. Despite the absence of a reducing effect on malaria incidence in our study, the intervention should be continued in order to maintain good ownership of LLINs in the general population between mass distribution campaigns. To improve utilization of LLINs among pregnant women and children under 1 year, the NMCP recently initiated a community platform strategy, in which community health workers coordinate between public health authorities and local community leaders to raise awareness about the importance of LLIN use in the population. This strategy, which is part of the NSP 2023–2027, will be reinforced in coming years. Moreover, the NMCP is currently seeking financial support from international partners to increase the number of LLINs to be distributed via routine channels. It is also planning to provide training to health practitioners in health establishments with low coverage rates for LLIN distribution, the aim being to determine the source of the problem to propose strategies to correct it. Note that coverage for this intervention could be further improved by reinforcing access to care, including by making prenatal consultations free of charge and by offering higher-quality care to pregnant women.

Our analyses did not include IRS, as this intervention concerned only a few villages located in 2 health districts during the study period. Although a pilot study conducted in the central region of Segou found IRS to reduce malaria incidence by 70% [44], the intervention was discontinued in 2022 due to its very high operational cost.

Our study has some limitations. First, the specific impact of testing and treatment could not be determined because coverage for these two interventions is entirely dependent on incidence. The testing and treatment rates were nevertheless included as interaction terms in the modeling analysis to increase the power of results and to minimize the confounding by indication bias. Second, while some of the interventions target specific populations and/or age groups (children aged 3 to 59 months for SMC, pregnant women for IPTp, and pregnant women and children aged under 1 year for LLIN routine distribution), the modeling analysis only evaluated the impact of interventions on malaria incidence in the general population. Including these specificities in the analysis could have contributed to the tailoring of interventions. Nevertheless, our study offers a simple model that can be reproduced by the NMCP in future evaluations of implemented interventions.

On the other hand, our study has many strengths. First, our analyses were performed using routine time series data extracted from the epidemiological surveillance system [45, 46]. This was particularly appropriate given that data monitoring improved considerably in Mali following the establishment of a mechanism for this purpose, with the DHIS2 showing a mean annual rate of data completeness of 96.38% for the period 2017–2022 [4]. Second, administrative coverage rates were adjusted by rates of uptake/utilization to avoid underestimating the effect of interventions on malaria incidence [47]. Third, malaria incidence was adjusted by the rates of testing, reporting, and care-seeking to avoid underestimating the effect of interventions, based on WHO recommendations (Method 1) [1].

The malaria control strategy in Mali must be reinforced to ensure that the GTS 2016–2030 reduction target of 90% is reached by 2030 and to ultimately achieve elimination. As our study results indicate, this reinforcement should primarily consist of improving coverage and utilization rates in the general population and in the most vulnerable groups (including by increasing access to care and raising awareness about the importance of LLIN use) and of deploying larger numbers of community health workers where needed. Studies on the impact of malaria control interventions in Mali that include target populations and age groups in the analysis are also needed to help better tailor malaria control efforts in the country.

5 Conclusion

This study assessed the impact of control interventions at the health district level on malaria incidence in the general population of Mali considering rainfall. Our results confirm that the incidence of malaria increased slightly in the country between 2017 and 2022. An increase in coverage rates for testing, treatment, SMC, IPTp, and LLIN routine distribution was observed over the study period. The interventions that had some effect in reducing malaria in the general population were LLIN mass distribution and SMC.

To ensure that the GTS 2016–2030 reduction target of 90% is reached by 2030 and to ultimately achieve elimination, all interventions evaluated in our study must be reinforced, as recommended by the WHO. As our study results indicate, this reinforcement should primarily consist of improving coverage and utilization rates in the general population and in the most vulnerable groups (including by increasing access to care and raising awareness about the importance of LLIN use) and of deploying larger numbers of community health workers where needed. Studies on the impact of malaria control interventions in Mali that include target populations and age groups in the analysis are also needed to help better tailor malaria control efforts in the country.

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Author Contributions J.G., IS and M.C. designed the study; P.D. collected the data under the coordination of M.C.; J.G. developed the statistical analysis plan with the participation of I.S. and M.C.; M.C. carried out the statistical analysis under the supervision of J.G. and IS; M.C. performed the cartographic analysis with the participation MM; M.H.S., D.T., S.F., M.K., and N.D. validated the results; V.S. and M.H.M. participated in the statistical analysis; M.C. and J.G. wrote the manuscript; all authors read and approved the final manuscript.

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Data Availability Data can be shared on request.

Declarations

Conflicts of Interest The authors declare no competing interests.

Ethics and Consent No individual data were collected nor analyzed for this study. Only aggregated data were used, extracted from the national information system DHIS2, at the district level and monthly scale. Our study was approved by the National Malaria Control Program (#042/MSDS-SG/PNLP, 14 January 2023), in accordance with Malian regulations on ethics and medical research.

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