Epidemiology and control profile of malaria in

Mali

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Contributing authors

Name	Affiliation
Madina Konate Diahara Traore	Programme National de Lutte contre le Paludisme (PNLP), Ministère de la Santé et de l'Hygiène Publique
Drissa Coulibaly Ogobara Doumbo	Malaria Research and Training Center (MRTC), University of Bamako, Bamako, Mali
David Kyalo Joseph K. Maina Peter M. Macharia Emelda A. Okiro Robert W. Snow Pamela N. Thuraniira	KEMRI-Wellcome Trust Research Programme, Nairobi, Kenya
Emanuele Giorgi	CHICAS, Lancaster Medical School, Lancaster University, UK
Nicholas Dellasanta Lauren Hashiguchi Ruth Lorimer Caroline Lynch	London School of Hygiene & Tropical Medicine (LSHTM), UK

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Abbreviations

ACT	Artemisinin-based Combination Therapy
AI	Aridity Index
AL	Artemether-lumefantrine
ANC	Antenatal Care
AQ	Amodiaquine
AS	Artesunate
ASACO	Association de Santé Communautaire
ASC	Agents de Santé Communautaires
CQ	Chloroquine
CREDD	Cadre de Relance Economique pour le Développement Durable
CSCOM	Centre de Santé Communautaire
CSCRP	Cadre Stratégique pour la Croissance et la Réduction de la Pauvreté
CSREF	Centre de Santé de Référence
DDT	Dichloro-diphenyl-trichloroethane
DESAM	Développement Sanitaire du Mali
DFID	Department for International Development
DHIS 2	District Health Information System 2
DHS	Demographic and Health Survey
DNS	Direction Nationale de la Santé
DPM	Direction de la Pharmacie et du Médicament
DRS	Regional Health Directorates
ECOWAS	Economic Community of West African States
EIR	Entomological Inoculation Rate
EP	Exceedance Probability
EVI	Enhanced Vegetation Index
FEMATH	Fédération Malienne des Associations des Tradithérapeutes et Herboristes
GDP	Gross Domestic Product
GTFAM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GIS	Geographic Information Systems
GMEP	Global Malaria Eradication Programme
GPS	Global Positioning System
GPSP	Groupe Pivot de Santé et Population
HIS	Health Information System
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
iCCM	Integrated Community Case Management
IDP	Internally Displaced Person
IMF	International Monetary Fund
INLA	Integrated Nested Laplace Approximations

IPTc	Intermittent Preventive Therapy in Childhood
IPTp	Intermittent Preventive Therapy in Pregnancy
IRS	Indoor Residual Spraying
ITCZ	Intertropical Convergence Zone
ITN	Insecticide Treated Net
KDR	Knock-Down Resistance
KWTRP	KEMRI-Wellcome Research Trust Programme
LAMP	Loop-Mediated Isothermal Amplification
LLIN	Long-Lasting Insecticidal Net
LSHTM	London School of Hygiene & Tropical Medicine
M&E	Monitoring and Evaluation
MAE	Mean Annual Values
MAP	Mean Annual Precipitation
MARA	Mapping Malaria Risk in Africa
MBG	Model-Based Geostatistics
MDG	Millennium Development Goal
MINUSMA	Multidimensional Integrated Stabilization Mission in Mali
MIS	Malaria Indicator Survey
MNLA	National Movement for the Liberation of Azawad
MPR	Malaria Programme Performance Review
MRTC	Malaria Research and Training Center
MSF	Médecins Sans Frontières
NEP	Non-Exceedance Probability
NGenIRS	Next Generation Indoor Residual Spraying
NGO	Non-Governmental Organisation
NIH	National Institutes of Health
NMS	National Malaria Strategy
NTD	Neglected Tropical Disease
ODA	Overseas Development Assistance
OSPSanté	Outil de Suivi des Produits de Santé
PAR	Populations at Risk
PCR	Polymerase Chain Reaction
PET	Global Potential Evapo-Transpiration
PMI	President's Malaria Initiative
PNLP	Programme National de Lutte contre le Paludisme
PPM	Pharmacie Populaire du Mali
PPN	Politique Pharmaceutique Nationale

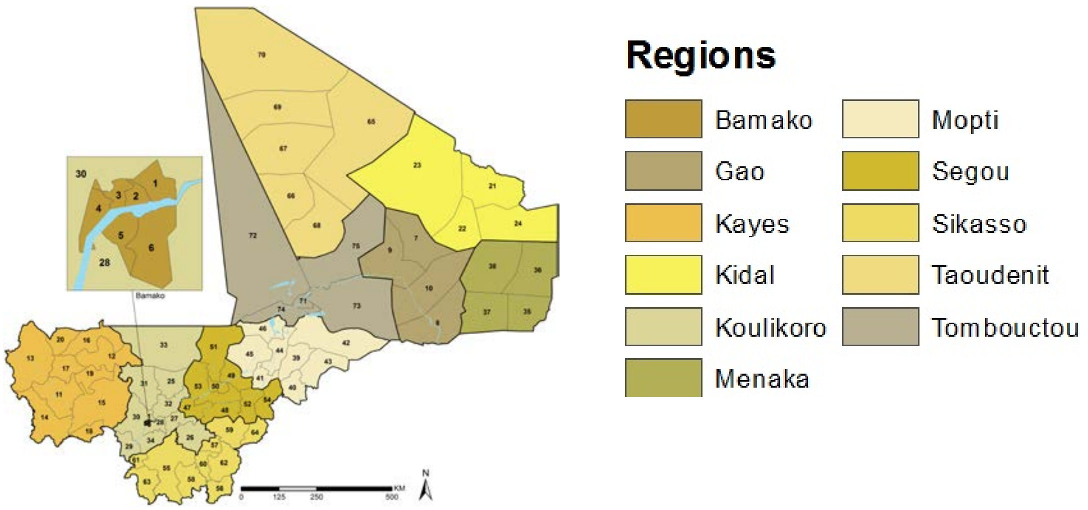
PPP	Purchasing Power Parity
PDDSS	Plan Décennal de Développement Sanitaire et Social
PRODESS	Programme quinquennal de Développement Sanitaire et Social
PSI	Population Services International
RA	Mean Monthly Extra-Terrestrial Radiation
RBM	Roll Back Malaria
RDT	Rapid Diagnostic Test
RTA	Reports Tirmestriels d'Activités
SAE	Small Area Estimation
SDADME	Schéma Directeur d'Approvisionnement et de Distribution des Médicaments Essentiels
SDG	Sustainable Development Goal
SIAPS	System to Improve Access to Pharmaceuticals and Services
SIMR	Système de Surveillance Intégrée des Maladies et de la Riposte
SLIS	Système Local d'Information Sanitaire
SMC	Seasonal Malaria Chemoprevention
SP	Sulphadoxine-pryimethamine
SPDE	Stochastic Partial Differential Equations
TD	Mean Monthly Temperature Range
TES	Therapeutic Efficacy Study
TSI	Temperature Suitability Index
UN	United Nations
UNEP	United Nations Environment Programme
USAID	United States Agency for International Development
WAEMU	West African and Monetary Union
WHO	World Health Organization
WHO AFRO	World Health Organization Regional Office for Africa
WHOPES	World Health Organization Pesticide Evaluation Scheme

Map overview and data access

This profile represents data on malaria risk and control in Mali using a series of maps, serving as an update to a profile generated in 2014. Key maps are presented below with more detail on them in the report.

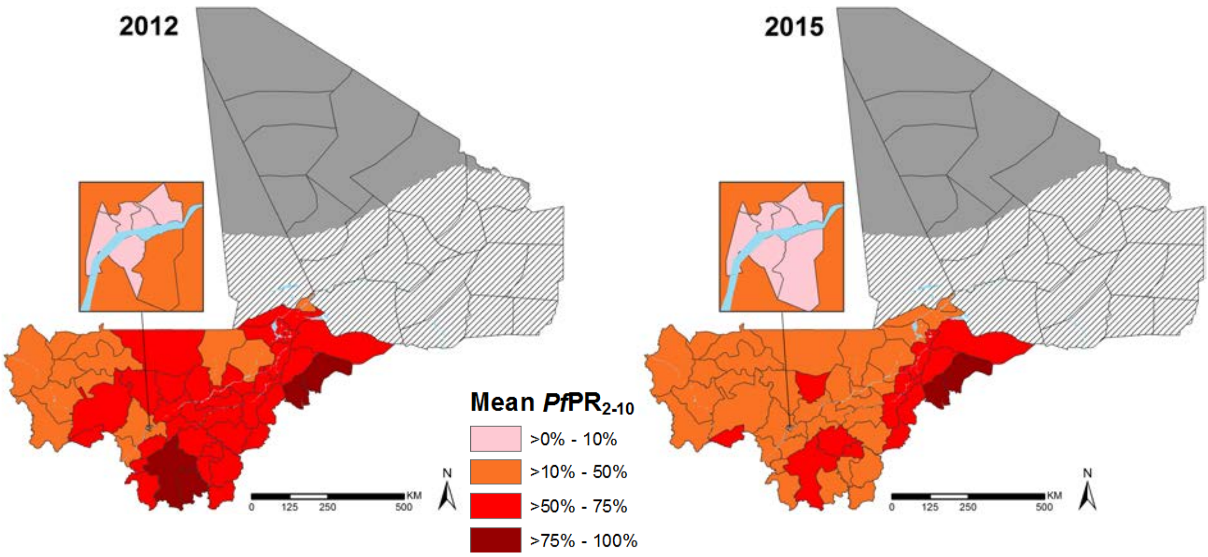
All data and maps used for the generation of this profile have been shared with the PNLP on disk drives. The PNLP should be consulted if further reference is of interest.

75 health districts of Mali within 11 nominal regions

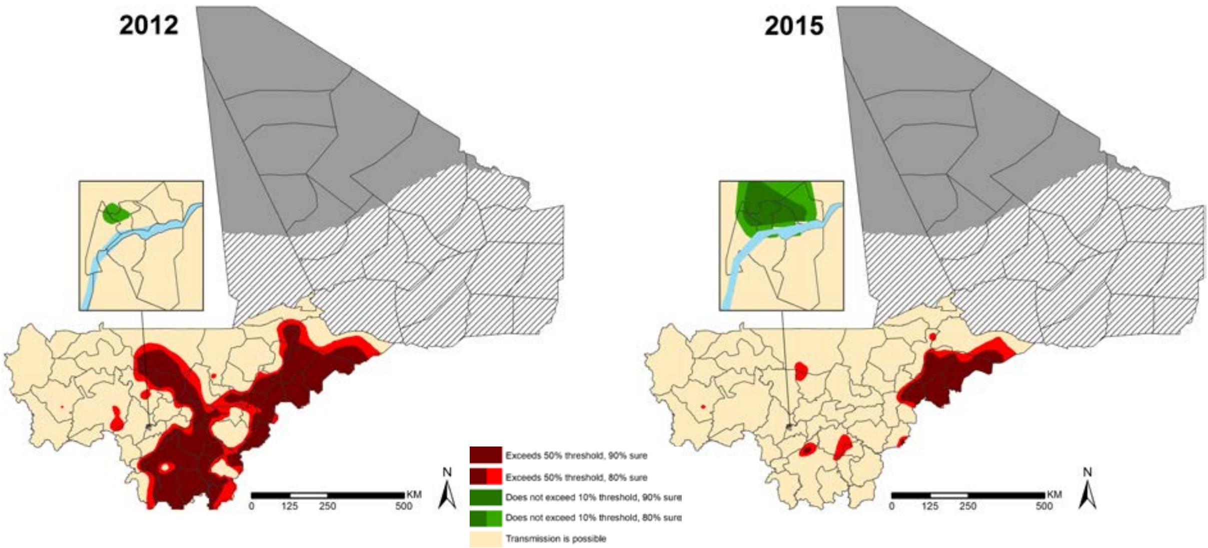


Region	District	Map Code
Bamako	Commune I	1
	Commune II	2
	Commune III	3
	Commune IV	4
	Commune V	5
	Commune VI	6
Gao	Almoustrat	7
	Ansongo	8
	Bourem	9
	Gao	10
Kayes	Bafoulabe	11
	Diema	12
	Kayes	13
	Kenieba	14
	Kita	15
	Nioro	16
	Oussoubidiagnan	17
	Sagabari	18
	Sefeto	19
	Yelimane	20
Kidal	Abeibara	21
	Kidal	22
	Tessalit	23
	Tin-essako	24
Koulikoro	Banamba	25
	Dioila	26
	Fana	27
	Kalaban Coro	28
	Kangaba	29
	Kati	30
	Kolokani	31
	Koulikoro	32
	Nara	33
	Ouelessebougou	34
Menaka	Anderamboukane	35
	Inekar	36
	Menaka	37
	Tidermene	38
Mopti	Bandiagara	39
	Bankass	40
	Djenne	41
	Douentza	42
	Koro	43
	Mopti	44
	Tenenkou	45
	Youwarou	46
Segou	Baraoueli	47
	Bla	48
	Macina	49
	Markala	50
	Niono	51
	San	52
	Segou	53
	Tominian	54
Sikasso	Bougouni	55
	Kadiolo	56
	Kignan	57
	Kolondieba	58
	Koutiala	59
	Niena	60
	Selingue	61
	Sikasso	62
	Yanfolila	63
	Yorosso	64
Taoudenit	Achouratt	65
	Al-ource	66
	Araouane	67
	Boujbeha	68
	Foum-elba	69
	Taoudenit	70
Tombouctou	Dire	71
	Goundam	72
	Gourma-rharous	73
	Niafunke	74
	Tombouctou	75

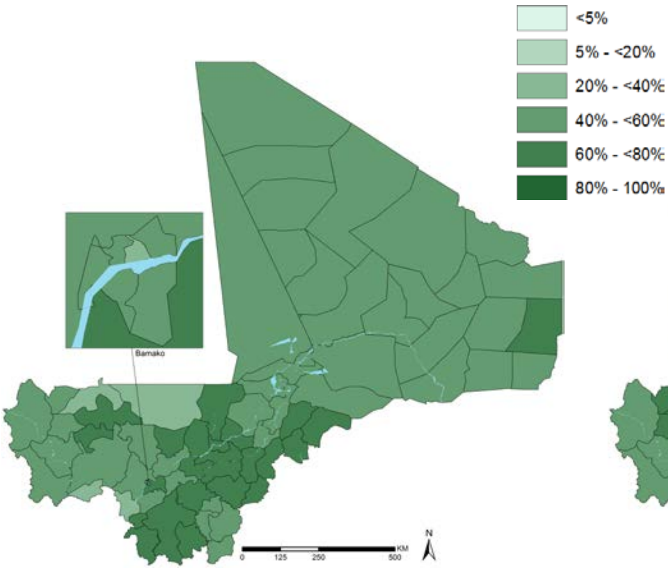
Health district mean *Pf*PR$_{2\text{-}10}$ in 2012 and 2015



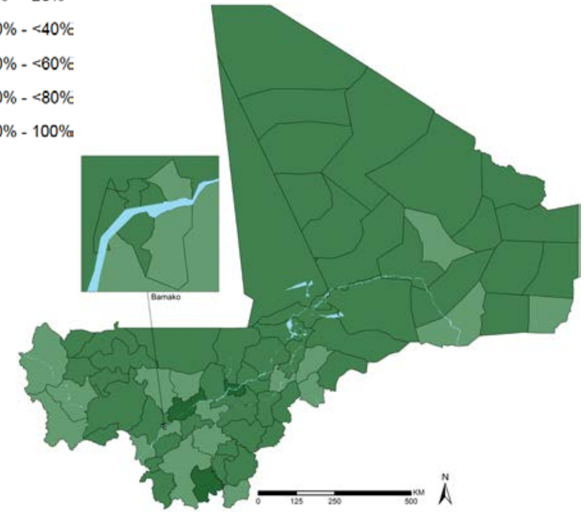
Probability that *Pf*PR2-10 is ≤ 10% and ≥50% per health district



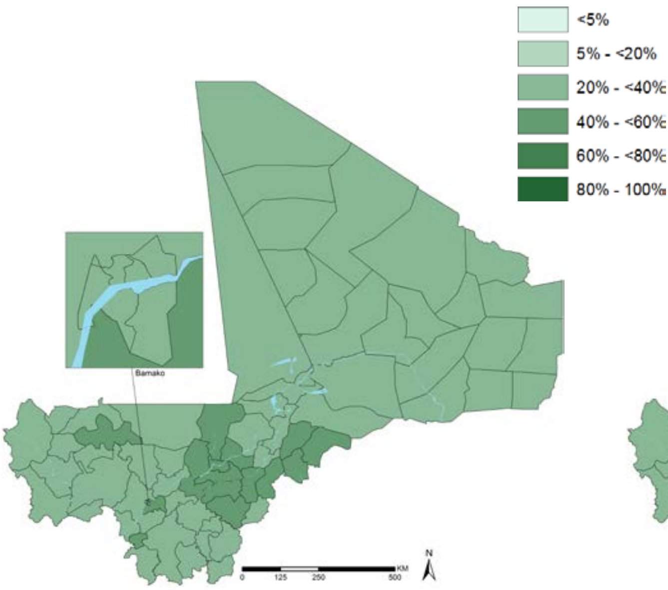
Proportion of the population sleeping under an ITN in 2012/13



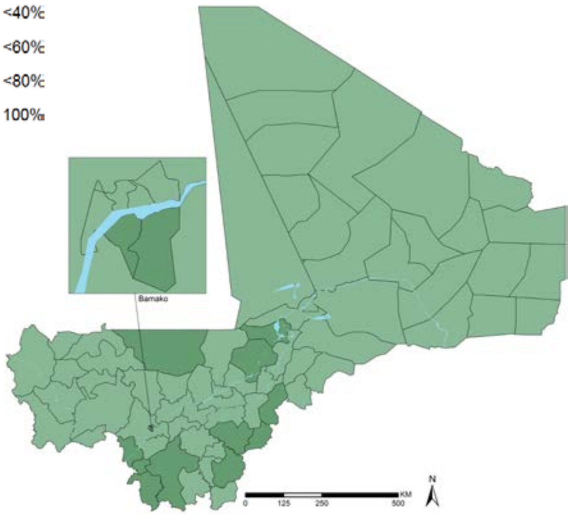
Proportion of the population sleeping under an ITN in 2015



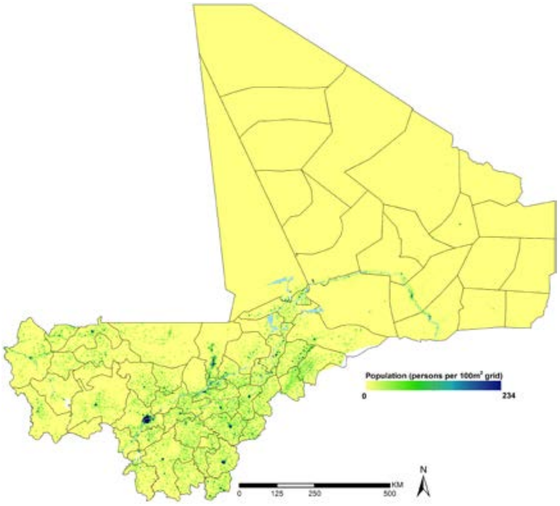
Proportion of households with at least one ITN for every two persons in 2012/13



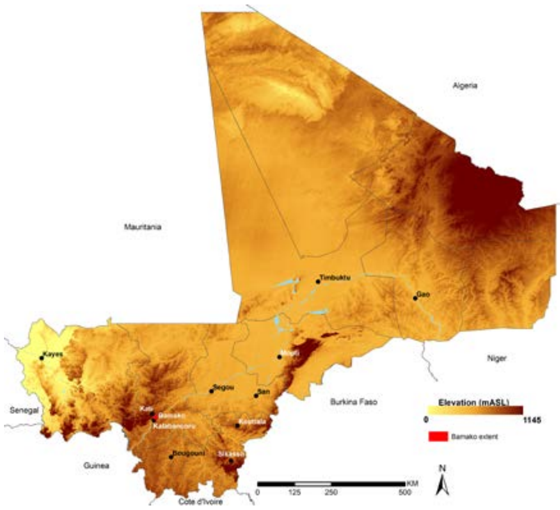
Proportion of households with at least one ITN for every two persons in 2015



Modelled 2015 population density per 100 m²



Major relief features, rivers, lakes and urban areas (red)



Executive summary

This epidemiological profile results from a collaboration between the Programme National de Lutte contre le Paludisme (PNLP), PNLP partners, the WHO Regional Office for Africa (WHO AFRO) and the LINK Programme (London School of Hygiene & Tropical Medicine [LSHTM] and KEMRI-Wellcome Research Trust Programme [KWTRP]). The profile was developed to support national- and district-level malaria control actors in aligning most recent malaria burden data and intervention coverage data with efforts to improve evidence-based reduction interventions in line with the Malian Plan Strategique de Lutte contre le Paludisme (National Malaria Strategic Plan) 2018 - 2022.

This report builds on work produced in 2014 by the KWTRP to develop an epidemiological profile of malaria to district levels. Since the report's publication, administrative boundaries have shifted and conflict in the northern region of the country has hindered monitoring and control efforts. At the same time, new sources of data have become available, namely a national Malaria Indicator Survey (MIS) in 2015. The MIS is designed to provide highly accurate results at the regional and national level; however, district-level estimates are best-suited for national planning. Therefore, we apply model-based geospatial techniques to render district-level estimates from the data available in nationally-representative surveys and smaller prevalence studies.

This report updates national spatially-defined data on malaria parasite prevalence, vector species occurrence, human population settlement, health service location and vector control coverage. The updated databases for this profile are owned by the PNLP and Ministère de la Santé et de l'Hygiène Publique as part of a national data repository. Using model-based geo-statistical (MBG) methods, this report presents updated maps of malaria risks in Mali since the publication of the first epidemiological profile in 2014. The maps are based on parasite prevalence among children aged 2-10 years (*Pf*PR_{2-10}) and are transformed into district population-adjusted estimates of risks to review burden and change over time across 75 health districts to support planning and resource allocation. The maps include the two new administrative regions of Taoudenit and Menaka, formally recognised by the Ministère de la Santé et de l'Hygiène Publique at the time of modelling. Additionally, the maps in this profile do not broadly incorporate Demographic and Health Survey (DHS) data; however, the NMCP may update these maps in-country moving forward, particularly with the standard DHS being carried out in 2018.

Malaria transmission in Mali is subject to extreme variation based on eco-climatic conditions, particularly between the north and south. In the Saharan Desert regions of the north (as well as Nara, Nioro, Diéma, Yélimané and Kayes), transmission is dependent on rainfall and is more subject to epidemics due to arid condition constraints, with all age groups considered at risk for severe malaria.[1] The Sudano-Guinean zone is subject to seasonal transmission of six months or more, while the Sahelian zone contrastingly has a seasonal transmission of three months or less.[1]

Plasmodium falciparum is responsible for the majority of malaria cases in Mali (95%), followed by *P. malariae, P. ovale and P. vivax.*[1–3] *P. vivax* was more recently identified in Bandiagara, Gao, Tombouctou and Kidal.[1,4] The primary vectors responsible for transmission in Mali include the *Anopheles gambiae* complex and the *An. funestus* group.[1] The distribution of these vectors is highly dependent upon spatial and temporal variations, with *An. funestus* abundant during the cool and dry season, *An. gambiae* during the rainy season in the South-Sudanian savannah nearby streams and *An. coluzzii* ubiquitously throughout Mali.[3,5–7]

Mali is making major strides in the control of malaria. Major intervention activities include universal long-lasting insecticidal net (LLIN) coverage campaigns, indoor residual spraying (IRS), integrated vector management, scaling-up of seasonal malaria chemoprevention (SMC) and improved essential care at the community level through case management by community health workers and health worker trainings.[1] Unfortunately, ongoing conflict challenges the efforts of the PNLP and partners in the delivery of interventions and data collection.

The number of LLINs distributed to pregnant women and children under five years of age has increased significantly from 2011 to 2016 in Mali, from 531,791 to 952,860, respectively. Regarding their use, the 2015 MIS found that 39% of households had at least one LLIN for every two persons and that 68% of all persons at risk slept under an LLIN the night before being surveyed. IRS coverage has shifted from two districts in 2015 to four districts in Mopti Region in 2017, targeting nearly 650,000 persons. Upon the release of the Plan Strategique de Lutte contre le Paludisme 2018–2022, 90% of the population at risk in targeted areas were protected by IRS in the previous 12 months. SMC coverage increased from 343,752 children in five districts in 2013 to 3,906,696 children in all districts in 2017. New targets seek to provide 90% coverage to children three to 59 months with a combination of sulphadoxine-pryimethamine (SP) and amodiaquine (AQ) by 2022 via SMC. The PNLP and partner organisations perform ongoing entomological monitoring in 15 sentinel sites throughout Mali.

The current Plan Strategique de Lutte contre le Paludisme 2018–2022 aims to reduce the incidence of malaria and malaria mortality rate by at least 50% by 2022 compared to 2015, and to completely eliminate malaria by 2030. To achieve these goals, the PNLP currently seeks to target interventions on the basis of epidemiological characteristics, to maintain access to quality interventions, to improve coordination and management capacities, to strengthen partnerships, to contribute to health system sustainability, and to promote malaria surveillance interventions.[1]

The geospatial maps in this profile, alongside geospatially-represented LLIN coverage maps, can assist the PNLP identify sub-national targets for interventions to promote progress towards its 2022 targets and beyond.

Introduction

1.1 History of malariometric data, maps and epidemiological intelligence in malaria control

The use of survey data, maps and epidemiological intelligence was a routine feature of control planning across most African countries during the Global Malaria Eradication Programme (GMEP) era of the mid-1950s. Data included epidemiological descriptions of transmission, vectors, topography and climate. Over 50 years ago, the infection prevalence among children aged two to ten years ($Pf\text{PR}_{2-10}$) was recognised as an important source of planning data and used to define categories of endemic risk. This categorisation of endemic risk was used to guide and monitor progress toward malaria elimination targets.

The art and skills necessary to design malaria control programmes based on an understanding of spatial epidemiology were lost during the 1970s when the agenda for malaria control fell under a less specialised, integrated primary care mandate focused on managing fevers.

In 1996, a renewed appeal for better malaria cartography to guide malaria control in Africa was made.[8,9] Over the last decade there has been enormous growth in spatial data on malaria and populations which had not been available to malariologists or programme control managers 60 years ago. The growth in data was accompanied by the development of statistical approaches to model and map risk and intervention access in space and in time using MBG.[10]

At the launch of the Roll Back Malaria (RBM) partnership in 1998, there were calls for universal coverage of all available interventions in response to the epidemic that affected most of sub-Saharan Africa during this period.[11,12] A decade on, the international donor community is constrained by the global financial crisis; accessing overseas development assistance (ODA) and using limited national domestic funding for malaria control now requires a much stronger evidence-based business case. These future business cases must be grounded in the best possible epidemiological evidence to predict the likely impact of future interventions, assess the impact of current investment and, equally important, demonstrate what might happen should funding and intervention coverage decline.

1.2 Purpose of this profile

This profile was developed to support national-level planning, through the assemblage of an epidemiological evidence base required for a more targeted approach to malaria control in Mali. This report builds upon a previous profile produced in 2014 by INFORM (KEMRI-Welcome Trust) which sought to develop an epidemiological profile of malaria at district levels. The 2014 analysis allowed for a description of malaria risk based on parasite prevalence data from across Mali, predicting to the most recent period for which the majority of data were available.

In 2011, WHO AFRO developed a manual to assist countries in developing their National Malaria Strategies (NMS) including, as a prelude, the undertaking of a National Malaria

Programme Performance Review (MPR). It is recommended that the MPR should include a detailed review of the malaria epidemiology and stratification, including the geographical distribution of malaria burden, parasite prevalence and parasite species.

The MPR undertaken in Mali in 2011 states that "strengthening the fight against malaria is partly based on a better description of the epidemiology (transmission zones and stratification and collection of reliable data on morbidity and mortality)."[13] The PNLP more recently developed their national malaria strategy for 2018 to 2022 following a mid-term review of the 2013 to 2017 plan in March of 2016 and final review in January and February 2018. The new strategy is intended to be more closely aligned to the Programme quinquennal de Développement Sanitaire et Social (PRODESS), the Plan Décennal de Développement Sanitaire et Social (PDDSS), the Cadre de Relance Economique pour le Développement Durable (CREDD) and the Sustainable Development Goals (SDGs).[1]

Following the release of the previous profile in 2013, the burden and management of malaria in Mali has shifted.[14] This is largely attributable to the implementation of interventions, changes in the political landscape, funding and demographic fluctuation. Concurrently, new data sources have become available, including a MIS in 2015.

This updated epidemiological profile includes the latest evidence of parasite transmission risk. Risk is described at the level of Mali's health districts; offering data at a unit most useful for targeting sub-national control toward the achievement of the targets of the national malaria strategic plan. Importantly, this work is intended to support the PNLP's strategic planning and ongoing monitoring and evaluation (M&E) efforts.

Country context

1.3 Location and geographical features

Until the dissolution of the Mali Federation with Senegal in 1960, the Republic of Mali was part of the Empire of Mali from 1312 to 1337 and French Soudan from 1982 to 1959. Mali is located in the northern hemisphere of West Africa, landlocked with borders to Guinea and Senegal in the southwest; to Côte d'Ivoire in the south; to Burkina Faso and Niger in the southeast; to Algeria in the north; and to Mauritania in the west. Mali is the 25th largest country in the world and the eighth largest in Africa, with a surface area of 1,241,238 km^2.[15] Bamako, the capital of Mali, is located in the southwest of the country.

The terrain of Mali is considered mostly flat and comprised of rolling sandy plains to the north, rugged hills in the northeast and savannah to the south.[15] The mean elevation of the country is 343 m above sea level. The lowest point of the country (the Senegal River) is 23 m above sea level, while the highest (Hombori Tondo) is 1,155 m above sea level.[15] Additional significant relief features include the foothills of Fouta Djallon, Mount Manding (734 m above sea level) and the Bamboo Mountains in the southwest and west; the Adrar des Iforas extending to the Hoggar Saharan Massif (850 m above sea level) in the extreme north; and the Kénédougou Massif (800 m above sea level) in the southeast.[16]

The two main geological regions of the country are Kenieba and Bougouni.[17] The Kenieba region may be found south of Kayes and bordering Senegal, including the Tamaoura Escarpment 500 m above sea level to the east.[17] Bougouni is defined as the region bordering Côte d'Ivoire and Guinea to the south, including Bagoé, Bougouni-Keikoro, Yanfoliba and Kangaba.[17]

To the north of the country is the conflicted territory known as Azawad. This is a former unrecognised state that is made up of the regions of Tombouctou, Kidal, Gao and Mopti, and comprises about 60% of Mali's total land area. The National Movement for the Liberation of Azawad (MNLA) declared its independence following the driving out of the Malian army from the region by Tuareg rebels in 2012.[18,19]

The most prominent drainage features in Mali are the Sénégal River and the Niger River. The Sénégal River is comprised largely of the Bafing River and the Bakoye River, joined at Bafoulabé.[20] The Sénégal flows in a northwest direction in Mali around the Mandingue Plateau for about 670 km, also passing through Senegal and Mauritania from the Atlantic Ocean.[20] The Niger passes through Mali for about two-fifths (1,693 km) of its entire length in a northeast direction across the Mandingue Plateau, joining the Bani River and ultimately forming an interior delta before branching and making the characteristic Niger Bend southeast at Bourem towards Niger.[20] The Niger is the main source of water for domestic consumption, farming, irrigation and transportation for riverine populations, referred to as 'Mali's lifeblood.'[20,21]

Major relief features, rivers, lakes and major urban areas are depicted in Figure 1.[i] The major urban areas shown on the map are all cities with a population of more than

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[i] Mali's Digital Elevation Model used is the 30m resolution Advanced Spaceborne Thermal Emission and Reflection Radiometer

50,000 according to the 2009 Population and Housing Census.[22] These are (in order of population size): Bamako, Sikasso, Koutiala, Ségou, Kayes, Mopti, Kalabancoro, Gao, Kati, San, Bougouni and Tombouctou.

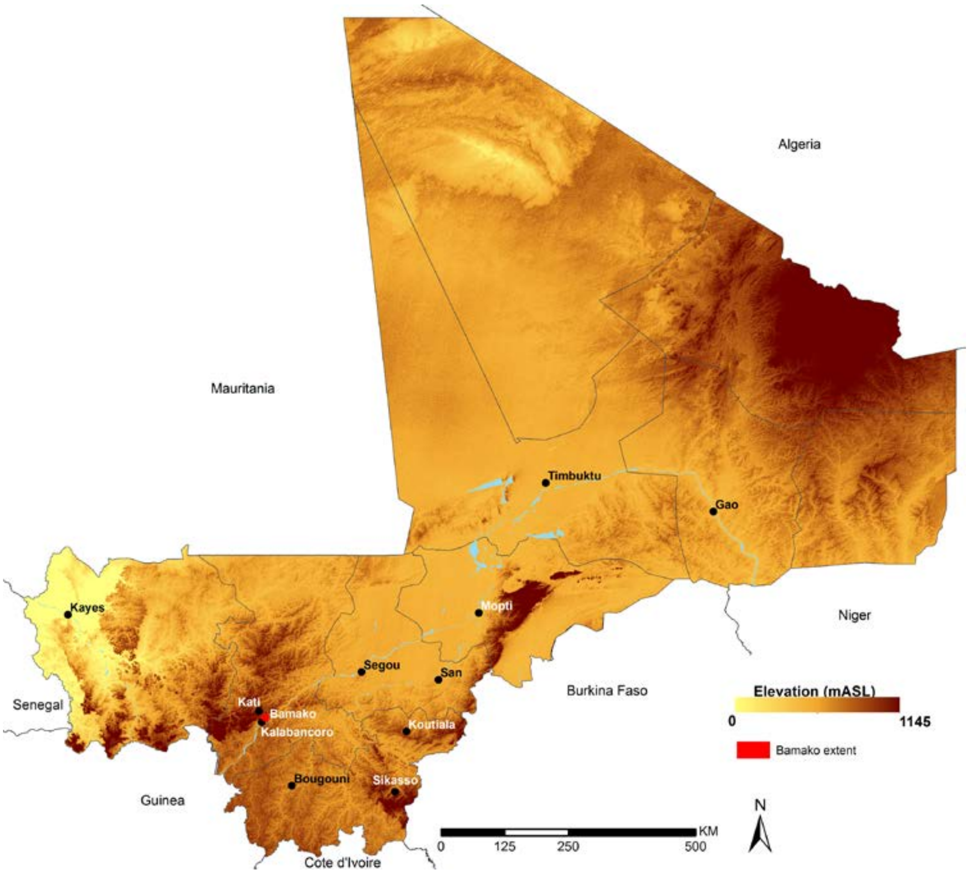


Figure 1 Major relief features, rivers and lakes, and indication of major urban areas (highlighted in red)

1.4 Climate

The seasons of Mali range from hot and dry from February to June; rainy, humid and mild from June to November; and cool and dry from November to February.[15] The four climatic zones of the country are comprised of the primarily agricultural Sudanese and Guinean zones in the south, and semi-arid Sahelian and arid Saharan zones to the north. The majority of the country's topography (65%) is composed of desert or semi-desert conditions.[21] The eco-climatic zones may be visualised in Figure 2.

(ASTER) Global Digital Elevation Model Version 2 (GDEM V2) accessed at (https://gdex.cr.usgs.gov/gdex/) on 16/03/18.

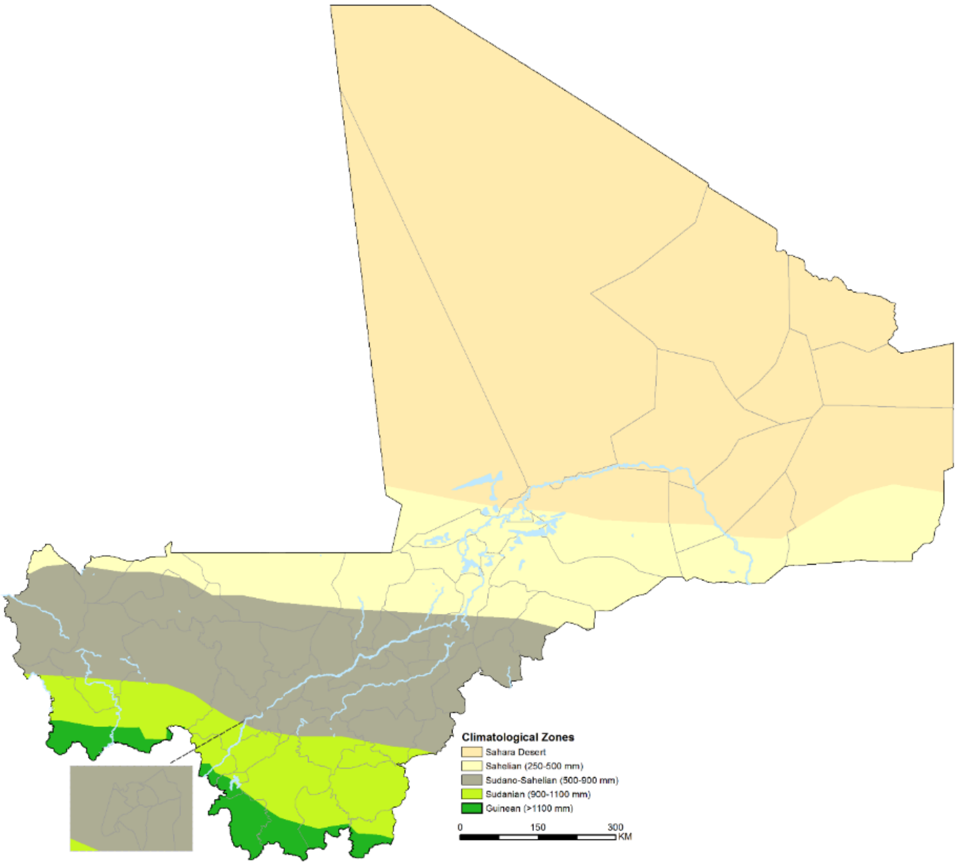


Figure 2 Adapted map of the eco-climatic zones of Mali[23]

Yearly fluctuations in latitudinal oscillations in the Intertropical Convergence Zone (ITCZ) result in large inter-annual variations in rainfall.[24] When in the northern position, usually from June to October, the ITCZ brings rains averaging 300 mm per month to the south, while barely any rain is experienced from November to March.[23,24] Consequently, Mali is prone to frequent droughts.[24]

Daily rainfall estimates from the Africa Rainfall Estimates version 2 (RFE 2.0) data from 2002–2009 were resampled to 1 x 1 km spatial resolution and used to identify seasonal areas. Within each health district, the proportion of the population that was in an area where ≥60% of rainfall occurred within any three consecutive months was computed. Health districts were identified as seasonal if 80% of population lived in areas where ≥60% of rainfall occurred in three consecutive months, and are mapped in Figure 3.[25] This was a replication of methods developed by Cairns et al.[26]

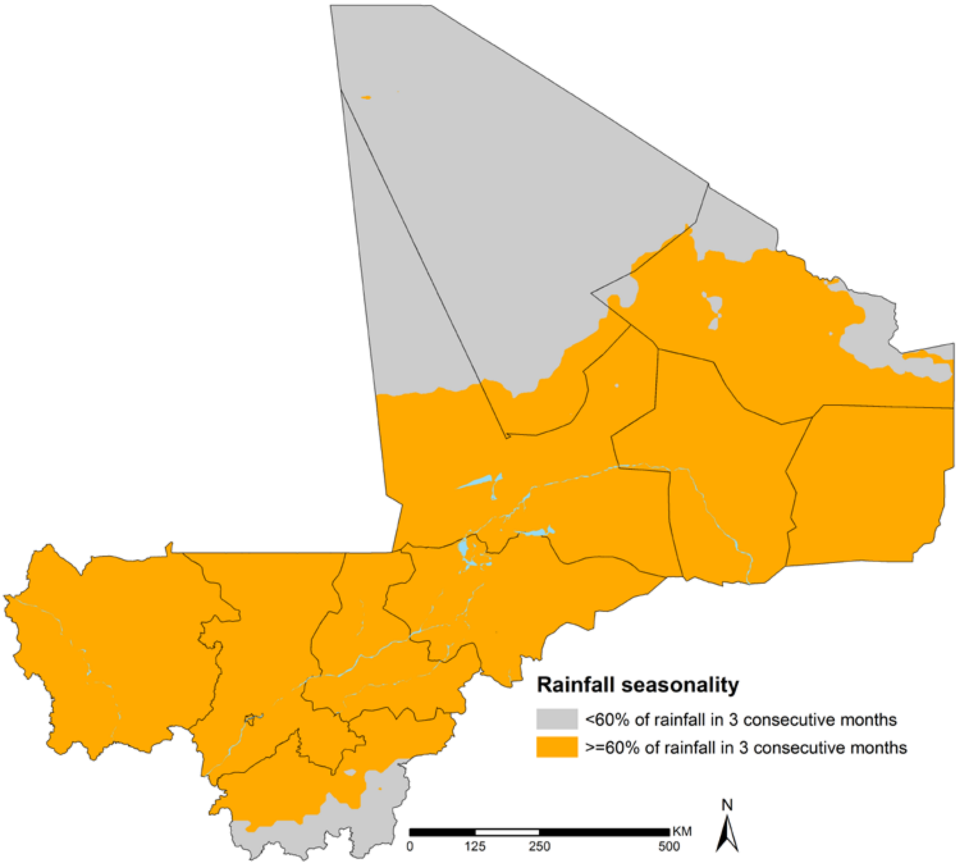


Figure 3 Rainfall seasonality in Mali

The mean temperature in Mali ranges between 27° and 30° C. While cooler temperatures ranging from 25° to 27° C may be found in the mountainous regions, northern temperatures may range from 27° to 35° C in the summer and drop to 15° to 25° C in the winter.[24] Temperatures are largely influenced by the winds, including the alize (blowing northeast from November to January) and the harmattan (blowing from the east from March to June).[20]

To demonstrate the aridity of Mali, the Global Mean Aridity Index from 1950-2000 at 30 arc seconds (or ~ 1km at the equator) spatial resolution may be utilised.[27] The aridity index is calculated using the following equation:

Aridity Index (AI) = Mean Annual Precipitation /Mean Annual Potential Evapo-Transpiration

AI values increase for more humid conditions and decrease with more arid conditions.

Mean annual precipitation (MAP) values were obtained from the WorldClim Global Climate Data, for years 1950 to 2000.[28] The Global Potential Evapo-Transpiration (PET) layers estimated on a monthly average basis were used to generate/aggregate mean annual values (MAE). PET is a measure of the ability of the atmosphere to remove water through the evapo-transpiration process. PET is calculated using the following equation:

$$PET = 0.0023 \bullet RA \bullet (Tmean + 17.8) \bullet TD0.5 \ (mm / day)$$

where *Tmean* is mean monthly temperature, *TD* is mean monthly temperature range and *RA* is the mean monthly extra-terrestrial radiation. The Hargreaves method has consequently been utilised, relying on monthly average temperature sourced from the WorldClim database and monthly extra-terrestrial radiation, calculated using a methodology presented by Allen et al., 1998.[29–31] Temperature range (*TD*) is a proxy to describe the effect of cloud cover on the quantity of extra-terrestrial radiation reaching the land surface.

The United Nations Environment Programme (UNEP) developed a classification based on the aridity index in 1997, further defined in Table 1.

Table 1 Aridity Index classifications according to the UNEP

Aridity Index Value	Climate Class
<0.03	Hyper-arid
0.03-0.2	Arid
0.2-0.5	Semi-arid
0.5-0.65	Dry sub-humid
>0.65	Humid

These metrics have been used since then and the hyper-arid regions of Mali may be demonstrated by Figure 4 using such methods.

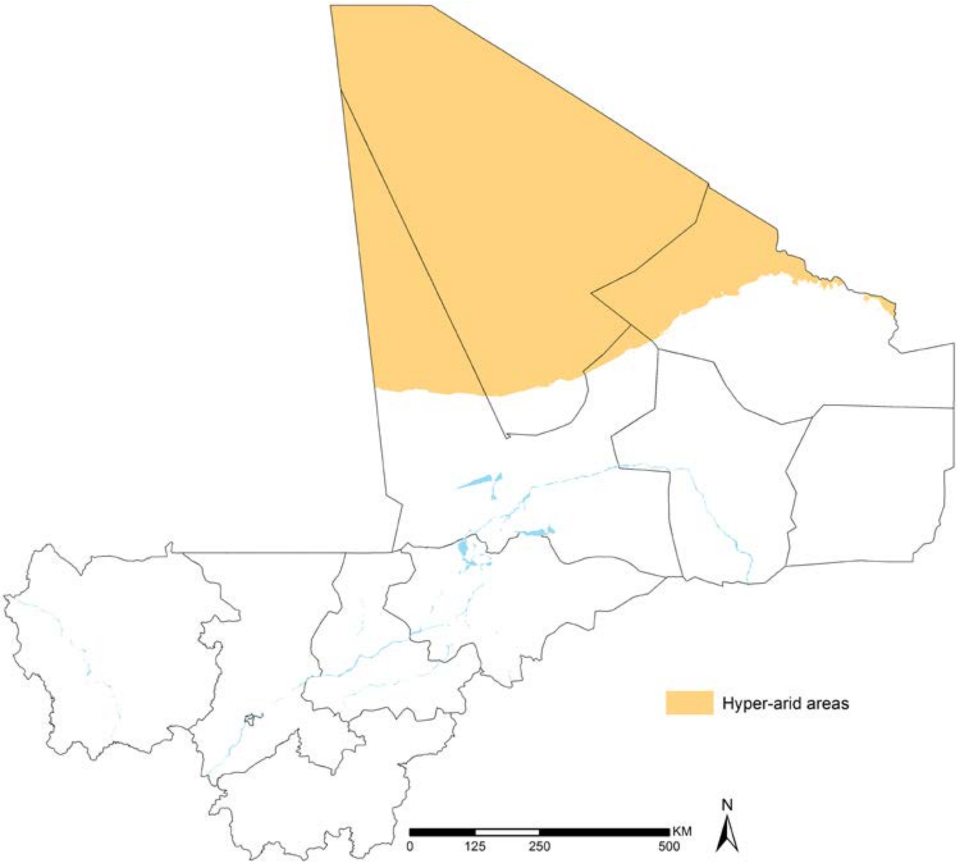


Figure 4 Hyper-arid regions of Mali

More than a third of the land in Mali is used for agricultural purposes, with 5.6% considered arable, 28.4% considered permanent pasture and 0.1% used for permanent crops.[15] Countries in the Sahelian region, including Mali, face environmental challenges such as droughts, desertification, soil erosion and reduced water supplies.[21,32] Due to the environmentally-linked economic and political reforms of the 1970s, droughts in the Sahel have been rigorously studied since the 1970s.[33]

One of the worst droughts in the Sahel in recorded history occurred from 1972 to 1984, in which an estimated 100,000 people died. By 1974, more than 750,000 people in Mali, Niger and Mauritania were wholly dependent upon food aid.[34] A famine subsequently struck the Sahel in August of 2010, resulting in crop failure in several countries amid record temperatures and almost complete rain failure. This led not only to widespread food shortages and starvation, but also to diseases related to poor nutrition, sanitation and pollution.

Power shortages have also been known to result from water shortages in hydroelectric dams.[35]

1.5 Political and conflict evolution and implications

In January 2012, the Tuareg rebel group MNLA began an insurgency against the government in the northern regions of Tombouctou, Gao and Kidal. This conflict led to significant deterioration of security in these regions and the displacement of large populations.[36] The MNLA remained in control of these regions until April 2013 following the intervention of the French government army in January 2013 to assist Malian government forces reclaim control of the north. In July 2013, the United Nations Multidimensional Integrated Stabilization Mission in Mali (MINUSMA) was deployed.[37] The security situation has improved since this deployment, although the region of Tombouctou and Gao are still considered of high risk with frequent skirmishes between the insurgents of government forces.

Ibrahim Boubacar Keïta, the democratically-elected president of Mali since 2013, signed an internationally-mediated peace accord in June 2015 with the militant groups in the north.[15] However, these agreements have yet to be met and groups that were not included continue to cause unrest in rural areas.[15] A state of emergency was enacted in November 2015 and recently extended in October 2017 for another year.[38]

As of 2017, Mali was ranked 25th in the world for terrorism impact, with groups including the Al-Qa'ida-affiliated Jama'at Nusrat al-Islam wal-Muslimin, Al'Qa'ida in the Islamic Maghreb, the Islamic State of Iraq and the Levant in the Sahel, Al Murabitoun, Ansar Dine, Boko Haram and Libération du Macina.[15,38,39] Twelve percent of terrorism attacks (equating to 10% of terrorism-associated deaths) in Mali in both 2012 and 2016 are attributed to the Libération du Macina. These attacks have included indiscriminate violence, kidnappings, improvised explosive devices and attacks against peacekeeping forces with extremism often tied to unemployment, lack of opportunity, weak religious institution regulation, reduced family values, the formation of an Islamic state and flaws in public administration and judicial processes.[38,39] Such groups are primarily active in the Mali-Niger and Mali-Burkina Faso border regions.[15]

This volatile situation inhibits the capabilities of humanitarian aid, either slowing or altogether blocking access to local populations in need.[40]

1.6 Population and economy

Population

Mali's population is comprised of a number of Sub-Saharan ethnic groups, including (in order of size) the Bambara, Soninké, Malinké, Fulani, Peul, Sénoufo, Dogon, Songhai, Diola, Bobo, Oulé, Tuareg and Moors/Maur.[21]

Since gaining independence, there have been four national population censuses undertaken in Mali. These were conducted in 1976, 1987, 1998 and 2009 and indicate unstable population demographics. The average annual population growth decreased from 1.75% in 1976 to 1.41% in 1987 before drastically increasing to 2.60% in 1998.[41] This trend continued until 2007 with a growth of 3.34% before dropping slightly again in 2009 to 3.26%.[41] Current estimates indicate a rise in annual growth at 2.97% after achieving a decline to 2.90% in 2013 (Figure 4).[41]

As of mid-2017, the population was 18.9 million.[42] It is projected that by 2023 the population will reach 22.96 million and 27.5 million by mid-2030.[42,43]

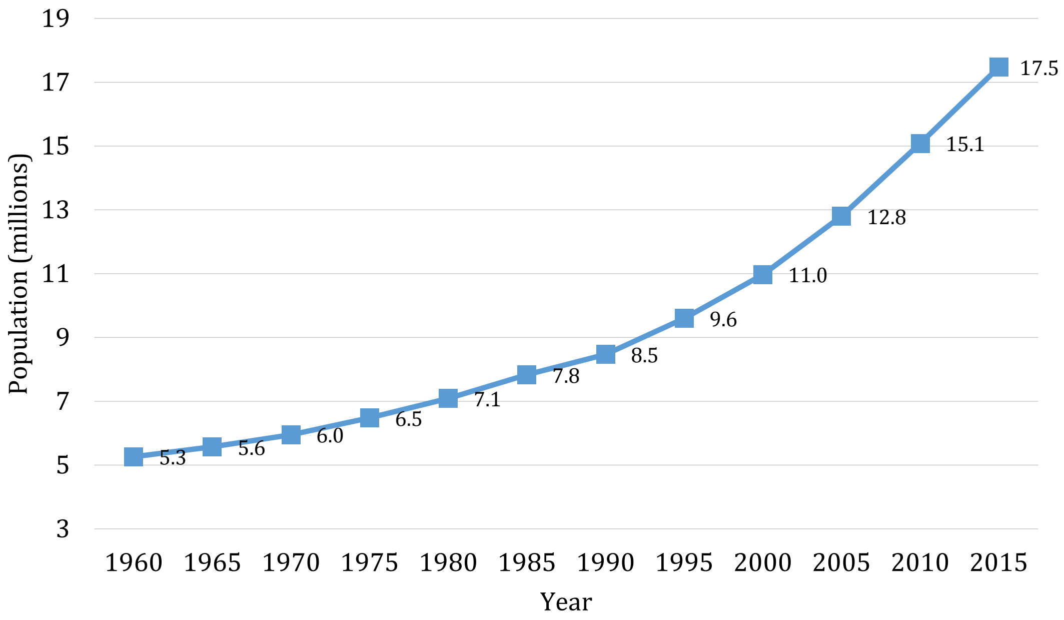


Figure 5 Population estimates in Mali, 1960 to 2015

To improve our understanding of human settlement patterns, spatial modelling techniques were developed to reallocate populations within census units to finer gridded surfaces.[44] In brief, a dasymetric modeling technique was used to redistribute population counts within 687 spatially-defined communes (administrative level 4 units) used during the 2009 national census and land cover data sets derived from satellite imagery.[45] A different population weight was assigned to each land cover class in order to shift populations away from unlikely populated areas (for example game reserves or arid deserts) and concentrate populations in built-up areas.

The net result was a gridded dataset of population distribution (counts) at 0.1 x 0.1 km resolution. The population distribution datasets were projected to years used to predict malaria risk and LLIN coverage (see later) using United Nations (UN) national rural and urban growth rates and made to match the total national population estimates provided by the UN Population Division for these years.[46,47] The resulting modelled population density for 2015 may be found in Figure 5.[ii]

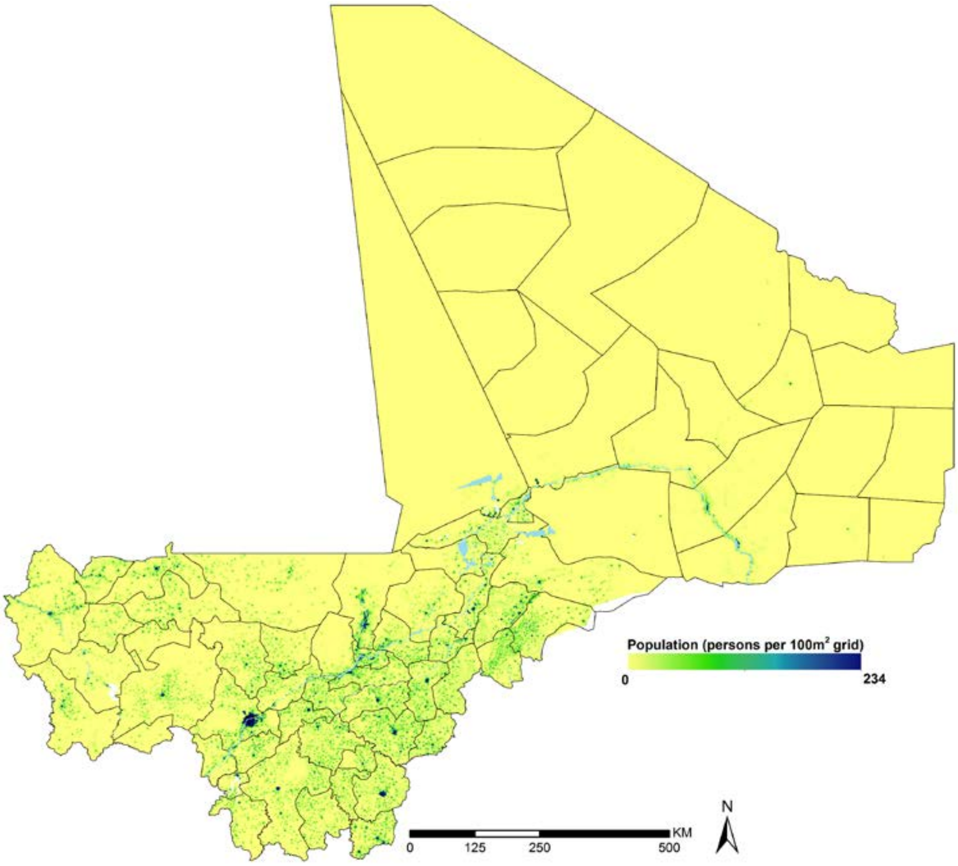


Figure 6 Modelled 2015 population density per 100 m^2

Population distribution mapping and malaria prevalence estimations could be improved using updated census data.

As of 2016, the population density of Mali is quite low at an estimated 15 persons per km^2 compared to the aggregated Sub-Saharan Africa population density of 44 persons per km^2.[41] In comparison to bordering countries, the population density of Mali is greater than Mauritania, but lower than that of Niger, Algeria, Guinea, Burkina Faso, Côte d'Ivoire and Senegal (Table 1).[48]

[ii] Dataset used was the alpha version 2015 estimate of numbers of people per grid square, with national totals adjusted to match UN population division estimates (http://esa.un.org/wpp/) and a spatial resolution of 0.00833333 decimal degrees (approximately 100 m at the equator). A geographic, WGS84 projection was utilised using a land cover based mapping approach described by Linard, C., Gilbert, M., Snow, R.W., Noor, A.M., and Tatem, A.J., 2012.

Table 2 Population density (people per km^2 of land area) of Mali and neighbouring countries for 1987, 2009 and 2016

Country	**1987**	**2009**	**2016**
Mali	7	12	15
Algeria	10	15	17
Burkina Faso	30	55	68
Côte d'Ivoire	35	63	75
Guinea	22	43	50
Mauritania	2	3	4
Niger	6	13	16
Senegal	36	65	80

Urbanisation

Mali's population is rapidly urbanising (Figure 6). In 1976, 17.5% of the population of Mali (1.1 million) was classified as urban and were concentrated primarily in Bamako City and other main urban areas such as Ségou, Sikasso, Mopti, and Koutiala, Kayes, Tombouctou, Gao and Kati. By 2009, this figure had risen to 33.6%, to 34.7%, in 2013 and 41.4% in 2017.[15] This can largely be attributed to population movements as a result of the conflict in the north, with 22% of internally displaced persons (IDPs) moving to Bamako alone.[49]

Estimates from 2015 to 2020 place urban growth at about 4.9% per annum.[15] The majority of the population lives in the south of the country, particularly along the Burkina Faso border.[15]

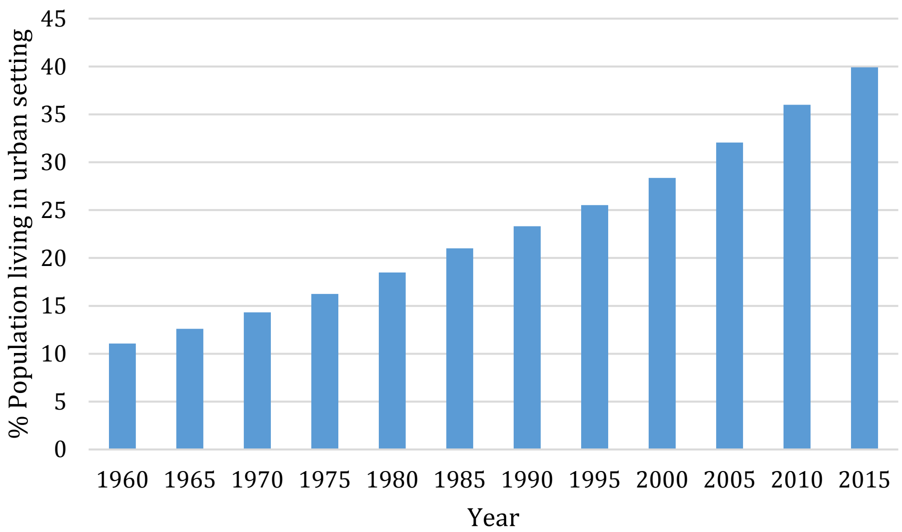


Figure 7 Percentage of the total population residing in urban areas of Mali between 1960 and 2015 according to *World Urbanization Prospects: 2014 Revision* of the United Nations Population Division 2014

Population movement

A potential major driver of malaria epidemics is the large and unplanned movement of people. These movements, in turn, lead to a strain on the health system and hinder detection, treatment and surveillance capacities.[50]

Prior to the eruption of conflict in 2012, Mali maintained fluid borders for populations and served as a transit country to the north.[49] In the 1990s, large numbers of Tuaregs returned to Mali from Algeria and Libya due to drought and increasing tensions.[21] Mali has also served as a refuge for 15,624 refugees and 2,497 asylum seekers from bordering countries, in particular, during the Mauritanian-Senegal war in 1989, the civil war in Côte d'Ivoire in 2002 and the conflicts in Sierra Leone in the 1990s.[49]

The military coup in 2012 was a major driver for a migration crisis in Mali and the continued conflict has resulted in the flight of the local population to neighbouring countries and to southern Mali.[49] An estimated 8.6% of the Malian population has fled the conflict zone in the pursuit of improved security.[49] With such a low population density in the north, this movement resulted in significant programme management complications.[49]

There are approximately 38,172 IDPs currently living in Mali.[40] In parallel, the country is struggling to cope with the problem of Malian refugees returning post-stabilisation, with 526,505 IDP returnees and 63,107 returning refugees in 2017.[40] Many IDPs are from the nearly malaria-free northern desert regions, therefore making them largely non-immune and a large risk group for potential malaria epidemics.

Before the migration crisis, up to a third of the Malian workforce would seasonally migrate to urban areas or to neighbouring countries for pastoral purposes, especially in the context of the country's high drought vulnerability.[49] Additionally, Mali was used for trafficking labour across neighbouring borders, with Gao and Tombouctou serving as major hubs with limited border control enforcement.[49] An estimated 5% to 10% of the Malian population is considered nomadic, potentially contributing to an increased risk of malaria transmission in lower prevalence areas.[15,21]

Economy

Upon gaining independence, Mali transitioned to a socialist economic approach including the nationalisation of resources.[21] This reform did not last long, as Mali rejoined the Franc Zone in 1967 due to a faltering economic system.[21] Turmoil associated with a coup in 1968 and drought from 1968 to 1974 further stalled the economy and attempted reforms.[21] The economic system was gradually improved after the signing of structural adjustment agreements with the International Monetary Fund (IMF).[21] Mali is now a member of the Economic Community of West African States (ECOWAS) and the West African and Monetary Union (WAEMU), but still ranks 176th out of 188 countries evaluated by the UN Human Development Index.[51]

Mali struggles with widespread poverty, ranking among the 25 poorest countries in the world; 90% of the Mali's poor live in rural areas in the south of the country.[15,51] These conditions are largely the consequence of ongoing conflict and recurrent droughts, with a particularly noticeable decline in gross domestic product (GDP) from USD 12.98 billion in 2011 to USD 12.44 billion in 2012 coinciding with a significant period of conflict.[51] This is demonstrated in Figure 8, which illustrates Mali's GDP growth (current USD) for the period from 2008 to 2017. Notably, overall poverty rates declined from 55.6% to 45% between 2001 and 2013, driven by growth in the agricultural and services sectors, with an overall GDP growth rate of 5.8% in 2016.[51] Both private consumption and gross fixed investments are on the rise by 5.1% and 14.9%, respectively, attributable to infrastructural improvements and agricultural yields.[51]

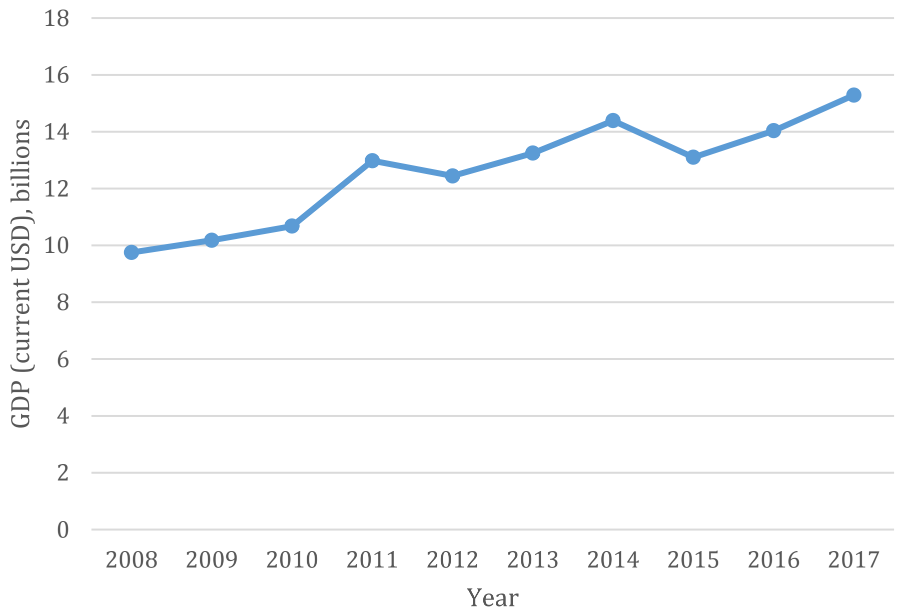


Figure 8 GDP (current USD) in billions for the period 2008 - 2017 in Mali[41,48]

The primary agricultural products of Mali include millet, corn, rice, peanuts and vegetables.[15] Natural resources found in Mali include bauxite, copper, gypsum, diamonds, iron ore, gold, limestone, phosphates, manganese, salt, silver, zinc, lithium and uranium.[21] However, a number of these mineral resources are not considered viable for commercial purposes or are difficult to access due to ongoing conflict.[21] Few of Mali's resources are exported, but those that are include cotton, gold and livestock (cattle, sheep, goats). These resources are exported to Switzerland (30.4%), India (12.2%), Ukraine (5.1%), China (5.1%), Burkina Faso (4.9%), Senegal (4.3%) and France and South Africa (4%).[15] Due to the agricultural nature of these products, they are dependent upon environmental factors and may fluctuate severely according to conditions.[15,51] The economy of Mali is subject to major shocks, as nearly 80% of the population is involved in fishing and/or agriculture industries, sectors which make up 40.9% of GDP.[15]

Current economic conditions are promising and are expected to maintain the current inflation drop of -1.8% and increase GDP (USD 14.035 billion as of 2016).[41,51] Major obstacles to this trend continuing are thought to be corruption and political turmoil, as experienced in 2012 with the political coup.[15]

Unemployment in Mali is estimated to affect 8.1% of the population and 36.1% are below the poverty line.[15] As of 2017, GDP per capita purchasing power parity (PPP) was

USD 2,200.[15] ODA to Mali is increasing, with USD 1,210 million provided in 2016 compared to the annual average USD 715 million from 2000 to 2009.[52] However, Mali is a highly indebted country with debt estimated at USD 4.296 billion as of 2017.[15]

Health in Mali overview

Although Mali has achieved significant progress in health and experienced a large reduction in child and infant mortality rates, the country still has some of the poorest health indicators globally. Median infant and under five mortality rates are 68 and 110.6 deaths per 1,000 live births, respectively. This is a decline from the figures reported in 2010 of 79.5 and 136.5 deaths per 1,000 live births, respectively.[53,54]

The total fertility rate of 6.0 children per woman of childbearing years remains the sixth highest globally, but this has declined from 2010, when the average fertility rate was 6.6 children per woman of childbearing years.[42] This decline is likely due to the increase in the number of women 15 to 49 years of age using modern methods of contraception from 6% to 15% for the same time period.[39,52] As of 2016, the maternal mortality ratio of Mali remains high at 379.6 deaths per 100,000 live births, a decline from 397 deaths per 100,000 live births in 2010.[56]

The age distribution of the population is heavily skewed; 48% of the population is less than 15 years of age and 3% of the population is more than 65 years of age.[42] Men and women maintain a relatively equal life expectancy at birth at 57 and 58 years of age, respectively.[42] Life expectancy at birth has increased since 2010, when the average life expectancy for men and women was 50 and 53 years of age, respectively. [55]

All-cause mortality is driven primarily by deaths from diarrheal diseases and lower respiratory infections, accounting for 21.02% (17.61%-25.18%)of total deaths in 2016. These are followed by neglected tropical diseases (NTDs) and malaria (19.29%, 15.99%-22.8%), neonatal disorders (13.52%, 11.84%-15.2%), cardiovascular diseases (9.45%, 8.01%-11.13%), neoplasms (5.61%, 4.67%-6.58%), HIV/AIDS and tuberculosis (4.62%, 3.68%-5.63%) and nutritional deficiencies (4.11%, 2.48%-6.19%). The remaining 22.38% is comprised of factors such as chronic respiratory diseases, digestive diseases and war and disaster.[56] The primary causes of death are similar to 1990, when diarrheal diseases and lower respiratory tract infections were responsible for 33.42% (28.71%-39.62%) of deaths, NTDs and malaria for 12.88% (9.83%-16.39%), neonatal disorders for 11.49% (10.26%-12.79%) and cardiovascular diseases for 8.24% (7.34%-9.11%).[56]

Rates of HIV infection in Mali are declining, with slight differences in gender distribution. At present, 0.3% of males and 0.6% of females in Mali aged 15 to 24 have been diagnosed with HIV/AIDS, a reduction from 2007/2009 measures of 1.2% and 1.7%, respectively.[42,55]

An estimated 24.9% of children under five years of age suffer from stunting and 11.1% of children under five years of age suffer from wasting in Mali.[56]

1.7 Administration and policies

Government

Mali is a multiparty, democratic, semi-presidential republic managed by a president and a presidentially-appointed prime minister.[15] The president is elected by popular vote for a five-year term and the presidential appointment is limited to two terms. President Ibrahim Boubacar Keïta has served since 2013 following the military seizure of power in 2012 and interim government rule.[15] The most recent election was carried out in July of 2018 and required a runoff vote since no candidate received more than 50% of the vote. President Keïta was subsequently re-elected, defeating his primary opponent, Soumaïla Cissé, of the Rally for Mali party. The presidential cabinet, or Council of Ministers, is composed of individuals appointed by the prime minister.[15]

The legislative branch of Mali is comprised of 147 seats to form the Assemblee Nationale (National Assembly) elected by constituencies for five-year terms. Malians abroad are responsible for the election of 13 seats.[15]

The highest level of the judicial branch of Mali is composed of the Cour Supreme (Supreme Court) of 19 members appointed by the Ministry of Justice for five years, as well as the Constitutional Court of nine members selected by the president. Below the Cour Supreme are the subordinate courts of the Court of Appeal, the High Court of Justice, magistrate courts, first instance courts, labour dispute courts and a special court of state.[15]

There are a number of political parties in Mali, including: the African Solidarity for Democracy and Independence; the Alliance for Democracy in Mali-Pan-African Party for Liberty, Solidarity and Justice; the Alliance for Democracy and Progress; the Alliance for the Solidarity of Mali-Convergence of Patriotic Forces; Alternative Forces for Renewal and Emergence; Convergence for the Development of Mali; the Economic and Social Development Party; the Front for Democracy and the Republic; the National Congress for Democratic Initiative; the Party for National Renewal; the Patriotic Movement for Renewal; Rally for Mali; and the Union for Republic and Democracy.[15]

Levels of decision-making

The most recent decentralisation of government functions (such as health as policy) began in 1992 when it was outlined in the constitution and implemented in 1999 with the formation of elected local governments.[57] This was envisioned as a means to free the country from unilateral post-colonial decisions, and potentially resolve ongoing tension with the north of the country.[57]

Through the decentralised scheme, the majority of administrative decisions are made at the commune level. The central government provides a large proportion of budgetary support to local governments. Local government and commune leaders are elected through universal suffrage and are responsible for collecting local revenues. Local governments serve on average 20,000 inhabitants at the commune level and are comprised of councillors, a mayor and administrative staff.[58]

Health system administrative divisions

Administratively, Mali is divided into 11 regions. These 11 regions contain 75 districts (cercles) administered by arrondissements (sous-préfectures) (Figure 8, Table 2). The districts are further sub-divided into communes which are made up of villages or quarters.

Since 2014, the government has newly-defined two regions:

1. Taoudenit (formerly in Tombouctou region) which includes six districts; and
2. Menaka (formerly in Gao region) which includes four districts.

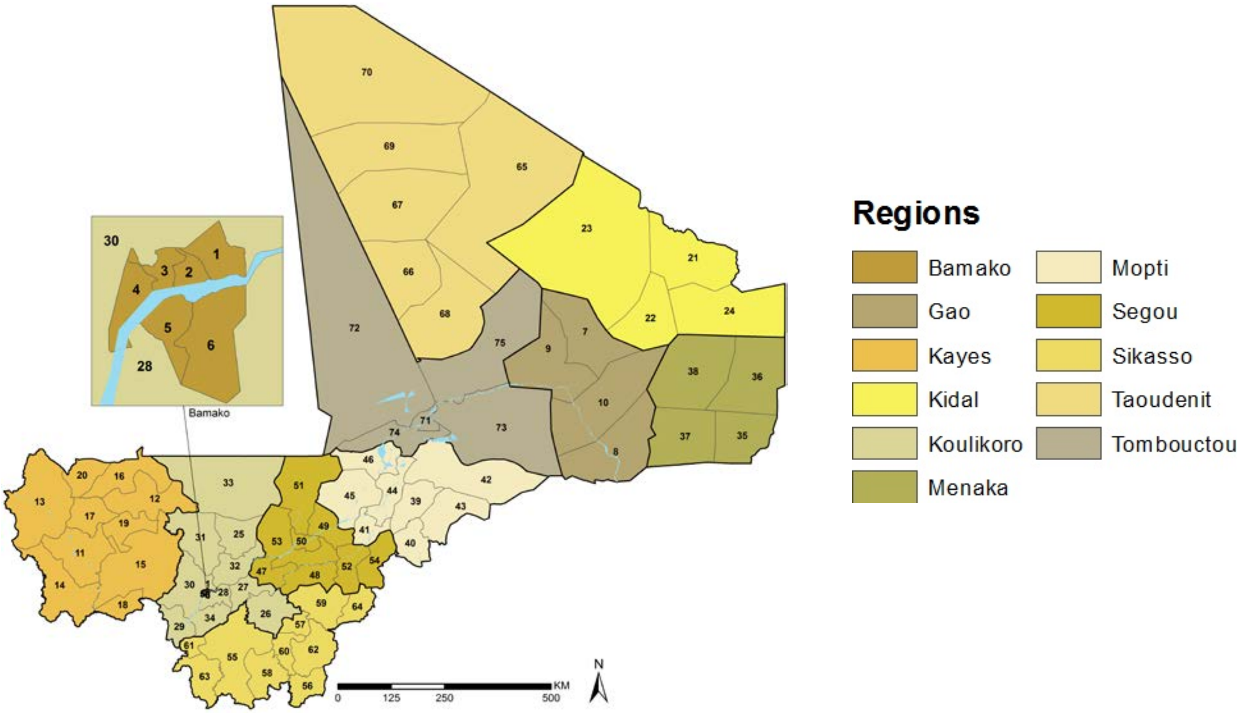


Figure 9 75 districts of Mali within 11 nominal regions. The methods for validating and preparing this figure are provided in *Annex A*

Table 3 75 Districts by region for Mali

Region	District	Map Code
Bamako	Commune I	1
	Commune II	2
	Commune III	3
	Commune IV	4
	Commune V	5
	Commune VI	6
Gao	Almoustrat	7
	Ansongo	8
	Bourem	9
	Gao	10
Kayes	Bafoulabe	11
	Diema	12
	Kayes	13
	Kenieba	14
	Kita	15
	Nioro	16
	Oussoubidiagnan	17
	Sagabari	18
	Sefeto	19
	Yelimane	20
Kidal	Abeibara	21
	Kidal	22
	Tessalit	23
	Tin-essako	24
Koulikoro	Banamba	25
	Dioila	26
	Fana	27
	Kalaban Coro	28
	Kangaba	29
	Kati	30
	Kolokani	31
	Koulikoro	32
	Nara	33
	Ouelessebougou	34
Menaka	Anderamboukane	35
	Inekar	36
	Menaka	37
	Tidermene	38
Mopti	Bandiagara	39
	Bankass	40
	Djenne	41
	Douentza	42
	Koro	43
	Mopti	44
	Tenenkou	45
	Youwarou	46
Segou	Baraoueli	47
	Bla	48
	Macina	49
	Markala	50
	Niono	51
	San	52
	Segou	53
	Tominian	54
Sikasso	Bougouni	55
	Kadiolo	56
	Kignan	57
	Kolondieba	58
	Koutiala	59
	Niena	60
	Selingue	61
	Sikasso	62
	Yanfolila	63
	Yorosso	64
Taoudenit	Achouratt	65
	Al-ourche	66
	Araouane	67
	Boujbeha	68
	Foum-elba	69
	Taoudenit	70
Tombouctou	Dire	71
	Goundam	72
	Gourma-rharous	73
	Niafunke	74
	Tombouctou	75

Health system

Historical perspective of the health system

Upon gaining independence, Mali restricted healthcare services to the public sector through a ten-year development plan.[59] Through this scheme, a pyramidal service provision structure (described later) was reinforced and drugs were provided through the Pharmacie Populaire du Mali (PPM) to ensure a consistent supply chain.[59] In the 1980s, care was offered free of charge, but services were minimally utilised.[60] This under utilisation of public services was largely due to distance from facilities (30% of the Malian population lived within 15 km of a health centre in the 1980s), more readily available traditional healers and poor quality of care.[61] Additionally, the number of civil servants in the health sector declined when private practice was re-authorised in 1985 in urban areas.[59,60]

The first health sector reform in Mali, the Politique Sectorielle de Santé et de Population, and the joint Bamako Initiative between the WHO and UNICEF to increase essential drug and healthcare service availability through decentralisation, brought about the establishment of community health centres (CSCOMs) in the 1990s.[62] CSCOMs were implemented to resolve deficient health service utilisation, and responsible for the provision of care to 10,000 persons apiece, overseen by a locally-elected association de santé communautaire [association for community health (ASACO)].[60] By 1997, there were approximately 500 public health care facilities throughout the country.[59] Among these there were 14 hospitals, 52 health district health centres and 270 district health centres.[59] Community empowerment, technical and financial partner strengthening, private sector and civil society relations and essential medicines were further sought to improve through these efforts.[1]

The subsequent decentralisation reforms in Mali's healthcare system were driven by politically-backed structural adjustments. The recruitment of healthcare professionals declined progressively over time, resulting in a ratio of qualified staff to the population up to eight times higher in urban areas than in rural areas.[58,60] To address this discrepancy, young doctors were encouraged to pursue employment in rural areas of the country by the Faculty of Medicine of Bamako and supported by the non-governmental organisation (NGO) Santé Sud.[60] By 2005, 74% of field doctors were practicing with a CSCOM and only 15% were active in private practice.[60] Rural doctors are expected to uphold a high quality of care while simultaneously considering ability to pay, generic drug and minimum package of care provisions, implementation of social protection mechanisms, health promotion and education activities.[60]

In 2013, the government of Mali adopted the PDDSS 2014-2023 and the PRODESS 2014-2018. The PDDSS and PRODESS serve as the primary reference documents for health interventions and social development in Mali, with both seeking a multisectoral and decentralised stance in the transfer of power to communities.[1] A new PDDSS has recently been developed, set to more closely monitor objective achievement and align with the Cadre Stratégique pour la Croissance et la Réduction de la Pauvreté (CSCRP).[1]

As of 2010, there were 0.1 hospital beds per 1,000 persons in Mali and less than 0.09 physicians per 1,000 persons.[41] While the number of nurses and midwives is slightly better at 0.443 per 1,000 persons, the number of community health workers is even lower at 0.007 per 1,000 persons.[41] Response to unmet need is heavily reliant upon missionary groups and international development organisations, particularly in the northern regions of the country.[21] Missionary groups and faith-based organisations only recently became active in Mali, as their presence was discouraged post-independence.[61]

Due to the ongoing conflict in Mali, access to medical staff and/or supplies is limited. Medical staff have fled from regions such as Tombouctou, creating a demand for external support. This gap has primarily been filled by Médecins Sans Frontières (MSF), now responsible for hospital and health centre support, chronic disease treatment, nutrition and laboratory services, mental healthcare, maternal healthcare, surgery, emergency care, and seasonal malaria prevention in Gao, Kidal, Koutiala and Tombouctou.[63] On a national scale, bilateral and multilateral organisations are widely active, with the Groupe Pivot de Santé et Population (GPSP) coordinating NGOs and the Ministère de la Santé et de l'Hygiène Publique.[62]

Health system governance

The primary health care system is currently composed of individual-oriented curative services, preventive services and promotional services.[58] Government expenditure has increased from 4.3% of GDP in 2001 to 6.9% of GDP (Intl USD 108 per capita) in 2014, with out-of-pocket expenses as a percentage of current health expenditure still high despite declining from 71% to 47% in the same years.[21,57,64,65]

The Ministère de la Santé et de l'Hygiène Publique oversees health policy development, while the Direction Nationale de la Santé [National Health Directorate (DNS)] oversees implementation efforts.[66] Both the Ministère de la Santé et de l'Hygiène Publique and DNS report to the Secretary General.[3] The Regional Health Directorates (DRS) and the four national hospitals are responsible for the regional operation of the national health policy.[62,66] Regarding malaria, the PNLP was previously under the direction of the Disease Control Division of the DNS. This shifted in 2007 when the PNLP became a directorate and began reporting directly to the Secretary General.[3] The PNLP is composed of four technical groups and a financial and administrative division.[3]

Daily management, financing and decision-making are delegated to ASACOs and locally elected governments.[58] ASACOs are comprised of a management committee and a board of directors made up of representatives from the commune, the village and health staff.[61] The local governments work in partnership with the ASACOs responsible for medicine and supply stock management, financing of services, facility maintenance and staff recruitment.[58,61] Recruited physicians may be hired on different contract schemes through the ASACOs, either as partners or employees.[60]

Service provision hierarchy

Health districts are primarily responsible for planning, budgeting and managing health development, while the regional levels are responsible for technical support of the health districts. The national level defines strategies and determines operational investments.[1]

Providers of care within the health system include para-statal health centres, health centres belonging to enterprises, military health centres, insurance companies, public and private medical and allied health schools, pharmacies, NGOs and traditional healers.[62] Traditional healers are registered under the Fédération Malienne des Associations des Tradithérapeutes et Herboristes (FEMATH), which collaborates with the Ministère de la Santé et de l'Hygiène Publique to integrate traditional and modern medicines.[1]

In the public sector, Mali relies upon a pyramidal service provision system (Figure 9), which operates on a referral basis with basic services at the base of the pyramid and the most specialised at the top. At the community/village level, community health workers are primarily responsible for care. At the district level, the centre de santé de référence (CSREF) serve as referral health centres between CSCOMs to the regional hospitals, with linkages to the regional health directorates.[66] As of 2017, there were 74 active CSREFs in Mali.[1] CSREFs, funded primarily by the government and donors, provide emergency care, obstetrics and surgical operations. Additionally, CSREFs have a malaria focal person for CSCOM support.[3] Each CSREF head oversees the CSCOMs which provide primary care services in their respective district.[62,66] If the necessary care is outside the remit of a CSREF, patients may be referred to one of the eight regional hospitals in the country, located in Gao, Kayes, Kati, Mopti, Sikasso, Ségou, Tombouctou and Bamako.[3,62,66] At the top of the pyramid are five tertiary reference hospitals, a national public health research institute, a national blood transfusion centre, a national health laboratory and two research centres.[1]

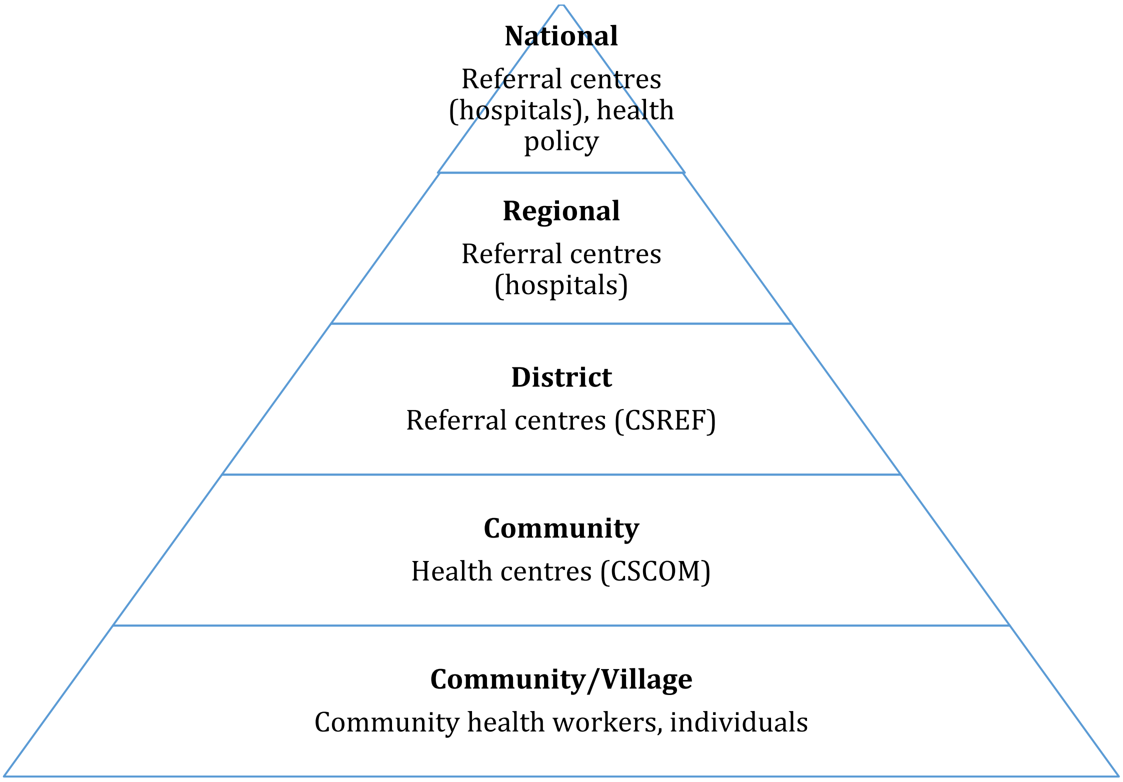


Figure 10 The health service provision pyramid in Mali

Since 2016, there have been 1,294 CSCOMs actively operating in Mali.[1] CSCOMs are typically staffed by a nurse, a midwife and an individual responsible for the drug supply.[61] However, staffing depends upon funding available at the community level and staff appointment needs.[3] CSCOMs are intended, under the National Health Plan of Mali, to provide a local health service to members of the population within 15 km, responding to 90% of facility-based services.[61] This includes preventive, promotional and curative health services.[58] To establish a CSCOM, communities must undertake a basic set of tasks, including the establishment of an ASACO, the hiring of personnel and the provision of a minimum of 10% of the costs associated with building a CSCOM.[3] Revenue for CSCOMs is generated through membership fees, drug sales and user fees which vary according to ASACO determinations.[3,61]

At the community level are Agents de Santé Communautaires (ASCs), which service villages and households with an integrated community case management (iCCM) package if they are more than 5 km from a health facility.[3] iCCM includes uncomplicated malaria treatment, malnutrition treatment, newborn primary care and family planning services. As of 2017 there were 2,337 trained ASCs in Mali.[3] ASCs are assisted by relais volunteer workers which primarily provide social and behaviour change communications.[3]

Health facility mapping

Accurate health system information is the cornerstone of effective decision-making and reliable assessments of disease burden and resource need.[67,68] Efforts to tackle the enormous burden of ill-health in low-income countries are hampered by the lack of functioning health information structures to provide reliable health statistics.[69–71] Central to a fully operational Health Information System (HIS) is a basic inventory of all functioning health facilities and the services that they provide. Such an inventory requires a spatial dimension, allowing facilities to be linked to the populations they serve by level of care and other proximate determinants of health such as environment, poverty and education. This spatial linkage can be provided by geographic information systems (GIS). The use of GIS for health services planning is widespread in developed countries, but there are few examples of their development and operational use in resource-poor settings in Africa.[72–76]

The location of clinical service providers is critical for planning future health sector requirements, a tactic that is not unfamiliar to Mali.[74] For example, mapping during Guinea worm eradication efforts proved particularly useful in planning interventions (Figure 10).

The final database used to generate an updated map included 1,447 geocoded public health facilities, comprised of 78 hospitals, 1,262 community health centres and 105 clinics. The final map of health facilities may be found as Figure 11.

The associated data was drawn from Humanitarian Data Exchange 2015, WASH Cluster Mali 2016, and the Ministère de la Santé et de l'Hygiène Publique 2016.[77–79] Nineteen duplicates were excluded and 30 coordinates and facility ownership were missing. No data was available on private facilities or those that provide specialist services (eg. maternity) or non-publically available services (police and prisons). The data was geocoded using global positioning system (GPS) sources (1,394), Google Earth (8), Encarta (9), Geonames (12), other sources (13) and a combination of other sources (11).

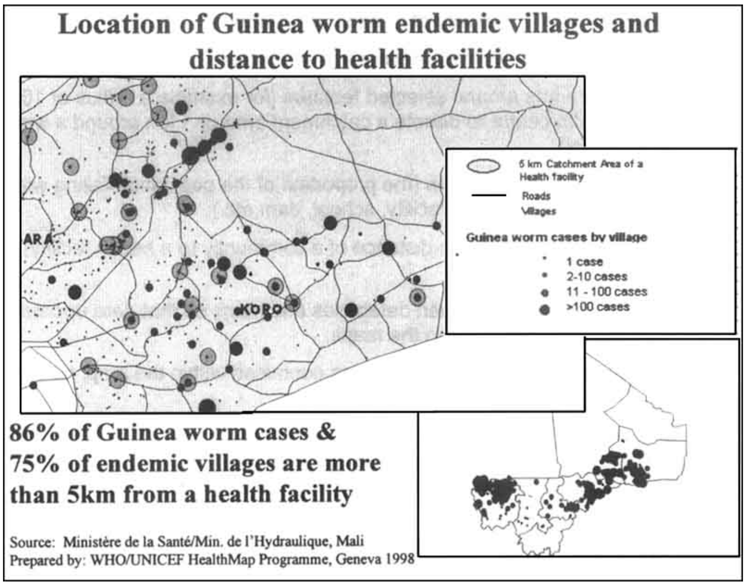


Figure 11 Location of health facilities with 5 km buffers used during the Guinea worm eradication effort in Mali

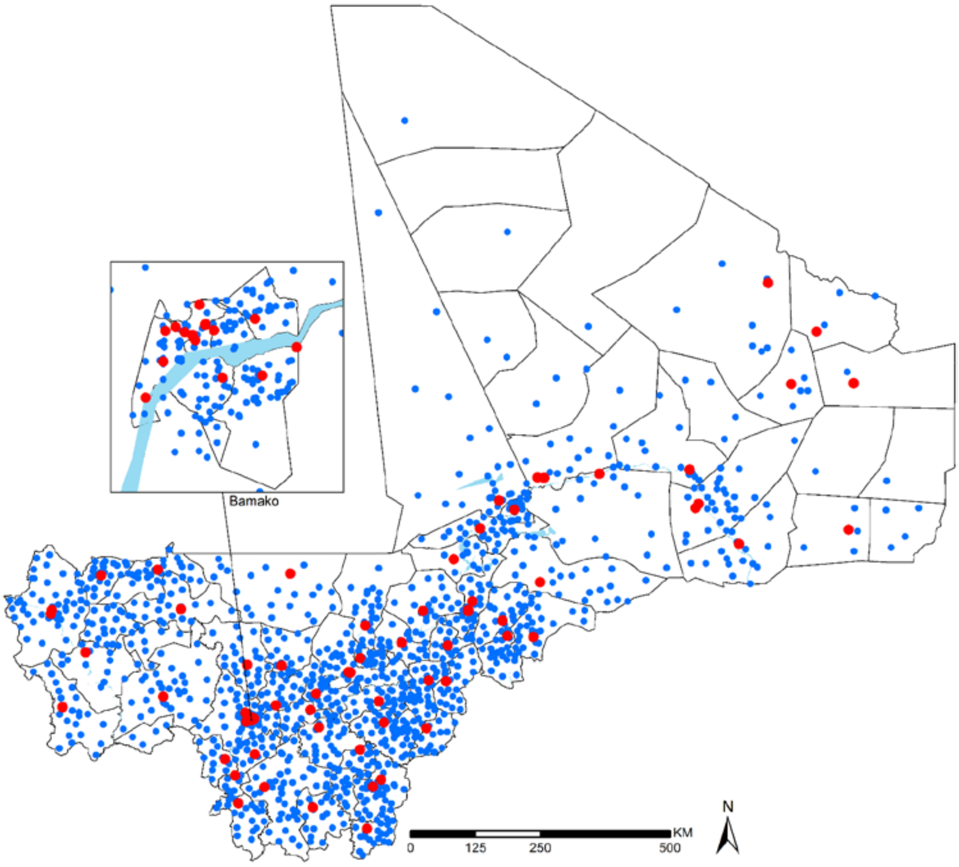


Figure 12 Distribution of 1,447 public health facilities: 78 hospitals (red), 1,264 community health centres and 105 clinics (blue) in 2016

Health context and priorities

The PDDSS 2014-2023 seeks to improve the coordination between the Ministère de la Santé et de l'Hygiène Publique, the Ministry of Labor, Social Affairs and Humanitarian Affairs; and the Ministry for the Promotion of Women, Family and Child. The PDDSS seeks to align to the Millennium Development Goals (MDGs) while simultaneously reducing the burden of poverty through the provision of quality universal health care. The document further stipulates that the values underpinning health policy should be linked to fairness, respect for human rights, respect for cultural identity, patient rights, gender and good governance. To this end, there are 11 priority objectives:[80]

1) Reduce maternal, neonatal, infant, and child morbidity and mortality;
2) Reduce morbidity and mortality related to communicable diseases;
3) Reduce morbidity, disability and mortality related to non-communicable diseases;
4) Promote a healthy environment by confronting the social determinants of health;
5) Reduce the health consequences of disaster-related emergencies and minimise their social and economic impact;
6) Increase the supply and use of quality health services and meet the needs of the population in a more equitable manner;
7) Ensure improved access, quality and use of pharmaceutical products, including laboratory reagents, vaccines and blood products;
8) Ensure the fair distribution of human resources (men and women) that are qualified, competent and efficient;
9) Develop a financing system that allows for improved mobilisation and use of financial resources for health, access to health services and transparent management which encourages providers and users to be more efficient;
10) Ensure the production, analysis, dissemination and use of reliable health information disaggregated by sex, with measures of up-to-date determinants of health, performance of the health system and health status;
11) Ensure that health system governance enables improved gender mainstreaming, improved strategic and operational planning, effective involvement of all stakeholders, improved coordination of the implementation of interventions and strengthened audits (internal and external).

Particular attention is drawn to strengthening the health system in the north of Mali, specifically efforts towards reinforcing infrastructure, equipment and human resources.

1.8 Malaria in Mali

Endemicity of malaria varies significantly in Mali, largely attributable to the diversity in the eco-climatic regions. Transmission varies based on factors of rainfall, altitude, temperature, urbanisation and hydro-agricultural development. The Système Local d'Information Sanitaire (SLIS) of Mali reported that malaria was responsible for 34% of all outpatient visits to health facilities in 2015, the result of 2.37 million clinical cases.[3] The MIS conducted in 2015 reported the prevalence of malaria in children under five years at 36% and 32% by microscopy and rapid diagnostic test (RDT), respectively.[3] Malaria is consequently a priority area targeted by the government's health agenda, the responsibility of the PNLP and partners.

A timeline of malaria control in Mali

As part of the earlier 2014 malaria risk profile, a comprehensive written history of malaria control in Mali was prepared to capture a historical perspective of control to be applied to today's control ambitions and to maintain an institutional memory of control efforts. To ground the discussion of malaria control in Mali, this report summarises major events between 1900 and present day. The events highlighted below were selected by the PNLP and partners during a meeting in Bamako that took place in July of 2018.

Readers are encouraged to reference the written history in full and to view the Mali Malaria Control Timeline (available at linkmalaria.org).

Year	Event
1904	European and African settlements in urban areas such as Bamako and Kayes implement 'hygiène prophylactique' environmental interventions to reduce mosquito populations
1906-1908	Execution of the earliest detailed study of mosquitoes in French Soudan
1920-1934	The creation of a large irrigation scheme, Office du Niger, instigates a rapid increase in mosquito density and associated malaria transmission. This ultimately calls for the establishment of health services across the scheme and a hospital in Ségou
1940-1949	Primary malaria control measures involve household visits to eliminate mosquito breeding sites and chemoprophylaxis
1950-1957	Dichloro-diphenyl-trichloroethane (DDT) spraying conducted in Bamako one to four times a year based on mosquito densities
1955-1956	Centre Muraz in Bobo-Dioulasso, Burkina Faso, undertakes one of the largest malariometric surveys of Mali at the time in Gao, Kidal, Koulikoro, Mopti, Sikasso and Ségou
1977	Chemoprophylaxis is recommended for pregnant women from the second trimester after a strong association is identified between pregnant Malian women with anaemia and malaria
1978	Vertical malaria control programmes are embedded in the primary health care system with presumptive treatment of febrile patients serving as the main approach to control
1984	Initial studies of insecticide resistance performed around the Sélingué hydroelectric dam indicate that *An. gambiae* complex are susceptible to DDT and organophosphates but resistant to dieldrin
1987	The Bamako Initiative, signed in Bamako as a joint initiative between the WHO and UNICEF, is adopted by African heads of state as a formal agreement to increase essential drug and healthcare service availability in Sub-Saharan African countries, with a large emphasis placed on the decentralisation of health service provisions

1991	Doumbo et al. publish a paper on the epidemiology of malaria in Mali based on data from nine locations, serving as the main reference for the epidemiology of malaria in the country and subsequent national policy documents[2]
1992	Establishment of the Malaria Research and Training Center (MRTC) within the Department of Epidemiology of Parasitical Diseases at the University of Mali (University of Bamako) through a partnership between the Faculty of Medicine, Pharmacy and Dentistry; the United States National Institutes of Health (NIH); the University of Rome (La Sapienza); the University of Marseille; Tulane University; the University of Maryland; the Rockefeller Foundation; and the WHO
1993	Establishment of the PNLP following the Amsterdam Conference[1]
	The PNLP developed and launched the Five-Year Action Plan 1993-1997
1996	Identification of high rates of sulfadoxine/pyrimethamine (SP) resistance among residents of two villages using SP for the treatment of *P. falciparum* malaria
1997	A multi-phase study on seasonality, malaria and chemoprophylaxis with proguanil and chloroquine (CQ) in Sikasso region indicates a strong association between seasonality and the likelihood of a mother giving birth to underweight children (with a higher risk among infants of first and second pregnancies), with a suppressive effect on the association observed when the drugs were taken for 20 weeks or more
1998	Launch of the Ten-Year Health and Social Development Plan 1998-2009 (PRODESS II), expected to be implemented in two phases (1998-2003 and 2004-2009)
1999	United States Agency for International Development (USAID)-Netmark-Population Services International (PSI) project selects Mali as one of the first countries to be involved in the commercial distribution of insecticide-treated nets (ITNs)
	The PNLP develops and launches the 2001-2005 plan for malaria following the Abuja Declaration, targeting vulnerable populations through ITN coverage, intermittent preventive therapy during pregnancy (IPTp) and case management
2000	Creation of the first geostatistical prevalence-based malaria risk map of Mali using parasite rate data in children under ten years of age from 1960 to 2000
2001	Abolishment of taxes on ITNs and the insecticides used to treat them
	A national integrated strategy for ITN promotion increases the availability and use of ITNs among pregnant women attending antenatal consultations and children under five years of age participating in measles vaccination campaigns
	Establishment of an association between CQ resistance and the pfcrt T76 mutation in *P. falciparum*

2003	Approval of the Ministère de la Santé et de l'Hygiène Publique as the principal recipient for a Round 1 (R1) Global Fund grant of USD 2.6 million for malaria control activities
2006	Release of the 21 April 2006 MOH Circular Letter stipulating the free distribution of ITNs to children under five years of age and pregnant women
	The United States President's Malaria Initiative (PMI) selects Mali as a funding candidate[1]
2007	The PNLP develops and launches the first national strategic plan (2007-2011) as an update to the 2001-2005 plan for malaria
	First-line treatment of uncomplicated malaria shifts from CQ to Artemisinin-based Combination Therapy (ACTs) of artesunate-amodiaquine (AS+AQ)
	Introduction of IPTp with SP
	Identification of the ecological niches for the two main vectors of malaria in Mali, *An. gambiae* and *An. arabiensis*
	The PNLP is transformed into the Directorate of Programme National de Lutte contre le Paludisme, ratified through Ordinance No. 07-022/PRM through Law No. 07-060 of 30 November 2007[1]
	Routine distributions and universal coverage campaigns provide ITNs free of charge to children under five years of age[3]
2008	National scale up of malaria rapid diagnostic testing begins
2008-2013	Use of pyrethroids and carbamates for IRS
2010	Adoption of an iCCM package including free treatment for uncomplicated malaria, acute respiratory infections, diarrhea, micronutrient supplementation, primary care for newborns and select family planning — for use by community health workers (ASCs)
	Revision of the Schéma Directeur d'Approvisionnement et de Distribution des Médicaments Essentiels (SDADME) to improve the antimalarial supply chain
	ASC service provision financially incentivised by the local government and partners
	Revision of the national treatment policy to make AL the first-line drug for uncomplicated malaria and AS+AQ as the second-line treatment[3]
	National anaemia and parasitaemia survey
	Development of the first molecular map of CQ resistance
2010-2012	Save the Children, the PNLP, LSHTM and the French National Center for Scientific Research implement a randomised control trial on the impact of malaria interventions (prevention education combined with LLIN distribution and treatment with a three-day course of AS+SP regardless of infection status) among children in 80 schools in Sikasso, with results indicating a positive impact on ITN use and behaviour, infection prevalence and anaemia

2011	Intermittent preventive treatment of malaria in children (IPTc) with AS+AQ found to provide substantial protection against *P. falciparum* in children between three and 59 months of age using an LLIN in three localities of Kati
2012	Review of the Plan Strategique de Lutte contre le Paludisme 2007–2011
	DHS 2012
	PNLP adopts SMC measures following the WHO recommendation for scale up in children three to 59 months of age in areas where more than 60% of cases of seasonal malaria transmission occurs during a period of up to four months or where 60% or more of the annual rainfall occurs in three consecutive months
	MSF Mali and the PNLP begin an SMC pilot in Koutiala in 42 health treatment centres and 26 villages, first using door-to-door and fixed distribution points every four weeks. The average cost of the intervention was estimated to be EUR 4.50 per child, with results indicating declines in paediatric uncomplicated malaria, hospitalisations and deaths
	P. vivax identified as the cause of 30% of confirmed cases in five health facilities in Tombouctou, Gao and Kidal
2013	PNLP develops and launches the 2013-2017 national malaria strategic plan
	Consolidation of the Global Fund R10 malaria grant and R6 Phase 2 grant[3]
	The government of Mali adopts the PDDSS 2014–2023 and the PRODESS 2014–2018
	The Nouakchott Initiative launches to coordinate the SMC response in The Gambia, Chad, Mali, Mauritania, Niger, Senegal and later Burkina Faso and Nigeria
	Two vector susceptibility tests for insecticides made available in all sentinel sites, with resultant sentinel site data outputs serving as the determinant for subsequent IRS insecticide classes
2013-2017	Scale up of SMC to all districts (from a targeted 343,752 children in five districts) using two rounds of SP+AQ and two rounds of AQ
2014	IRS shifts to organophosphates after the identification of short carbamate half-life and resistance to pyrethroids[3]
	RDTs made free for all ages[3]
	Change from two doses of SP to three or more doses for IPTp
2015	Commencement of regular data audits at health district and regional levels[1]
	Training of all healthcare workers on malaria in pregnancy guidelines[3]
	PMI-supported IRS reduced to two districts due to costs associated with the organophosphate transition
	MIS 2015 conducted
	Introduction of District Health Information System 2 (DHIS 2) and integration with the Reports Tirmestriels d'Activités (RTA) and SLIS[108]

2015-2016	TES studies in Sélingué, Missira, with AL and AS+AQ ACT treatment arms, with both appearing to be efficacious
2016	DHIS 2 replaces Développement Sanitaire du Mali (DESAM)[1]
	The Global Fund approves Mali's concept note for approximately USD 70 million[3]
	PMI procures 1.25 million ITNs for distribution via routine channels[3]
	Assistance from the UNITAID Next Generation Indoor Residual Spraying (NGenIRS) project allows for IRS expansion to Baroueli, Fana and Koulikoro
	PMI supports the mass distribution campaign of one million nets in Gao and Tombouctou[3]
	PNLP initiates the production of monthly bulletins of malaria indicators[3]
2017	The Global Fund supports the mass campaign of 3.2 million ITNs in Kayes and Mopti to replace those distributed in 2013 and 2014[3]
	Establishment of a malaria M&E technical working group between the NMCP, PMI, the Global Fund and other partners[3]
	TES in Sélingué, Missira, with treatment arms including AL, AS/AQ and SP/AS/AQ (among parasitaemic children during SMC)[3]
	IRS shifts to four districts in Mopti Region following an evaluation of the 2015 MIS results and completion of IRS in previously designated districts[3]
2018	The Global Fund approves of Mali's 2019-2021 concept note for approximately 47 million euros
	DHS 2018 to be conducted
	PNLP develops and launches the Plan Strategique de Lutte contre le Paludisme 2018-2022

Plan Strategique de Lutte contre le Paludisme 2018–2022

The current framework issued by the PNLP that addresses the burden of malaria in the country is the Plan Strategique de Lutte contre le Paludisme 2018–2022, which uses a mosaic of strategies to target control malaria due to its diverse presentation throughout the country. The Plan Strategique de Lutte contre le Paludisme 2018–2022 replaced the strategy for the years 2013–2017.

The goal of the PNLP under this strategy is to guarantee universal and equitable access to malaria control interventions within the national health policy framework, with the vision to have a 'Malaria free Mali' by 2030.[1] The objectives under the current strategy seek to reduce the malaria mortality rate by at least 50% compared to 2015; to reduce the incidence of malaria by at least 50% compared to 2015; and to strengthen the coordination and management capacity of the PNLP at all levels.

To achieve these goals and to reduce the burden of malaria, the strategy pursues the following:

1) Targeting of interventions according to epidemiological characteristics;
2) Maintaining access to, and ensuring high coverage of quality interventions;
3) Strengthening of community approaches;
4) Improving coordination and management capacities;
5) Strengthening partnerships, particularly within the private sector;
6) Contributing to sustainability within the health system; and
7) Promoting malaria surveillance interventions.

An overview of current national malaria interventions

Vector control

Vector control in Mali is guided by the 2015 National Vector Control Strategy. Mali is pursuing vector control through universal LLIN coverage, improved capacity building, delivery of IRS in targeted districts, targeted larval control, insecticide resistance management and collaboration with the private sector.[1] The Plan Strategique de Lutte contre le Paludisme 2018–2022 aims to protect 80% of the population targeted through IRS, treat 95% of mosquito breeding sites and encourage the regular use of LLINs by 80% of the at-risk population by 2022.

The PNLP defines universal coverage of LLINs as one LLIN for every two persons.[1] The PNLP distributes LLINs through mass campaigns and through routine ANC distributions. Mass LLIN distribution campaigns are first organised at the health district level, while pregnant women are targeted from their first ANC visit and issued an LLIN voucher. The effectiveness of LLINs is monitored from the time of mass distribution at three or six months to determine their performance in the field.[1]

In alignment with the WHO IRS operational manual, IRS is carried out annually in targeted districts before high transmission periods.[1] Sentinel sites operated by the PNLP and partners collect relevant entomological data to support IRS targeting. Sentinel data is supplemented by mapping of households for operational purposes. Post-treatment of sprayed structure studies are conducted to monitor insecticide persistence to ensure that practices meet WHO thresholds.[1]

Larval control is undertaken by the PNLP and partners following a basic and targeted entomological/epidemiological survey and breeding site mapping. Through vector identification, breeding sites in selected regions may be targeted and destroyed through drainage, backfilling and landscape modification, supplemented by basic sanitation efforts carried out by communities and NGOs.[1]

Insecticide resistance monitoring is undertaken through the collection of entomological data in select health districts targeted for IRS, with annual monitoring of vector resistance. Under the Plan Strategique de Lutte contre le Paludisme 2018–2022, IRS is supervised at the district level for resistance monitoring, with relevant data managed by sentinel sites. There have been two vector susceptibility tests for insecticides in sentinel sites since 2013.[1] IRS insecticide class selections are based on this data.[3]

Drug policy

In accordance with the PDDSS, the Politique Pharmaceutique Nationale (PPN) has stipulated the need for equitable access to quality essential medicines.[1] The call for equitable access to quality medicines is echoed in the Plan Strategique de Lutte contre le Paludisme 2013–2017, which calls for a functional supply chain system for the provision of antimalarials.[3] In the public sector, the PPM manages central purchasing and essential drug supplies. These medicines are stored in PPM regional facilities for district supply purposes, with the exceptions of Gao, Kidal, Ménaka,and Taoudénit.[1] Communities obtain medical supplies from health centre depots.[1]

The PNLP works with USAID/PMI through the System to Improve Access to Pharmaceuticals and Services (SIAPS), the Direction de la Pharmacie et du Médicament (DPM) and the PPM to improve the antimalarial drug provision system according to SDADME which was revised in 2010.[1] Consumption of malaria control products is tracked by a health products monitoring tool, l'Outil de Suivi des Produits de Santé (OSPSanté). Acquisitions between 2013 and 2017 of LLINs, RDTs, CTAs, SP, SP/AQ are considered adequate according to the PNLP; however, injectable AS has been found to be in low supply.[1]

Antimalarials are quality-controlled according to international standards, with national health laboratories conducting quality control checks before medicines are distributed.[1] In theory, randomised checks are also conducted by the same laboratories at the local level during supervisory visits. Further analyses may be conducted at the regional level using laboratory quality control kits outfitted by USAID/PMI in 2010. Unfortunately, the storage of antimalarials has been deemed inadequate.[1] The Drug Regulatory Directorate supports the alert and response system concerning substandard drugs.[3]

According to the Plan Strategique de Lutte contre le Paludisme 2018–2022, RDT and microscopy diagnostics are offered free of charge to pregnant women and children under five years of age. Microscopy services are only offered at health facilities with an affiliated laboratory.[1]

In 2018, the PNLP advised the use of Artemisinin-Lumefantrine (AL) as the first-line treatment and Artesunate-Amodiaquine (AS/AQ) as alternative therapy for cases of malaria confirmed by RDT or microscopy.[1] Artemisinin-based combination therapies (ACTs) are used at all levels to treat uncomplicated malaria and should be freely available to pregnant women and children under five years of age. ACTs are to be used from the second trimester of pregnancy.[1]

Severe cases of malaria are to be treated using injectable artemisinin (artesunate or artemether) or quinine.

Community-based management

Community-based management was most recently a focal point of the 2016–2018 concept note submitted to the Global Fund.[1] Global Fund provisions are expected to mobilise partners to ensure motivation of health workers, expand the package of care offered at the community level (including children aged three to six months and those over five years of age), improve integration of humanitarian organisations in conflicted areas, link tuberculosis and malaria management, include community health worker malaria data into epidemiological surveillance data and communicate community management strategies.[1]

Community-based management was adopted as iCCM policy in 2010, supplemented by updated severe malaria treatment and pre-referral guidelines.[3] ASCs are largely responsible for RDT testing, ACT administration and SMC through iCCM.[3]

Diagnoses by RDT at the community level are carried out by ASCs if not at a health facility and the proportion of children under five years of age with suspected malaria has fluctuated since 2013 according to associated diagnostic data. In 2013, 93.66% of suspect cases were tested with RDTs, until a drop was experienced in 2015 to 74%, before rising to 97.06% in 2017.[1] The proportion of children under five years of age with confirmed malaria treated by community health workers with ACTs has declined since 2013 from 110.58% to 67.96% in 2017.[1]

The Plan Strategique de Lutte contre le Paludisme 2018–2022 anticipates the implementation of a weekly reporting system at the community level.

Malaria in pregnancy

Malaria in pregnancy in Mali is dependent upon a combination approach of LLIN distribution via antenatal care (ANC) channels, IPTp and case management.[3]

The treatment for uncomplicated malaria during the first trimester is oral quinine, followed by AL in the second and third trimesters. In cases of severe malaria, the first-line treatment is injectable artesunate or artemether.[3]

The current standard for IPTp is three doses of SP during pregnancy, implemented through the DNS and the respective reproductive health divisions.[1] IPTp coverage is low, likely due to quality of care, low demand by pregnant women and delays in receiving antenatal care despite a reasonable supply of SP at the facility level.[1]

ANC coverage has declined since 2015 from 74% to 57% in 2017, with similar trends in routine data concerning IPTp1(82% in 2015 to 72% in 2017) and second dose (59% in 2015 to 51% in 2017).[1] Coverage of IPTp3 is the only point noted to increase from 2015 to 2017 at 20% and 35%, respectively. The proportion of those that received IPTp3 during their last pregnancy has fluctuated but generally increased, rising from 0% in 2013 to 22% in 2015, to 35% in 2016 and 23.24% in 2017.[1]

ANC coverage indicators captured by routine data collection vary slightly from those reported in national surveys. The 2012 DHS found that the proportion of pregnant women receiving two or more doses of SP was 29% and the 2015 MIS found that this had increased to 38%.[3] The Plan Strategique de Lutte contre le Paludisme 2018–2022 aims to cover 80% of pregnant women with IPTp by 2022. Efforts and studies to improve ANC service delivery are underway in the form of enhanced intervention packages.[3]

Seasonal malaria chemoprevention

SMC aims to reduce acute seasonal risk of new infections by implementing blanket coverage of malaria prophylaxis to children in areas where vector proliferation is concentrated within a few months of every year.[81] Combinations of drugs, with at least one partner drug having a long half-life, may reduce the clinical consequences of new infections within a short window of transmission.[81–83] The clinical burden of malaria in children in acutely seasonal transmission areas is high as children are more adapted to synchronised infections leading to higher host parasite densities and because young children have poorly designed clinical immunity due to widely-spaced natural immunisation.[82,84,85]

The first SMC trials in Mali began in Bandiagara district through a randomised cohort study in which one arm of children received SP and the other received no treatment prior to the transmission season.[86] The findings of this study indicated that those who received SP had a delayed median time to their first clinical episode and parasite densities during disease episodes were lower than the control group.[86] A subsequent study demonstrated that in SMC with SP reduced overall malaria incidence by almost 43% among children six months to ten years of age in Kambila district.[87]

In February 2012, the WHO issued a recommendation for SMC using SP and AQ at monthly intervals in children three to 59 months of age, principally in the Sahelian region of Africa.[88] In 2012 it was estimated that 24.9 million children below five years of age lived in areas suitable for SMC, that is, areas of the Sahel or sub-Sahel with stable *P. falciparum* transmission and where 60% of annual rainfall was concentrated in three consecutive months.[26] In May of 2013, the Nouakchott Initiative was launched to coordinate the SMC response in The Gambia, Chad, Mali, Mauritania, Niger, Senegal, and later Burkina Faso and Nigeria.[89]

Between 2013 and 2017, SMC was scaled up nationally to all districts, increasing coverage from a targeted 343,752 children in five districts to 3,906,696 children in all districts.[1] The SMC coverage exceeded the 2013–2017 strategy goal of 80% of children receiving four doses of SMC (Figure 12). The decision to scale up SMC to the national level was largely the result of a pilot in Koutiala District in 2012 that was conducted by MSF in 26 villages through 42 health treatment centres. This study indicated a 42% reduction in malaria cases, with an average intervention cost of EUR 4.50 per child for four rounds.[3]

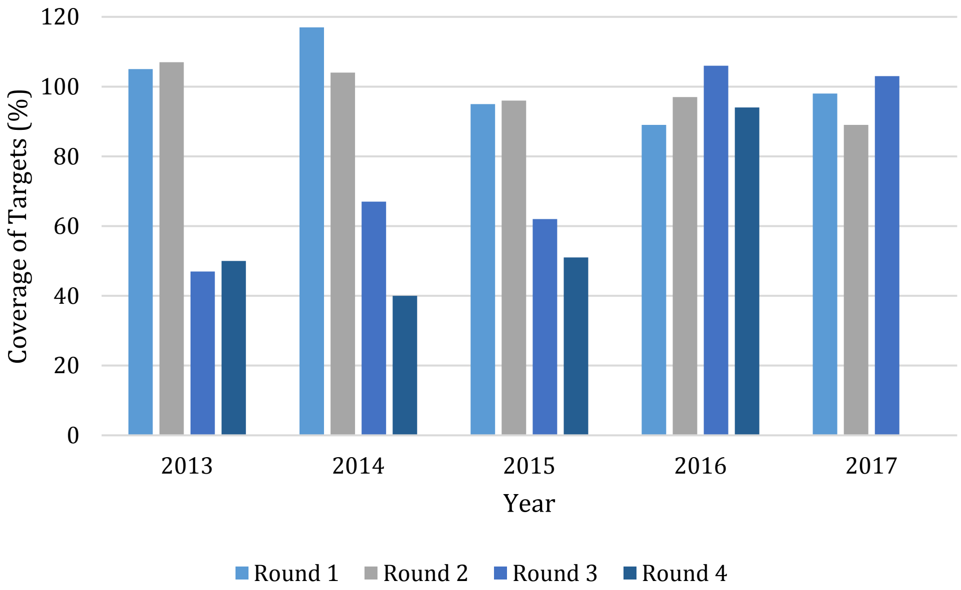


Figure 13 SMC Target coverage from 2013 to 2017, using data from the Plan Strategique de Lutte contre le Paludisme 2018–2022 (NMS, 2018 – 2022)

The Plan Strategique de Lutte contre le Paludisme 2018–2022 aims to achieve 90% SMC coverage among children three to 59 months of age. SMC coverage is to be completed through the delivery of a combination of SP and AQ during periods of high transmission (cases primarily occur in the north from September to December and in the south from August to November) once a month for four months. The first two rounds will include both SP and AQ and the final two doses will include AQ only.[1] SMC will be carried out by community health workers with a fixed strategy in large cities and a mobile strategy in small villages. Reporting during the campaign will be on a daily basis to the CSCOM, eventually escalated to the central level, with a final evaluation being conducted through a national survey.[1]

Structure and function of the National Malaria Control Programme

The PNLP coordinates malaria control at all levels in the public and private sectors. Centrally, the PNLP coordinates with partners for the implementation, monitoring, and evaluation of interventions. A malaria monitoring committee was established in 2009 to oversee the PNLP's strategy in effect. Regionally, the PNLP works with health district representatives to improve programme performance. The PNLP also trains private practitioners in malaria case detection and management and encourages regular data collection.[1]

Financing malaria control

The PNLP is funded by the National Health and Social Development Program on an annual basis, with yearly budgets determined by an evaluation committee.[3] Governmental contributions are allocated towards salaries, offices, operating costs, RDTs, LLINs, SMC and ACTs.[3] The amount of governmental budget allocated to health has increased from 5.65% in 2003 to 7% in 2016. This formulates the majority of health funding at 55.4% compared to external partners at 31.7%.[1]

Major external funders towards malaria control in Mali include the Global Fund to Fight HIV, Tuberculosis and Malaria (GTFAM) and PMI/USAID. These allocations and additional funders are graphically represented in Figure 14.

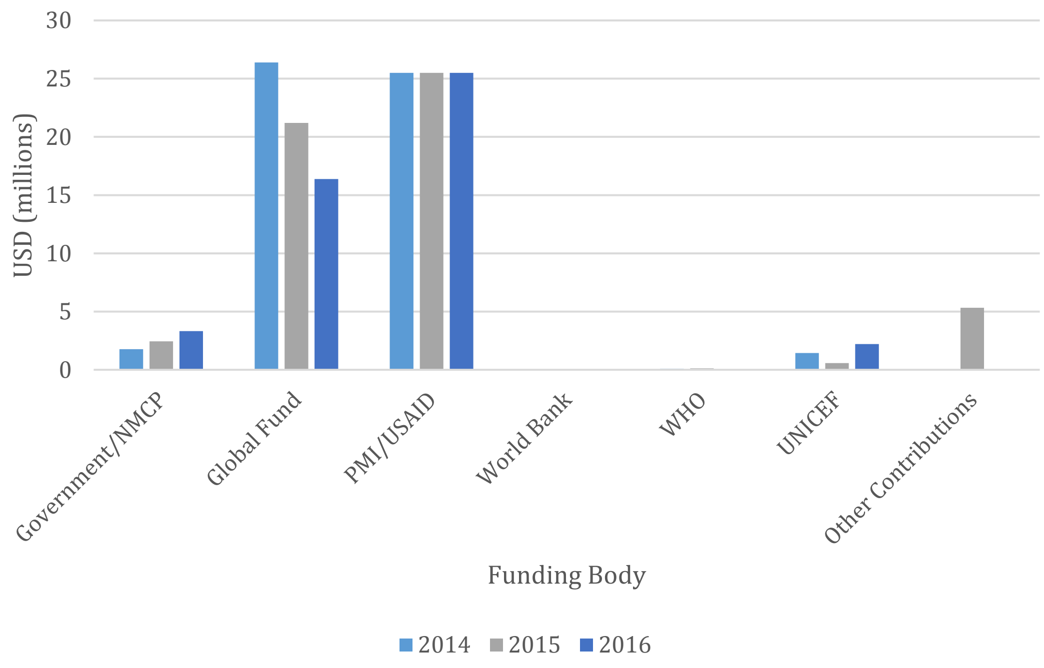


Figure 14 Estimated contributions for malaria reported by Mali, 2014 to 2016 (adapted from the World Malaria Report)[90]

The Plan Strategique de Lutte contre le Paludisme 2018–2022 calls for an annual investment of approximately USD 15.83 per capita for malaria prevention, control and treatment. This totals to a budget of USD 334,077,751.05 to be allocated over five years. These funds are expected to be drawn from USAID/PMI (28.87%), the Global Fund (9.71%), the government (6.39%), other partners (1.92%) and the WHO (0.20%).[1]

More than half of the PNLP budget (61.52%) is projected for allocation for purchasing and stock management, followed by SMC (19.64%) and M&E (6.82%).[1] A more comprehensive breakdown of expenses is presented in Figure 15.

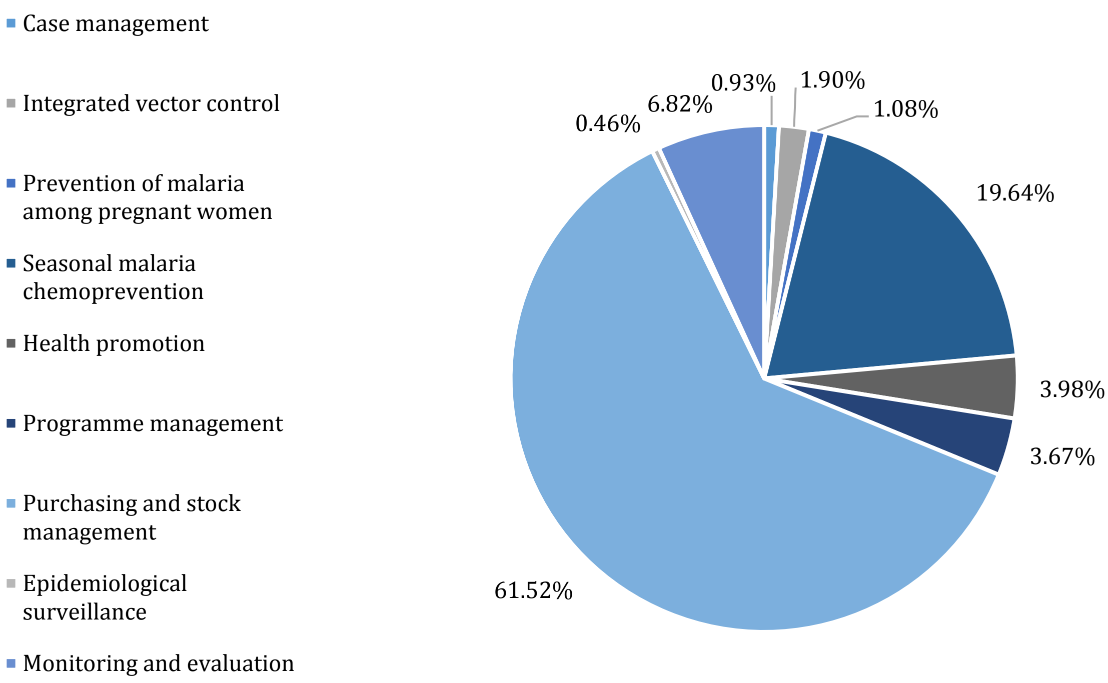


Figure 15 Allocation of the PNLP budget (adapted from the Plan Strategique de Lutte contre le Paludisme budget for 2018 – 2022)

Data relevant for malaria control

Data used to inform malaria control in Mali primarily comes from four sources: (i) routine health information, which gathers data from the public health system and may be complemented by other types of official data such as socio-demographic information; (ii) data from sentinel surveillance sites; (iii) large-scale household and health facility surveys; and (iv) operational research and intervention studies.

This report briefly describes the routine health information system and sentinel sites and gives examples of data generated through operational research.

Routine health information systems

Routine data in Mali was initially collected through le SLIS, composed through the transmission of data from the various health structures via Reports Trimestriels d'Activités (RTA). In 2015, the Développement Sanitaire du Mali system (DESAM), was integrated into DHIS 2, with reporting occurring on a monthly basis.[1]

DHIS 2 was rolled out nationally in 2017 with reports from all districts and 75% of all facilities.[3] Further data on priority diseases (including malaria) is collected at the facility level and sent to the central level through the Système de Surveillance Intégrée des Maladies et de la Riposte (SIMR). As of 2015, regular audits of data are conducted at the district and regional level.[1] Variations in reporting across all health areas have been attributable to computer access (Bamako) and insecurity (Gao, Kidal).[3]

Regarding malaria indicators gathered through routine systems, data completeness (defined as the percentage of health facilities reporting on a monthly basis) has dramatically improved since 2012 from 66%, to 76% in 2014 and most recently to 94.7% in 2016.[3] There is a malaria-specific dashboard included in the DHIS 2 system and monthly bulletins have been issued by the PNLP since October 2016.[3]

Mali has two major national health information system coordinating bodies, including the Groupe thématique d'Appui à la Statistique and a DHIS 2 implementation steering committee.

PMI supported both local and regional health sector staff for epidemic detection and response purposes in Mopti and the Northern Regions using surveillance data in 2015. Surveillance support has primarily been prioritised in response to the West African Ebola epidemic and aligned to the Global Health Security Agenda, intended to strengthen the health information system from the district to national levels.[3]

Data from the private sector has not been fully integrated into the DHIS 2 system.

Sentinel sites

Sentinel surveillance sites collect data related to malaria morbidity and mortality, as well as laboratory, entomology and drug therapeutic efficacy data.[1] Research is conducted and data collected at these sites for malaria prevention and management purposes, with 13 active sites since 2007.[1]

Large-scale household and health facility surveys

Several population-based surveys have been carried out in Mali since 2006. The first of these surveys was the 2006 DHS, followed by a national anaemia and parasitaemia survey in 2010, the DHS 2012, and the 2015 MIS. A 2018 DHS was being conducted at the time of this profile's publication.

The DHS are nationally-representative household surveys, which typically sample between 5,000 and 30,000 households and are conducted every five years. These surveys are designed to be precise at the regional and national level but are less precise in providing district- or sub-district-level estimates. Malaria-relevant data collected by DHS are: ownership and use of mosquito nets, prevalence and treatment of fever, IRS coverage and prevalence of anaemia. Sometimes these surveys include malaria-specific modules which include additional questions on IRS, as well as biomarker testing for anaemia and malaria. The DHS is carried out at various times in the year, not accounting specifically for malaria seasonality.

In contrast to the DHS, the MIS is a standalone household survey that collects national, regional, and/or provincial data. These surveys are timed to malaria transmission seasons and collect data for a set of malaria indicators. Key MIS indicators include:

- Household ownership of LLINs and their use, especially by children under five years of age and pregnant women;
- The type and timing of treatment of high fever in children under five years of age;

- Diagnostic blood testing of children under five years of age with a fever
- IPTp1-3 coverage; and
- IRS coverage.

The MIS can also collect data on malaria parasites and anaemia using RDTs or field microscopy.

Results of recent major household surveys

Five standard DHS have been completed in Mali, performed in 1987, 1995–1996, 2001, 2006 and 2012–2013. The 2006 DHS was the first to capture malaria data, through a module on bed nets. In the 2012-2013 DHS, additional malaria modules were added, capturing information on bed nets and diagnostics. A special survey on anaemia and parasite prevalence in children (EA&P) was completed in 2010, as was a MIS in 2015. The findings of the most recent surveys are summarised below.

2006 DHS

The 2006 DHS identified that 62% of households owned at least one ITN, with 27% of children sleeping under a net the night before the survey. Among pregnant women aged 15 to 49, 28.9% slept under an ITN the night prior to the survey.

According to the 2006 DHS, 4% of pregnant women received at least two doses of SP/Fansidar during an ANC visit.

2010 EA&P

The 2010 EA&P identified that the prevalence of malaria in children 6 to 59 months of age by microscopy was 37.5%, with the highest rates in Sikasso (59.2%) and Mopti (47.4%). These were followed by Ségou (42.1%), Koulikoro (41.8%), Kayes (28.6%), Tombouctou-Gao-Kidal (16.8%) and Bamako (2.2%).

The 2010 EA&P found that anaemia prevalence (measured as haemoglobin levels less than 8.0 g/dl) was 26% among children under five years of age, with the most severe cases being among those 12 to 17 months of age.

The 2010 EA&P identified that 84.7% of households had at least one LLIN, with 70% of children under five years of age utilising a LLIN the night before the survey. Among women aged 15 to 49 years of age, 62.7% utilised a LLIN the night before the survey.

2012–2013 DHS

While the north of the country was not captured in the 2012 – 2013 DHS, malaria prevalence was highest in Mopti (71%) and lowest in Bamako (10%). Prevalence in Kayes was relatively low (37%) compared to Koulikoro (50%), Ségou (56%) and Sikasso (62%).

The 2012–2013 DHS found that the prevalence of malaria among children aged six to 59 months tested by microscopy was 52% and indicated an increase in trend with the age of the child. Anaemia prevalence was particularly high, with 21% of children six to 59 months of age testing positively, with the highest rates in the 18 to 23 months age range.

The 2012 – 2013 DHS reported that 65% of households had at least one ITN, with 61% utilising the net the night prior to the survey. Use of ITNs increased from 2006 to 2012 – 2013, from 27% to 69%, respectively, among children under five years of age and from 29% to 73%, respectively, among pregnant women between the ages of 15 to 49.

According to the 2012 - 2013 DHS, at least 20% of pregnant women received at least two or more doses of SP, with at least one during an ANC visit.

2015 MIS

The 2015 MIS identified that (with the exception of Mopti and Bamako), the trend in parasite prevalence shifted by region since the 2012 – 2013 DHS. Mopti once again had the highest level of prevalence (60%), followed by Sikasso (42%), Ségou (37%), Koulikoro (35%), Kayes (27%) and Bamako (6%).

The prevalence of anaemia in children aged six to 59 months tested by microscopy was 20%, with the 18 to 23 months of age range remaining the largest contributor.

The 2015 MIS reported that 70% of households had access to ITNs, with 64% sleeping under a net during the night prior to the survey. A reported 71% of children under five years of age and 78% of pregnant women between the ages of 15 to 49 slept under a net the night prior to the survey.

According to the 2015 MIS, at least 38% of pregnant women received at least two or more doses of SP, with at least one during an ANC visit.

Elucidation of survey results

Progress with control is not expected to be homogeneous and it will become increasingly important to understand variations in malaria epidemiology with greater spatial resolution. DHS, MIS and other nationally representative household surveys are designed to be representative at the regional level (though domains contain districts which share similar malaria burden or have a shared malaria intervention which is to be investigated).

The modelling methods presented in later sections offer an approach to leverage data from these nationally representative surveys to offer district-level estimates.

1.9 Drug and insecticide resistance and response

Drug resistance

Therapeutic efficacy studies (TES) were carried out in 2015 and 2016 in Sélingué, Missira, with AL and AS/AQ ACT treatment arms. Of the genotyping conducted on 309 samples for K13 markers, only one had a mutation that is not associated with artemisinin resistance. AL and AS/AQ treatment still appears to be efficacious.[3]

Since 2017, there has been an ongoing TES in Sélingué, Missira, with treatment arms including AL, AS/AQ and SP/AS/AQ (among parasitaemic children during SMC). Two further studies in the same sites are to be carried out in 2018, separating the SMC arm from the others.[3]

Insecticide resistance

Initial studies of insecticide resistance were performed around the Selingue hydroelectric dam in 1984 and indicated that *An. gambiae* complex were susceptible to DDT, organophosphates (temephos, chlorpyrifos, fenthion, fenitrothion and malathion), but resistant to dieldrin.[91] The presence of pyrethroid resistance of the knock-down resistance (kdr) type were tested in samples collected in Bamako and Sikasso of *An. arabiensis* and the Mopti, Savanna, and Bamako chromosomal forms of *An. gambiae* areas. This study reported that the kdr allele was associated with the Savanna form and presented in samples dating back to 1987.[92] However, a subsequent study indicated an increasing frequency of the kdr allele and its presence in the Bamako form and absence in the M form of *An. gambiae.*[93]

Entomological data is collected in IRS sites, as well as nationally-selected surveillance sites.[3] Insecticides utilised for IRS have been alternated as a result of such monitoring, with pyrethroids and carbamates (used from 2008 to 2013) changed to organophosphates in 2014 after detected resistance and short half-life identification, respectively. Data from 2016 indicates widespread DDT and pyrethroid resistance (deltamthrin and permethrin), but susceptibility to organophosphates (pirimiphos-methyl) and carbamates.[3] Mosquito mortality varies for both permethrin (from 28% to 93%) and deltamethrin among *An. gambiae* spp. (53% to 91%). Reduced efficacy has been attributed to mud walls typical to Malian structures and plastering with kaolin post-IRS is under investigation.[3] Pyrethroid resistance is of particular concern due to Mali's use of ITNs/LLINs for malaria reduction purposes.

Further reports of insecticide resistance have provided evidence of resistance against organochlorines, pyrethroids, carbamates and organophosphates. A 2015 study using WHO tube tests and polymerase chain reaction (PCR) identified resistance-associated mutations provided comprehensive resistance information across classes of insecticides.[94] The 2015 study identified resistance to DDT 4% in Kita, Koulikoro, Kati, Niono, Bla, Baraoueli, Bougouni, Silengue, Kadiolo, Bandiagara, Bankass, Djenne and Bamako. Resistance to deltamethrin 0.05% was identified in Bandiagara, Bankass and Djenne, with possible resistance in Bougouni. Resistance to lambda-cyhalothrin 0.05% was identified in Kita, Koulikoro, Kati, Niono, Bla, Baraoueli, Silengue, Kadiolo and Bamako. Resistance to bendiocarb 0.01% was identified in Kita, Bla, Bougouni and Kadiolo, while possible resistance to fenitrothion 1% was identified in Niono, Baraoueli and Bougouni. Of additional concern was the evidenced development of resistance mechanisms in *An. coluzzii*, *An. gambiae s.s*. and *An. arabiensis,* with changes to kdr, ace-1^R, monooygenases and esterases.[94]

Resistance capacities in Mali are hypothesised to have resulted from the use of pesticides for agricultural purposes and from the deployment of LLINs and IRS as public health interventions.[94]

1.10 History of risk mapping in Mali

The early years:1900-1999

Most of the early descriptions of the epidemiology of malaria in French Soudan (Mali) were based on entomological studies that described the distribution of the *Anopheles* spp. vector.[95–98] These studies confirmed the predominance of the *An. gambiae* complex.[95,97] Another species, *An. funestus*, was also shown to be widespread. Early French researchers also described the ecological niches inhabited by the mosquitoes using the broad climatic categorisation which have since been adopted to describe the contemporary malaria ecology in Mali.[2,95,97] These zones are the following: the Saharan zone (the Sahara Desert area), the Sahelian zone (mean annual rainfall of 250-500 mm), the Sudano-Sahelian zone (also known as the dry savannah, mean annual rainfall of 500-900 mm), Sudanian zone (also known as the humid savannah, mean annual rainfall 900-1100 mm), and the Guinean zone (annual mean rainfall >1100 mm). On several occasions, reference is made to the various combinations of these zones either as Sahara-Sahelian or Sudano-Guinean zones.

Within these climatic ecologies, epidemiological studies on the levels of malaria infection rates in humans started in the early 1900s and were initially concentrated in Bamako. In 1909, *P. falciparum* prevalence was reported as high as 33% in one location and 20% in two locations in 1914 .[99] A much higher prevalence among a smaller sample size of about 79% in 1922 was reported in an area of Bamako.[100] Sautet and Marneffe (1943) conducted a study in 17 locations in Gao, Mopti and Tomboctou in 1942 on the epidemiology of malaria and bilharzia and reported *P. falciparum* prevalence ranging from 6% to 54%.[101] Perhaps the largest malariometric survey done in the early years in Mali was in 1955 and 1956 in the regions of Gao, Kidal, Koulikoro, Mopti, Sikasso and Segou and was organised by the Centre Muraz in Bobo-Dioulasso, Burkina Faso.[102] Surveys were undertaken in 358 villages with *P. falciparum* prevalence of greater than 50% reported in Mopti, Segou and Sikasso.

In the rest of the period after 1956 to 1999, several parasitological studies of different sample sizes have been undertaken in Mali, but many of these focused only on a handful of locations or regions. By the time the PNLP was established in 1993, the general understanding of the epidemiology of malaria in Mali was one of increasing transmission southwards from the Saharan zone (which was considered to be very low transmission and epidemic-prone) to the Guinean (where transmission was hyperendemic to holoendemic).[2] The frequency and size of the parasitological studies increased substantially after the establishment of the MRTC in 1992.

Malaria risk stratification: 2000-2013

By 2000, a map of the length of malaria transmission season in Africa was developed under the Mapping Malaria Risk in Africa (MARA) project (Figure 15).

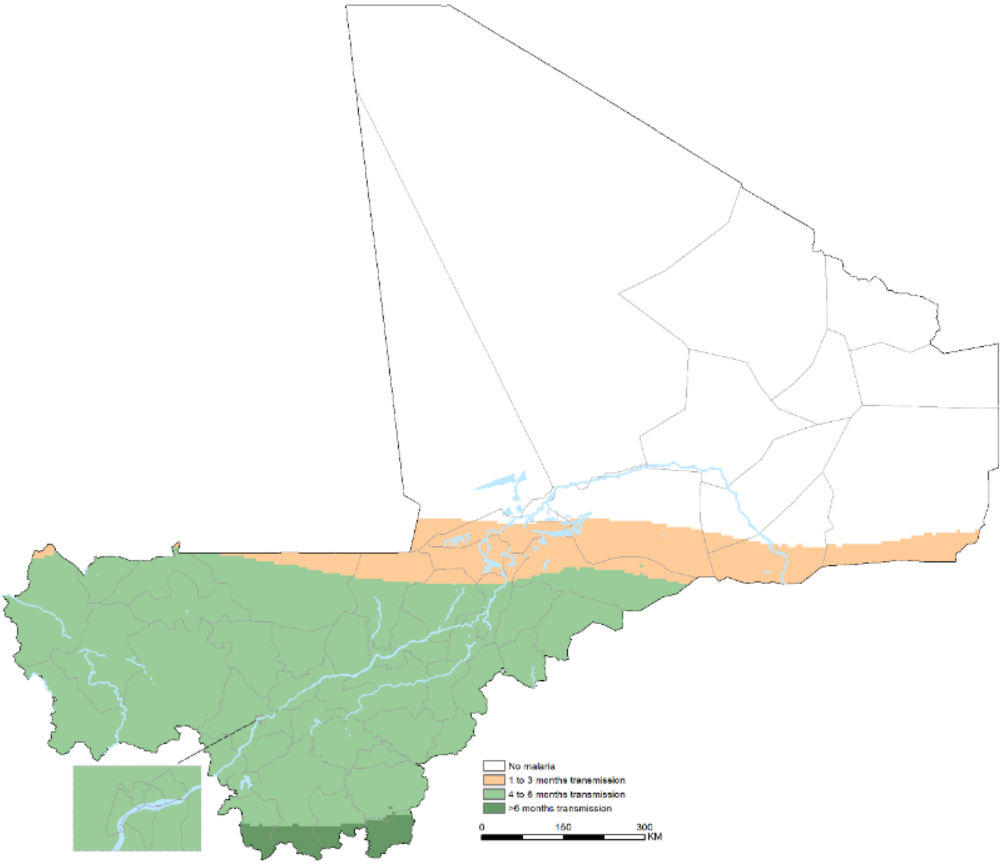


Figure 16 MARA climate malaria seasons map[iii]

The first geostatistical prevalence-based malaria risk map of Mali was developed using parasite rate data in children under ten years of age from 101 survey locations from 1960 to 2000.[103] This map (Figure 16) was developed by combining the parasite rate data with climatic, topographic and population data within a regression plus Kriging approach.

[iii] The MARA models of seasonality are defined using the combination of temperature and rainfall thresholds and a catalyst month. Areas where mean annual temperatures were <5°C were considered not to have a malaria transmission season. A pixel was considered 'seasonal' if the temperature range varied considerably or if annual rainfall was <720 mm. Seasonal zones classified according to the numbers of average months in which temperature was >22°C and rainfall >60 mm within a three-month moving window and at least one month of highly suitable conditions (>22°C, >80 mm) occurred as a catalyst month. For areas considered 'stable' the equivalent values were 19.5°C and 80 mm with no requirement for a catalyst month.

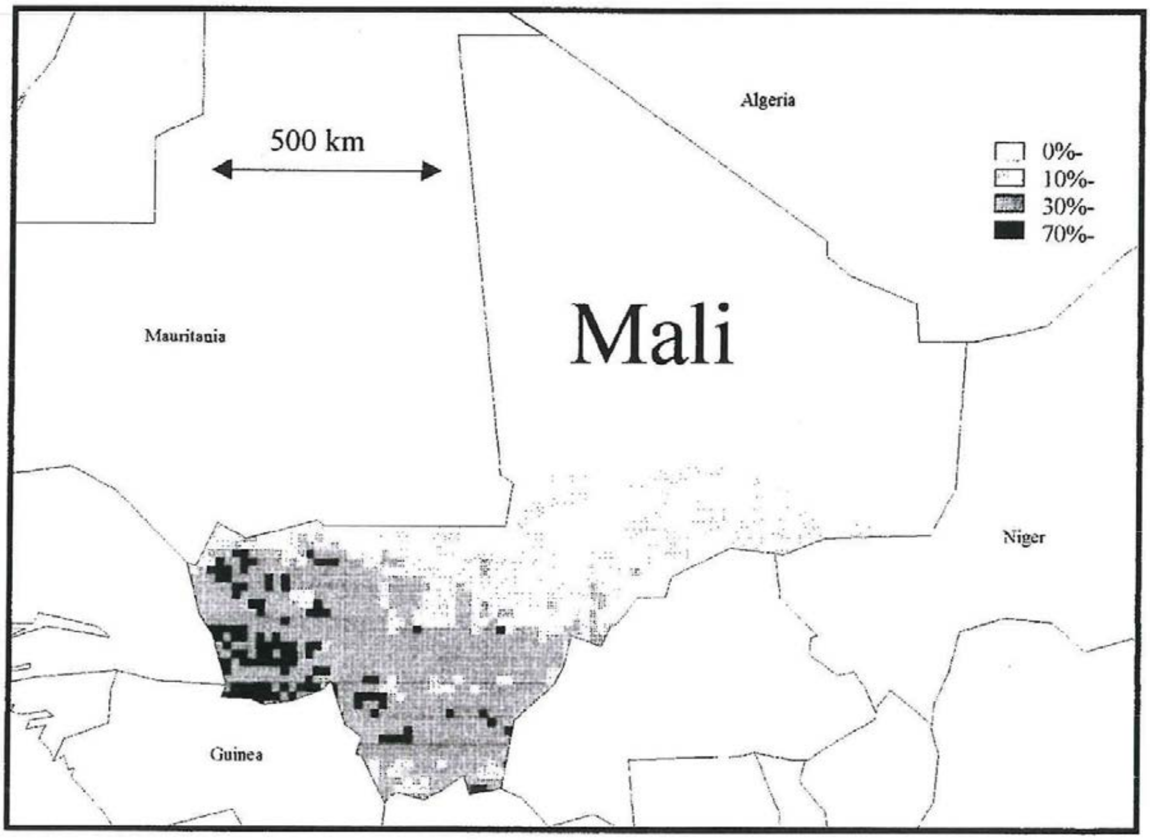


Figure 17 Map of malaria risk in Mali in 2000, predicted using regression plus Kriging approach[103]

A map combining the information on climatic zones, levels of infection prevalence from various studies and a length of transmission season was first developed by the time the first national strategic plan for malaria control from 2001 to 2005 was launched after the start of the RBM initiative.[104] This map (Figure 17) was developed through a collaboration between the MRTC and the PNLP and classified malaria risk in Mali in five zones.

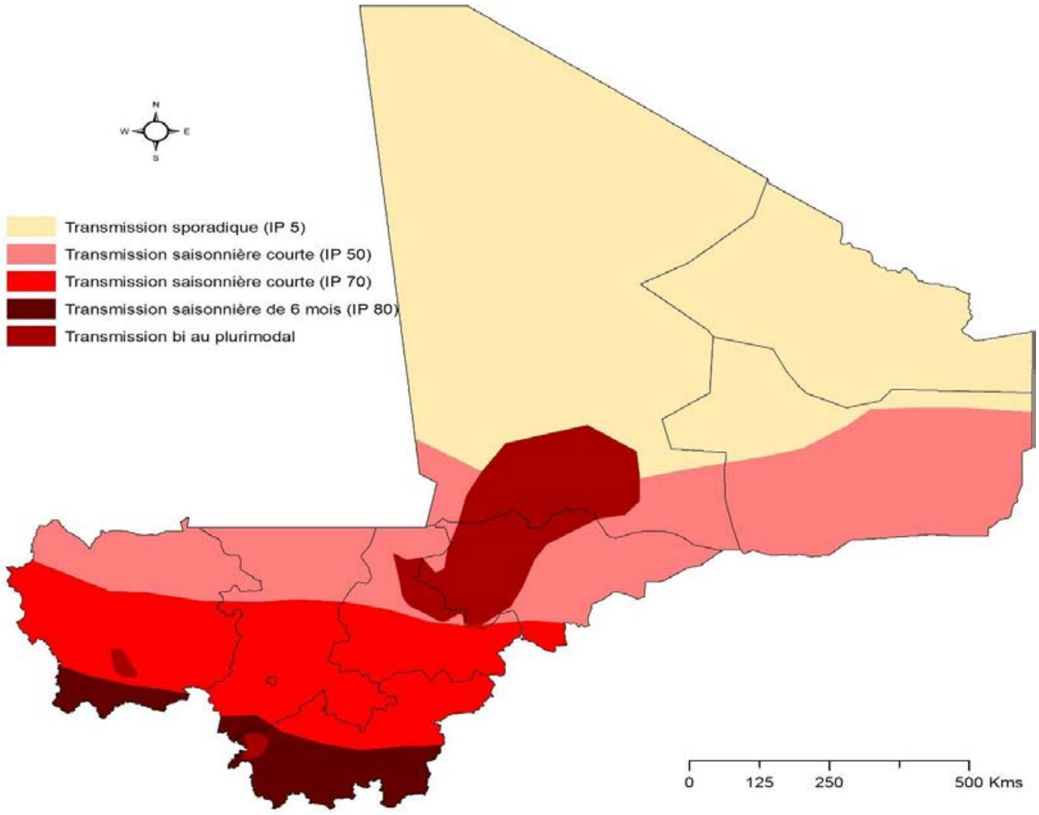


Figure 18 Map of malaria risk zones[iv] in Mali developed using a semi-quantitative combination of climatic zones, infection prevalence and length of transmission season

Another malaria risk map (Figure 18) was developed in 2001 by Kleinschmidt et al., but this map covered the whole of West Africa.[105] The map was developed using 450 survey data points with a minimum of 50 persons examined between 1970 and 2001. Predictions were undertaken separately within the main climatic zones (Sudano-Sahel, Guinean and Forest zones) and standardised to the age range of two to less than ten years of age. No predictions were made in large parts of the Sahara Desert. Predictions were undertaken within a Bayesian geostatistical framework combining the parasite rate data with environmental covariates. For Mali, the analysis predicted that most areas in the Sudano-Guinean zone (in which 67% of the population lived in 2001) had *P. falciparum* rates in children two to ten years of age of greater than 30%.

[iv] **Guinean zone:** seasonal, long transmission ≥6 months. In this area, the parasite rate in children is ≥80%. The status of acquired immunity is acquired by the age of five to six years of age. **Sudanian zone:** seasonal transmission and normally ≤3 months. In this area, parasite rates in children are between 50% and 70%. The status of acquired immunity is rarely achieved before nine to ten years of age. **Sudano-Sahelian zone:** areas of bi- or multi-modal transmission including the inland delta of the Niger River (Niono, Sélingué, Manatali, Markala). The parasite rate among children is between 40% and 50%. Anaemia remains a significant clinical phenotype. **Sahara-Sahelian zone:** sporadic or epidemic transmission corresponding to the northern regions and some areas of Koulikoro and Kayes (Nara, Nioro Diéma, Yélimané, Kayes). The parasite rate among children is below 5%. All age groups are at risk of severe malaria and epidemic risk is high populations migrating from this zone to the south. **Bi-modal or multi-modal zone:** very conducive to malaria infection, particularly in urban areas such as Bamako and Mopti where malaria is endemic-hypoendemic. Parasite rate is normally ≤10% among children and older age groups are also susceptible to severe and complicated malaria.

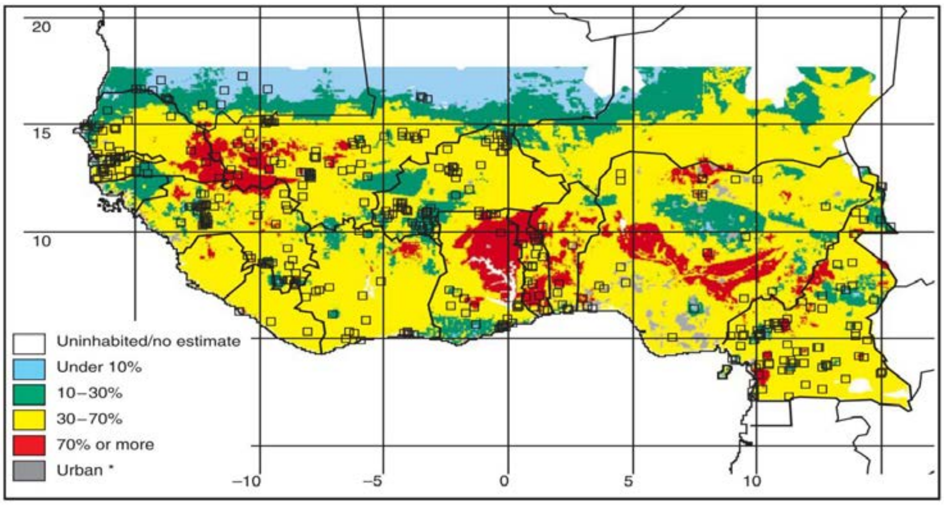


Figure 19 Predicted prevalence of *P. falciparum* parasite rates in children aged two to ten years of age in West Africa predicted using 450 parasite surveys with a minimum sample of 50 persons examined between the period of 1970-2001[105]

A map of entomological inoculation rates (EIR) was developed by the MARA project in 2006 using data from 164 surveys collected between 1965 and 1998 (Figure 19).[106] EIR estimates were first derived by fitting the Garki model to the parasite prevalence data.[107]

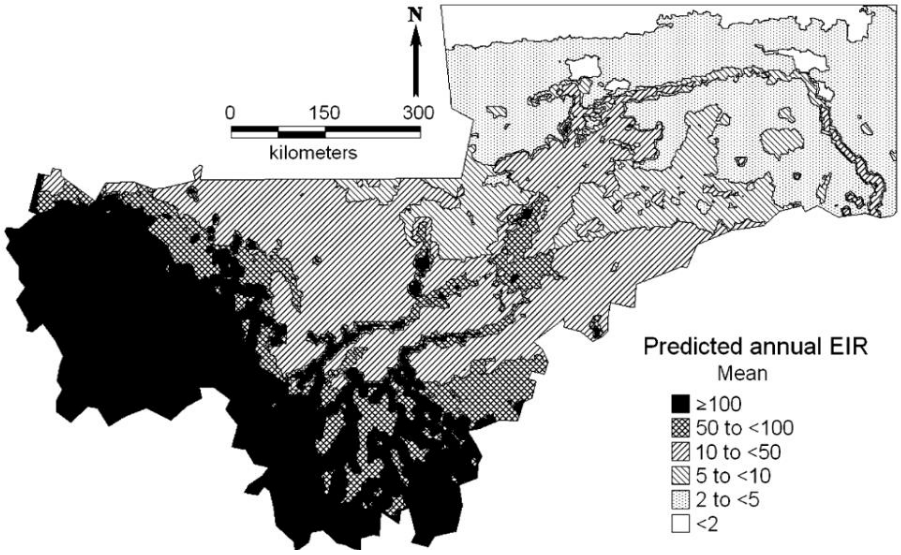


Figure 20 Spatial prediction of the mean annual entomological inoculation rate in Mali using 164 survey data at 147 locations from 1965 to 1998 collected by MARA. The map does not show most of the northern areas that coincide with the Sahara Desert[106]

Spatial modelling of EIR was then implemented using Bayesian geostatistical methods with the same climatic variable used by Kleinschmidt et al (2000) for estimation purposes. These estimates were then transformed back to the age-specific (less than five years of age and two to less than ten years of age) predictions of parasite prevalence. The parasite maps (Figure 20) indicated that the parasite rate among both age groups was greater than 20% across Mali below the Sahara Desert, with rates greater than 80% in most of the Sudano-Guinean zone.

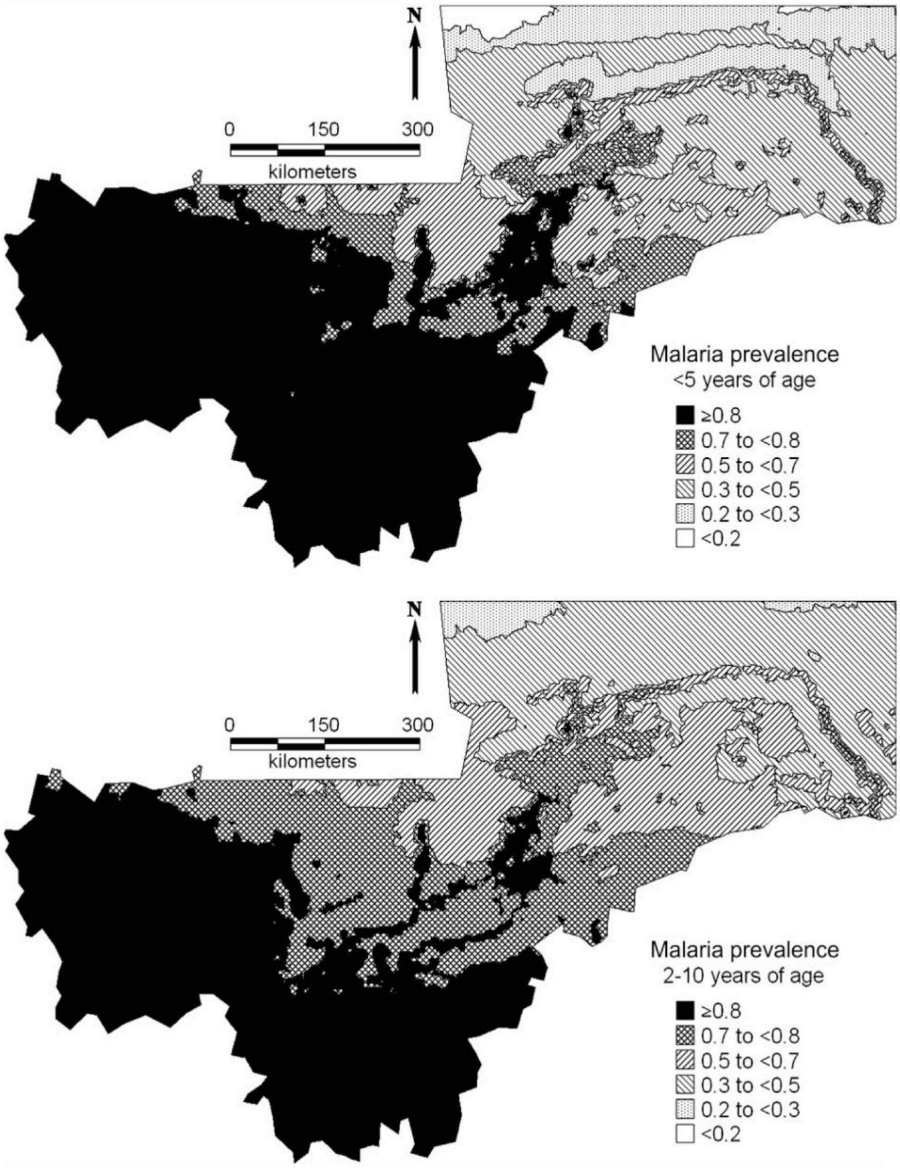


Figure 21 Spatial prediction of the age-specific parasite rates in Mali derived from a transformation of the EIR using a mathematical model. The maps do not show most of the northern areas that coincide with the Sahara Desert[106]

P. falciparum prevalence in children one to ten years of age in Mali between 1977 and 1995 was subsequently mapped by Gosoniu and colleagues using 89 data points.[108] This map (Figure 21) compared the results of stationary and non-stationary models and used the covariates of season length, vegetation, temperature, rainfall and proximity to water bodies in the model.[108] The analysis demonstrated that the non-stationary water models – which assumed directional heterogeneity in parasite rates – perform better. The maps of Sudano-Guinean zone had parasite prevalence rates greater than 50%, while most of the Sahelian region had predicted prevalence of less than 20%.

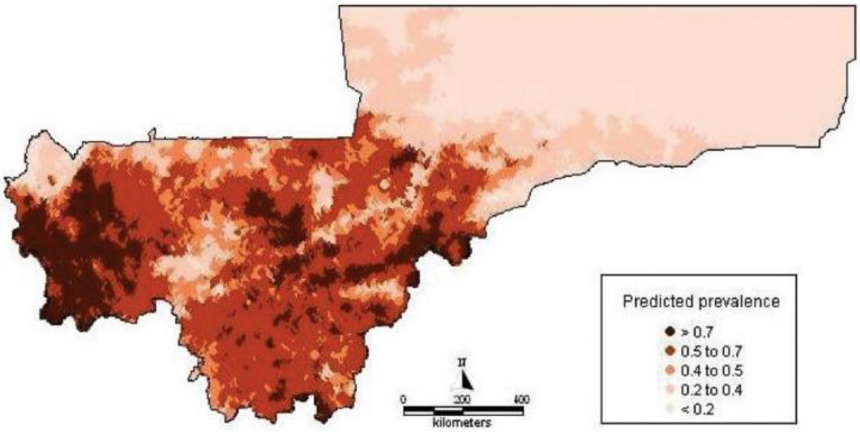


Figure 22 Spatial prediction of parasite rates in children one to ten years of age in Mali, derived from 89 data points from the period 1977 to 1995. The map does not show most of the northern areas that coincide with the Sahara Desert[108]

A map of malaria transmission intensity, Figure 22, was included in the 2013 to 2017 national strategic plan for malaria.[14] This map was based on 114 clusters from the 2010 national anaemia and prevalence survey among children and 413 clusters from the 2012–2013 DHS.[109] The map summarised the proportion of sampled children under five years of age that tested positive for *P. falciparum.* The survey results were summarised at regional levels and classified into three strata: (1) less than 30% parasite prevalence (Bamako, Tombouctou, Gao, Kidal); (2) 30% to 59% (Kayes, Koulikoro, Ségou); and (3) 60% or greater (Mopti, Sikasso).

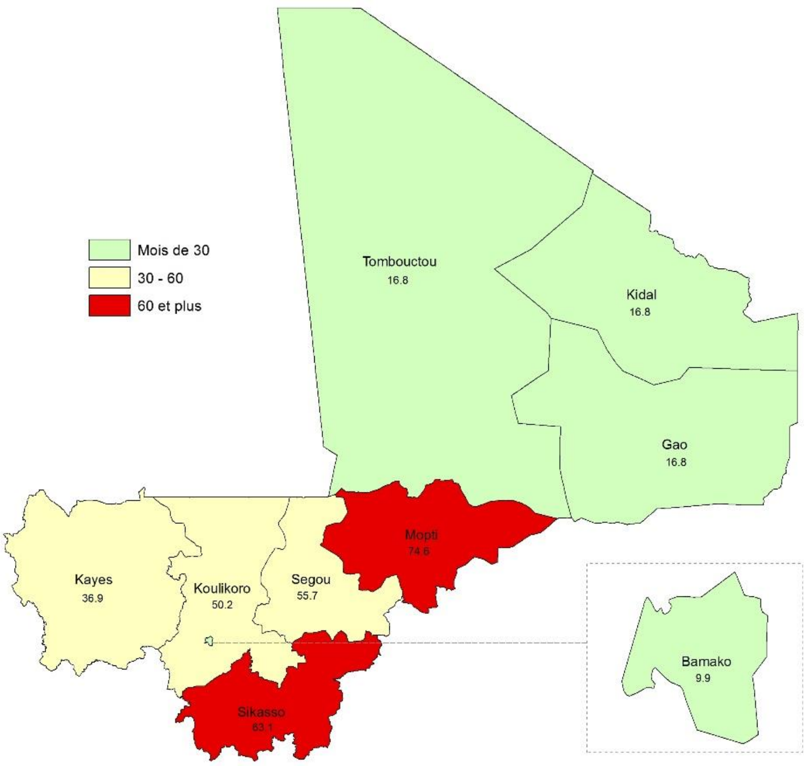
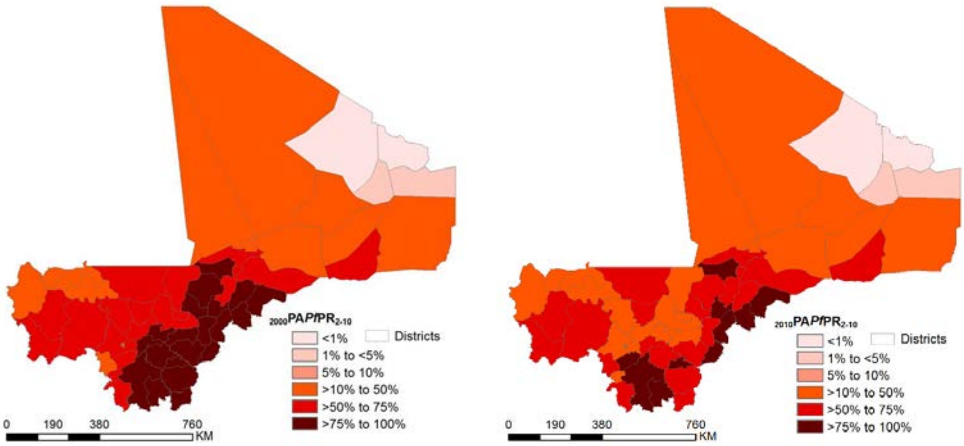


Figure 23 Malaria strata based on parasite prevalence among children under five years of age surveyed during the national household surveys of 2010 and 2013[109]

2014 to present

Mapping of malaria prevalence and relevant malaria intervention data was conducted by the LINK project in 2014, included in the first epidemiological profile of malaria in Mali generated by LINK. The parasite prevalence maps were developed using a comprehensive inventory of geo-coded prevalence data with rigorous Bayesian, MBG methods to interpolate estimates of *Pf*PR$_{2\text{-}10}$ across Mali in 2000, 2010 and 2013 and derived quantities of population-adjusted risk per district. Empirical data from parasite prevalence survey reports was assembled from online journal searches, investigations of material in Geneva and Brazzaville, the Institut Pasteur library in Paris and contact with national academics and research groups for unpublished data.

The final collection included 625 surveys from 1980 to 2013, which were subsequently standardised to the age group of children aged two to ten years of age. Final results of these standardisations indicated that risks of *P. falciparum* infection were marginally higher over the last decade compared to prevalence reported before 1999. However, the survey data was non-randomly dispersed over time and space, requiring the application of Bayesian hierarchical space-time models implemented through Stochastic Partial Differential Equations (SPDE) using Integrated Nested Laplace Approximations (INLA) for inference. In addition to urbanisation, the prevalence maps included used climate feature covariates of long-term annual precipitation, Fourier-processed enhanced vegetation index (EVI) and a temperature suitability index (TSI) all at a 1x1 km spatial resolution. Due to the aridity of the Saharan region and manifestation of malaria in the form of epidemics following unusually high rainfall, analysis was limited to areas with data south of the Sahara Desert.
Continuous maps of *Pf*PR$_{2\text{-}10}$ were generated and further classified into endemicity ranges. The modelled and population density grids were then used to extract populations at risk by district at each 1x1 km *Pf*PR$_{2\text{-}10}$ grid location using ArcGIS 10.1. These maps were generated for the years 2000, 2010 and 2013 (Figure 23).



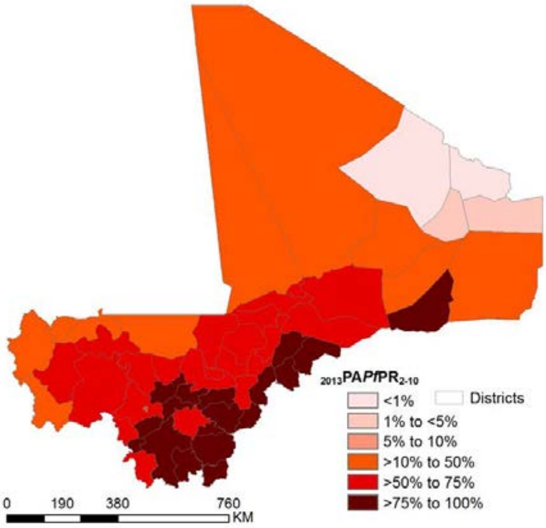


Figure 24 The population-adjusted 1939 *Pf*PR2-10 by health district (n=60) in Mali in 2000 (upper left); 2010 (upper right); and 2013 (bottom)

Malaria prevalence mapping using model-based geostatistics

Typically, national household surveys are designed to be precise at national and regional levels and rarely at lower levels, such as the district level. Therefore, aggregating survey data to provide district-level estimates of an outcome of interest are likely to result in values that are low in precision. Additionally, while smaller prevalence studies offer a detailed picture of malaria burden in a particular area, they are unable to provide insight to burden across a district or country alone.

In 2014, LINK reported a heterogeneous pattern of transmission of malaria in Mali, in which the southern districts in the Sudanese and Guinean eco-climate zones experienced predominantly hyperendemic to holoendemic malaria where the PA*Pf*PR$_{2-10}$ was ≥50%, in which about 66% of the population lived in 2013. By 2013, about 32% of the population lived in mesoendemic areas of mesoendemic transmission (PA*Pf*PR$_{2-10}$ >10% to 50%). Hypoendemic transmission appeared to be present only in Gao and Kidal regions while the PA*Pf*PR$_{2-10}$ was marginally above 10% due to the high concentration of the population of this region and in a few districts bordering the southern regions. Comparisons of populations at risk (PAR) indicated some achievements since 2000, especially in the hyperendemic and holoendemic transmission areas, where PAR reduced from 72.5% to 52% in 2010 between 2000 and 2010 before rising to 66% in 2013.

This profile builds upon survey and prevalence study data that is already available, using MBG to generate district-level estimates which are reliable and comparable over time, serving as an update to the maps generated in 2014.[110,111] The following details how the models of malaria prevalence in Mali were assembled and validated. Additionally, the maps of prevalence models which were produced using these methods will be presented.

1.11 Assembling malaria survey data into a single geo-coded repository

Data searches

Methods to identify sources of information have been opportunistic, cascaded approaches and included the use of personal contacts among the research communities in Mali. More traditional peer-reviewed publication searches were also performed, including: PubMed, Google Scholar, the WHO Library Database and African Journals Online. In all digital electronic database searches for published work the free text keywords "*malaria*" and "*Mali*" were used. Finally, surveyed data from the national household surveys in 2006, 2010, 2012 and 2015 were also identified. A full description of survey data assembly methods is provided elsewhere.[112]

All of those who aided in locating survey reports, university theses and unpublished data or provided help in the geo-coding of survey data are listed in the front of the report.

Data extraction

From each of the survey reports the minimum required data fields for each record were: description of the study area (name, administrative divisions and geographical coordinates, if available), start and end of survey dates (month and year) and information about blood examination (number of individuals tested, number positive for *Plasmodium* infections by species), the methods used to detect infection (microscopy, RDTs, Polymerase Chain Reaction [PCR], or Loop-mediated isothermal amplification [LAMP]) and the lowest and highest age in the surveyed population (decimal years). For data derived from randomised controlled intervention trials, data were only selected when described for baseline, pre-intervention and subsequent follow-up cross-sectional surveys among control populations. It was occasionally not possible to determine the month of the survey from the survey report. Descriptions of "wet" and "dry" season, first or second school term, or other information was used to make an approximation of the month of the survey.

Where age was not specified in the report but a statement was made that the entire village or primary school children examined, the age ranges of 0-99 years or 5-14 years were assumed, respectively. Surveys covered a number of age ranges, but to make a meaningful comparison in time and space a single standardised age range is required. Correction to a standard age for *P. falciparum* was performed using adapted catalytic conversion Muench models via static equations in R-script that uses the lower and upper range of the sample and the overall prevalence to transform the data into a predicted estimate in children aged two to ten years, $Pf\text{PR}_{2\text{-}10}$.[113]

Geocoding locations of each survey

During data extraction, each data point was recorded with as much geographic information from the source as possible and this was used during the geo-positioning, for example checking the geocoding placed the survey location in the administrative units described in the report or corresponded to other details in the report on distance to rivers or towns when displayed on Google Earth. According to their spatial representation, data were classified as individual villages, communities or schools or a collection of communities within an area covering a 5 km grid or approximately 0.05 decimal degrees at the equator (point). Preference was given to point data, however, areas more than 5 km^2 were classified as "wide-areas" (<10 km^2), and those where data was only available across larger administrative units included as "polygons," and excluded from the analysis.

More recent use of GPS during survey work enabled a re-aggregation of household survey data, to increase the sampling precision by combining clusters of small sample sizes in space, while maintaining the 5 km grid criteria. While in theory GPS coordinates should represent an unambiguous spatial location, these required careful re-checking to ensure that the survey location matched the GPS coordinates and all coordinates located on populated communities. To position each survey location where GPS coordinates were not available, a variety of digital resources were used: Microsoft Encarta Encyclopaedia, Google Earth, Fallingrain, African Data Sampler and digital place name gazetteers of schools and health centres in Mali.

We have selected as a data reference period 2000-2016, where data can be used to make a prediction to the years when national household sampling was undertaken in 2012/2013 and 2015. Between 2000 and 2016, a total of 971 independent survey points were identified at 853 unique locations (Figure 24). All data points were geocoded (Figure 25) and it was determined that there was not enough data available for mapping purposes in certain districts (Figure 26). The final survey locations used with years used to make predictions, 2012/2013 and 2015, may be seen in Figure 27. A total of 65,742 samples were collected at these sites, with all surveys relying on microscopy/blood examinations for parasite detection. The 2010 DHS is based on 109 clusters, 1,617 households and 9,624 respondents. The 2012-2013 DHS is based on 413 clusters, 10,105 households and 58,330 respondents. The 2015 MIS is based on 177 clusters, 4,240 households and 39,408 respondents.

The collected data points were geocoded, with 75.28% points geocoded using GPS, 9.37% using other means, 8.34% using Encarta, 2.68% using personal communications, 1.75% using Google Earth, 1.44% using a combination of means and 0.82% using Geonames. Three points were not geolocated. The maximum *Pf*PR_{2-10} value identified was 99.79%, the minimum was 0.0% and the median value was 42.64% (IQR:49.41%). A complete, geocoded database of survey data has been provided to the PNLP with this report.

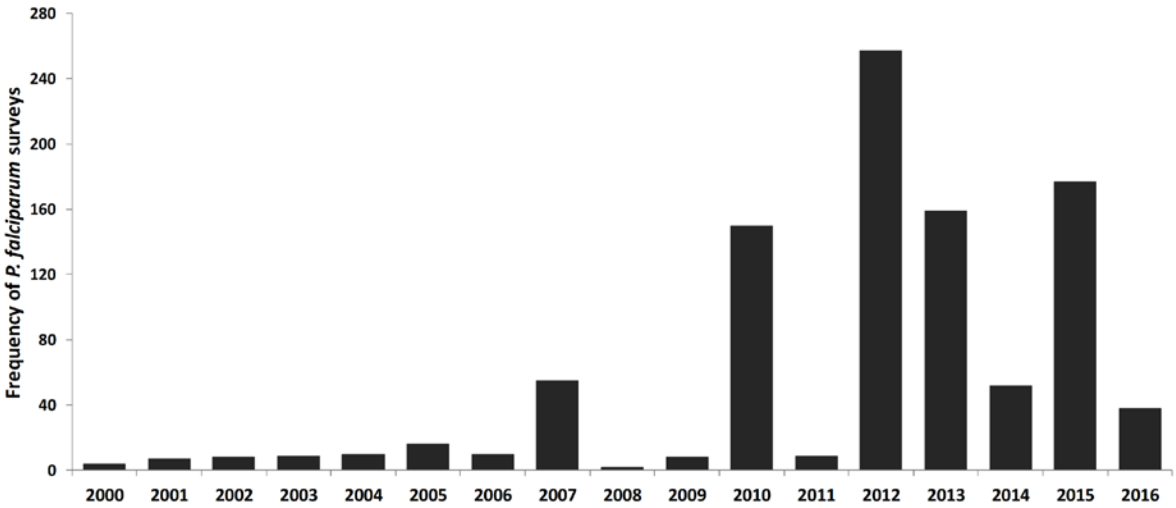


Figure 25 Frequency of *P. falciparum* surveys in Mali between 2000 and 2016

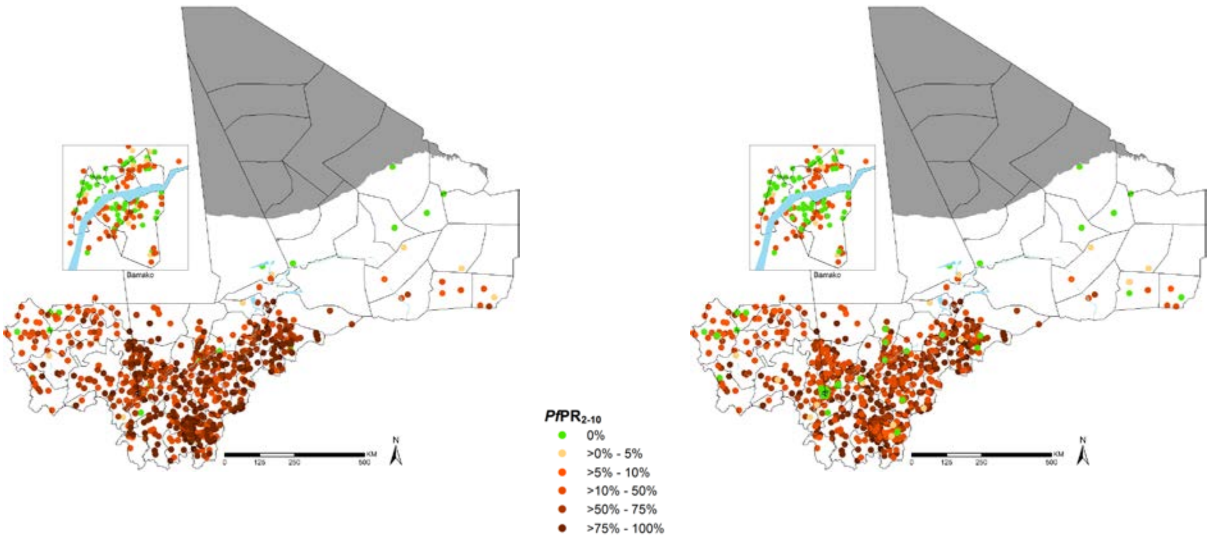


Figure 26 The age-corrected *P. falciparum* infection rates at 853 unique locations showing the highest values on top among 971 surveys from 2000 to 2016 (left) and lowest values on top (right)

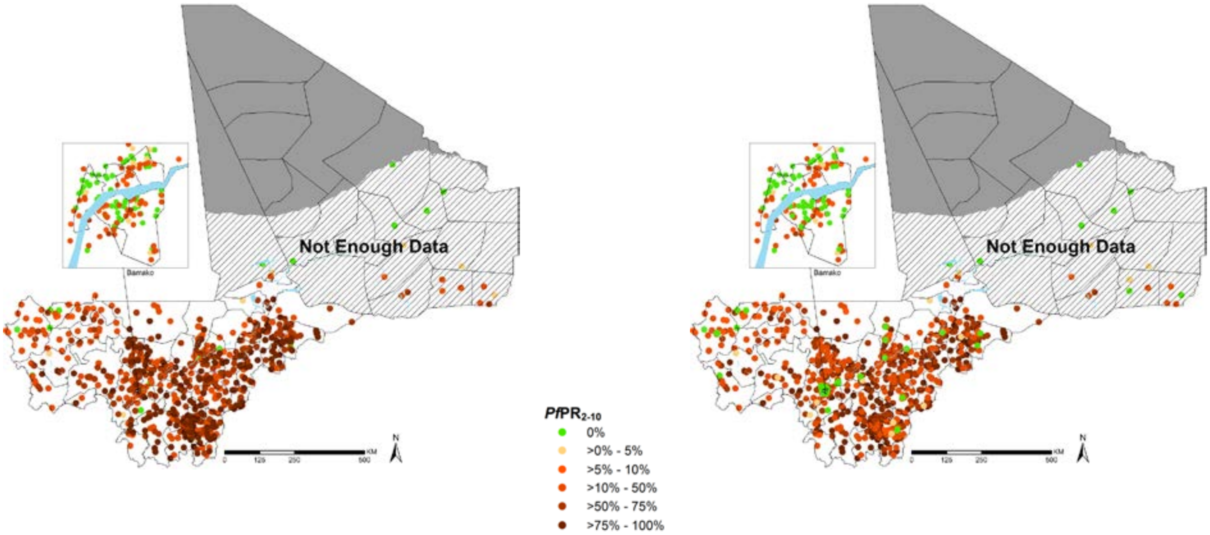


Figure 27 The age-corrected *P. falciparum* infection rates at 853 unique locations showing the highest values on top among 971 surveys from 2000 to 2016 (left) and lowest values on top (right), with districts with insufficient data for mapping indicated

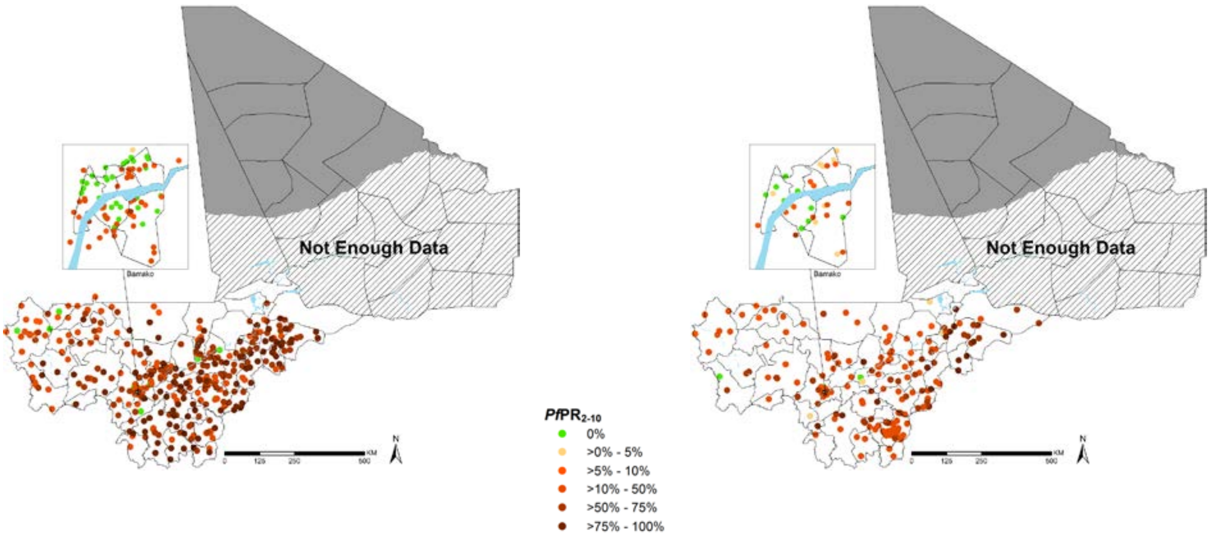


Figure 28 The age-corrected *P. falciparum* infection rates at 853 unique locations showing the years used to make predictions for mapping purposes with 2012/2013 on the left and 2015 on the right

1.12 Statistical approaches to locality risk mapping

Model form

The analysis of research data undertaken in different parts of Mali, regional school surveys and national household surveys in one combined way, requires MBG. MBG is a modeling framework that allows for the best possible use of data by providing a statistically principled approach to manage uncertainty. These statistical methods draw on the basic principle that things that are close in space and time are more related than distant things (also known as the first law of geography) (i.e. surveys conducted in the same district should have a more similar measure of malaria risk than surveys in different districts far from each other, or surveys that are one year apart should have a more similar malaria risk than surveys undertaken decades apart).[114] The mathematical details that translate the first law of geography into geostatistical models are described elsewhere and used recently to provide malaria risk maps in Somalia.[115,116]

In the current modelling exercise, no environmental covariates are used to assist in malaria predictions. These become important when data are very sparse, and there is a well-defined biological relationship in each setting with the covariates selected. For the current modelling exercise in Mali, it is assumed that the parasite prevalence at a given location is a product of the climate and control environment, without presuming the biology of climate to infection prevalence.

The spatio-temporal variation in *Pf*$PR_{2\text{-}10}$ was modelled using geostatistical methods to borrow strength of information across time and space. Let *x* be the location of a surveyed community in year *t*. We then use *S(x,t)* to denote the variation in malaria risk between communities (eg. variation due to different environmental conditions) and *Z(x,t)* the variation within communities (ie. genetic and behavioural traits). In statistical jargon, *S(x,t)* and *Z(x,t)* are so-called random effects that are used in a model in order to capture the effects of unmeasured malaria risk factors.

The input data was the observed *Pf*$PR_{2\text{-}10}$ values at location *x* (n=968) and year *t*. A logit-linear model for *Pf*$PR_{2\text{-}10}$ was defined as:

$$\log\left\{\frac{PfPR(x,t)}{1-PfPR(x,t)}\right\} = \alpha + \beta * f(mA) + \gamma * g(MA) + S(x,t) + Z(x,t)$$

where *f(mA)* and *g(MA)* are spline functions of the minimum and maximum age among the sampled individuals at location *x*. To predict *Pf*$PR_{2\text{-}10}$ we then set *mA*=2 and *MA*=10. The *S(x,t)* was modelled as a stationary and isotropic Gaussian process with spatio-temporal correlation function given by:

$$corr\{S(x,t),S(x',t')\} = exp\{-||x-x'||/\phi\}exp\{-|t-t'|/\psi\}$$

where ϕ and ψ are scale parameters which regulate the rate of decay of the spatial and temporal correlation for increasing distance and time separation, respectively. The notation *||x-x'||* represents the distance in space between the locations of two communities, one at *x* and the other at *x'*. The above equation then indicates that as the distance between *x* and *x'* increases, the spatial correlation will decay at a rate ϕ. A similar argument applies to *|t-t'|* which represents the time separation between two surveys.

The model parameters were estimated via maximum likelihood in the R software environment (version 3.4.2). The targets for the predictions were *Pf*$PR_{2\text{-}10}$ over the 1 x 1 km regular grid surface covering the whole of Mali. Maps of malaria risk were generated for the years 2012 and 2015 in ArcMap version 10.5 (ESRI Inc., Redlands, CA, USA) (Figure 29) and average *Pf*$PR_{2\text{-}10}$ binned to four classes of risk per district (Figure 30).

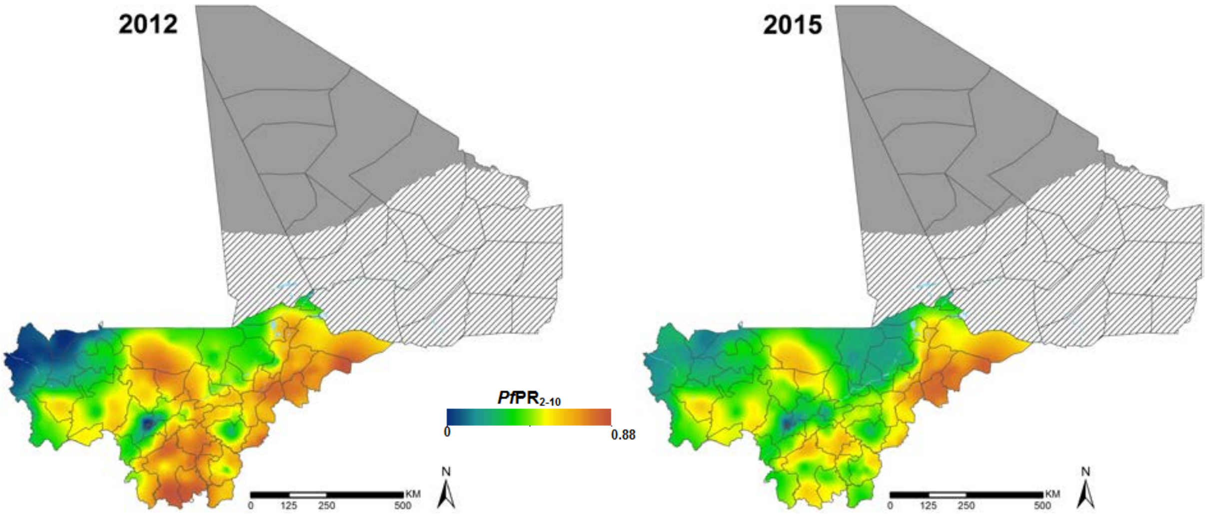


Figure 29 Continuous predicted *Pf*PR2-10 estimates for Mali in 2012 (left) and 2015 (right), ranging from low (yellow) to high (red) through intermediary prevalence (blue). Grey masks show areas unable to support stable transmission or areas with insufficient data.

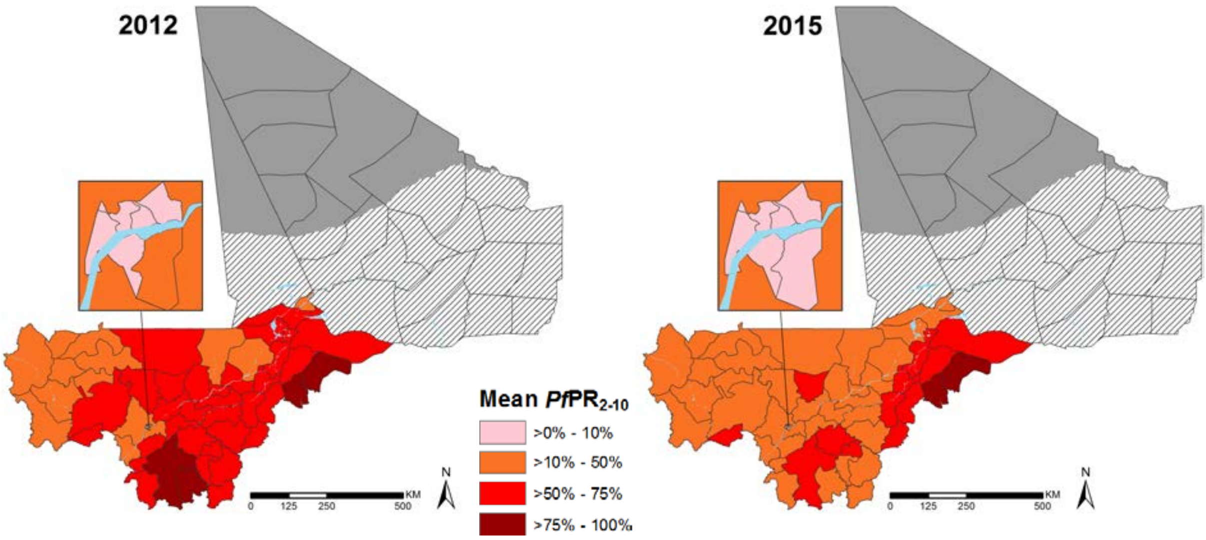


Figure 30 Binned predicted average quantities of *Pf*PR2-10 in 75 districts in 2012 and 2015: >0% - 10%, >10% - 50%, >50% - 75% and >75% - 100%

In general, malaria incidence decreased throughout all of Mali between 2012 and 2015, with the highest prevalence in Bankass and Koro of Mopti region.

1.13 How certain are we in our estimates of malaria prevalence?

One of the objectives of this profile is to identify areas of Mali that are below a certain malaria prevalence threshold. In countries where areas are transitioning to lower transmission, identifying areas which are below a particular threshold require consideration regarding the adaptation of strategies to meet universal coverage efforts. In doing so, intervention combinations may be considered more nuanced, cost-efficient and efficacious.[115]

However, classifying geographical areas into different endemic levels by estimated parasite prevalence creates an oversimplified picture of the malaria situation in that area.[116] As with any data measurement or modeling, we are making an estimate of malaria prevalence for a population in a certain place at a specific time. This estimate falls within a range of values that are likely to encompass the true prevalence of malaria.

To address the uncertainty of our estimates, we have calculated both an 'exceedance probability' (EP) and a 'non-exceedance probability' (NEP) that the prevalence of malaria in a given area is above the threshold of 50% and below threshold of 10%, respectively, based on available survey data. An EP close to 100% indicates that *Pf*PR$_{2-10}$ is most likely above the threshold *l*. If close to 0%, *Pf*PR$_{2-10}$ is most likely to be below the threshold *l*. In contrast, a NEP close to 100% indicates that *Pf*PR$_{2-10}$ is highly likely to be below the threshold *l* and if close to 0%, *Pf*PR$_{2-10}$ is highly likely to be above the threshold *l.* If close to 50%, *Pf*PR$_{2-10}$ is equally likely to be above or below the threshold *l*, corresponding to the highest level of uncertainty.

Estimates of *Pf*PR$_{2-10}$ at location *x* and time *t* (*Pf*PR$_{2-10(x,t)}$) have uncertainties that need to be taken into account when determining whether the prevalence in that area falls below a certain threshold, say *l*. We use the geostatistical model to derive a distribution of the values most likely that *Pf*PR$_{2-10(x,t)}$ can take. We then use this distribution to quantify how likely *Pf*PR$_{2-10(x,t)}$ is to be above a threshold *l* through an EP, formally expressed as:

$$EP = Probability\{PfPR_{2-10(x,t)} > \ l/data\}$$

where *l* is the prevalence threshold which we set to ≥50%. In other words, EP expresses how likely *Pf*PR$_{2-10}$ is to be above the threshold *l* based on the availability of survey data.

Regarding the NEP, the distribution may be used to quantify how likely *Pf*PR$_{2-10}$ is to be below a threshold *l*, formally expressed as:

$$NEP = Probability\{PfPR_{2-10(x,t)} < \ l/data\}$$

where *l* is the prevalence threshold which we set to ≤10%. In other words, NEP expresses how likely *Pf*PR$_{2-10(x,t)}$ is to be below the threshold *l* based on the availability of survey data.

Figure 31 indicates areas where the model allows for 80% and 90% certainty that the *Pf*PR$_{2-10}$ does not exceed 10% or exceeds 50% in 2012 and 2015 based on available data. These maps demonstrate an overall decline at both the 80% and 90% confidence levels that *Pf*PR$_{2-10}$ does not exceed the 50% threshold.

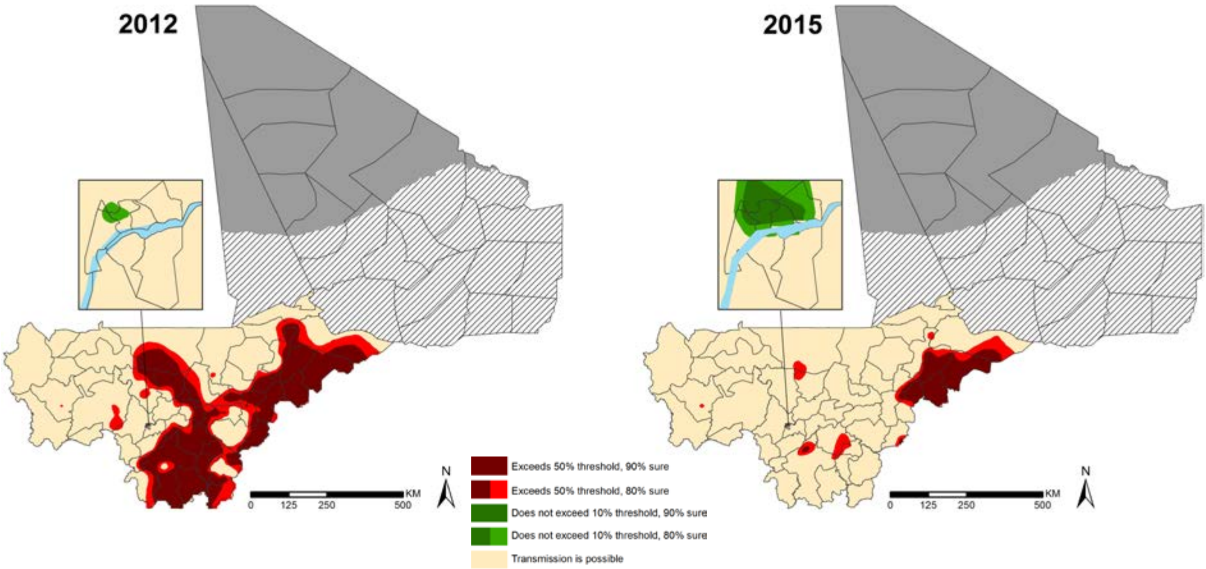


Figure 31 Probability that *Pf*PR$_{2-10}$ is ≤10% and ≥50% per health district

Entomological profile

1.14 Mosquito sampling sites

Entomological monitoring is carried out in 15 sites throughout Mali.[3] Monitoring includes both IRS and non-IRS regions, including Kayes, Koulikoro, Ségou, Sikasso, Mopti and Bamako. All sites gather information regarding vector-insecticide susceptibility, while those conducting IRS collect information about entomological densities, behaviour, longevity, infection rate and blood meal origins.[3]

Reasons for selection as sampling sites vary. Sites are included as a survey site if they are a:

- Former IRS sites (Koulikoro, Bla, Barouéli, Fana);
- New IRS site (Badiangara, Bankass, Djenne, Mopti);
- Non-IRS comparison site (Bamako);
- Major agricultural or irrigation site (Niono, Kati, Kita, Bla, Bougouni, Selingue, Kadiolo);
- Site of ITN distribution (Kita, Koulikoro, Barouéli, Fana, Selingue, Kadiolo); or
- Site of other vector control efforts (Kati).[3]

1.15 Summary of geocoded malaria vector data repository in Mali

National malaria vector studies in Mali have often excluded the northern and eastern desert areas since they are not receptive to *Anopheles*. Specifically, no *Anopheles* surveys could be identified from Taoudenit and Menaka regions in the north and east, respectively. The first nationwide entomological study was undertaken in the late 1950s and early 1960s, describing the Anopheline species found in Mali and their locations, complete with latitudes and longitudes. [95] The first national maps describing spatial distribution and chromosomal variation of *Anopheles gambiae s.s.* and *Anopheles arabiensis* were later developed in 1991 by Touré and colleagues.[117] This effort was part of a larger study which began in 1981 and covered diverse eco-climatic regions such as forest, savannahs and deserts. Similar mapping exercises continued later on within this project with data ranging from 1981 to 1994 and further to 1994 by Sogoba and colleagues.[118,119]

Data sources included in this repository included historical archives and published sources, with increased documentation of potential secondary vectors and more recent unpublished data from scientists and control agencies working within Mali. These have been used to develop a repository of data on malaria vectors for Mali. Full details of the data assembly, geo-coding methods and classifications of species according to their role in malaria transmission are provided elsewhere.[120]

The database has been arranged as a site-specific, referenced inventory to capture details of species identification recorded since the earliest surveys in 1906 through to the latest records in 2014. The full digital Pdf library, database and bibliography were delivered to the Ministère de la Santé et de l'Hygiène Publique with this report.

From each identified report, data extraction included whether a species was identified at a given site, methods used to capture adults or larvae and methods used to speciate each anopheline collection. "Y" was recorded if a species was identified and "N" was only recorded when the true absence of the species was reported. The database is therefore one of species presence, not absence and not proportional to the presence of various vectors.

The final database contained 446 site-specific reports of anopheline vectors in Mali, occurring between 1906 and 2014 for which it was possible to geo-locate the survey site (Figure 31). It was not possible to geo-locate two (0.4%) of the survey sites.

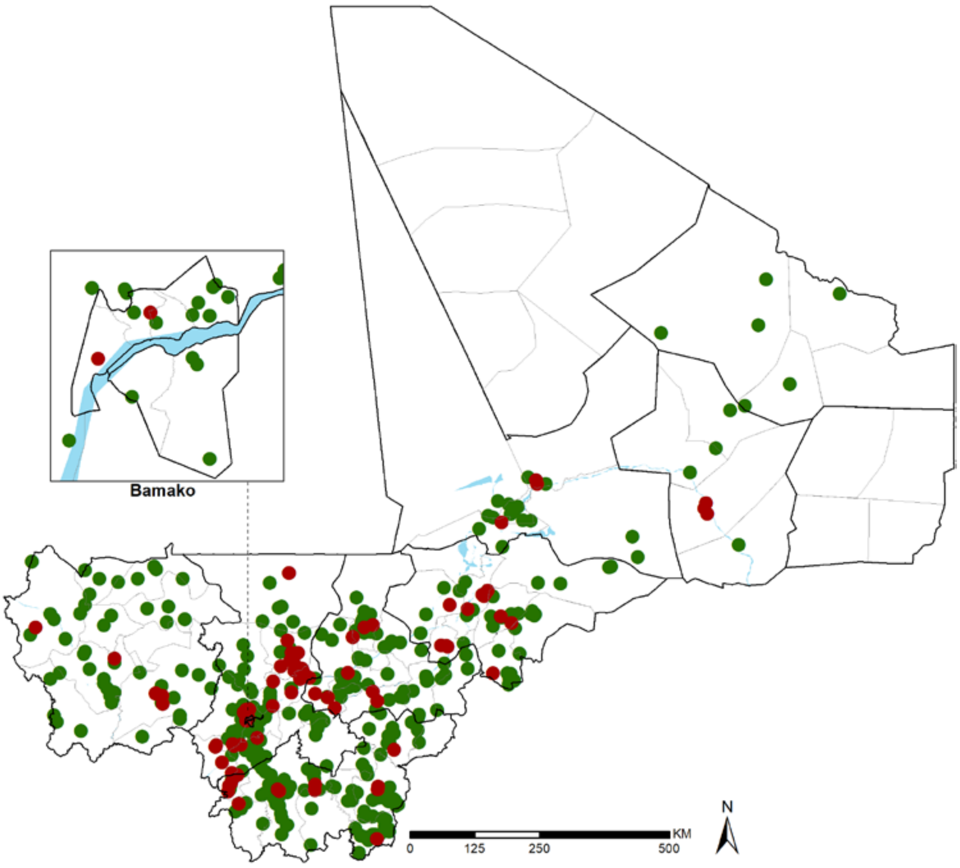


Figure 32 Distribution of 446 Anopheline survey locations sampled between 1906 and 2014 (82 red locations are sites sampled 2005-2014, 364 green are sites sampled before 2005)

The database includes the extensive mosquito survey data assemblies from 1981 to the late 2000s, undertaken in a long-term collaboration between the Département d'Epidémiologie des Affections Parasitaires of the Ecole Nationale de Médecine, de Pharmacie et d'Odonto-Stomatologie of Bamako and the Istituto di Parassitologia.[118,119]

1.16 Identified species

An. gambiae complex and *An. funestus* group are the major vectors of malaria in Mali, and occur in sympatry across the country except in the northeastern and southwestern regions, where *An. funestus* diminishes (Figure 32, Figure 33). *An. gambiae* complex in Mali comprises *An. gambiae s.s.* (previously known as S form), *An. colluzii* (previously known as M form) and *An. arabiensis*, all of which have been described in all of the regions of the country except for Taoudenit and Menaka and occur in sympatry within their range (Figure 34). The speciation of the members of the *An. funestus* group has not been studied extensively in Mali.

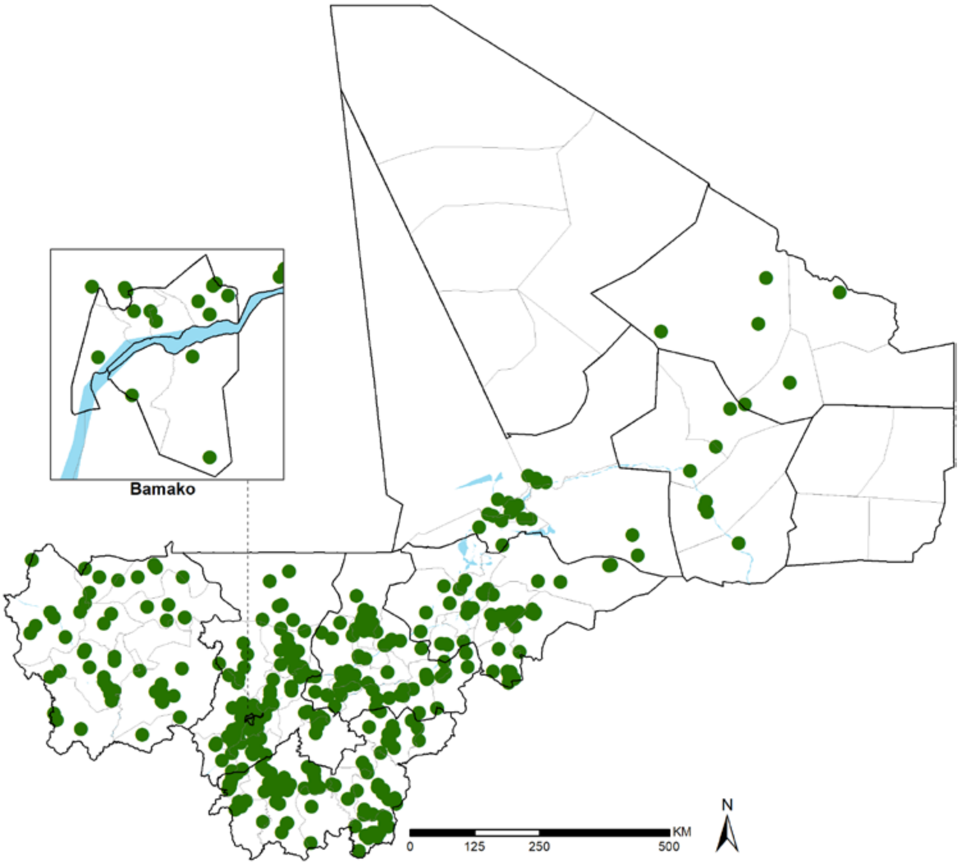


Figure 33 Distribution of documented *An. gambiae s.l.* (n=407)

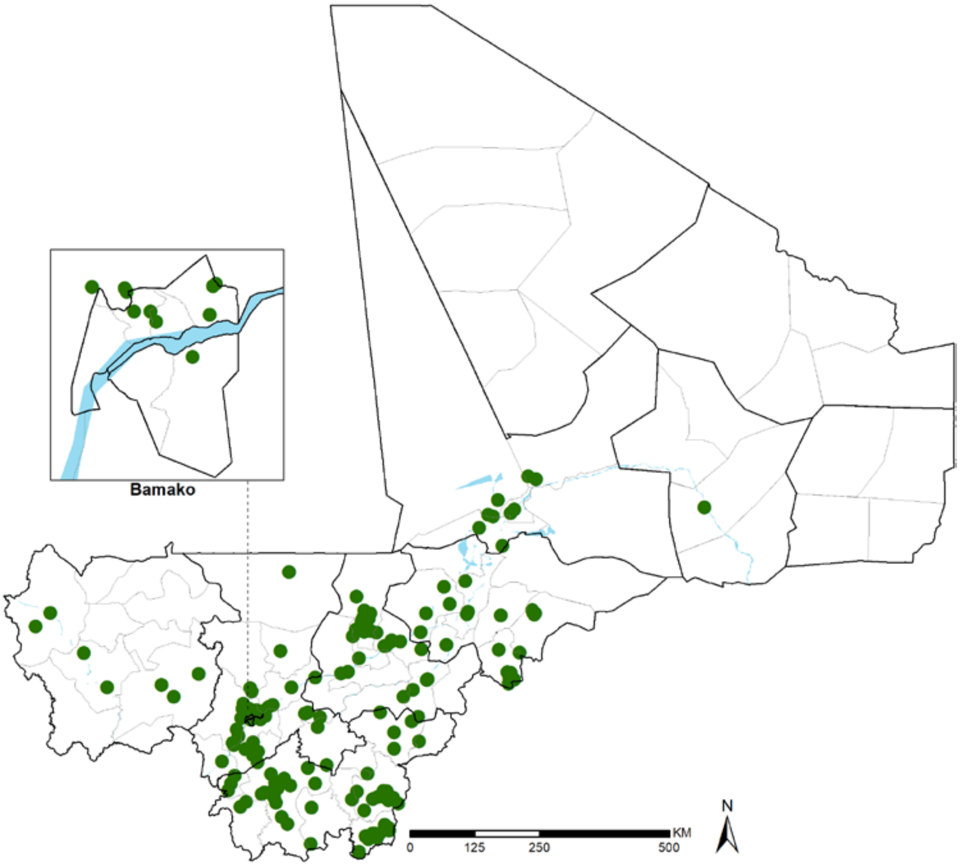


Figure 34 Distribution of documented *An. funestus s.l.* (n=173)

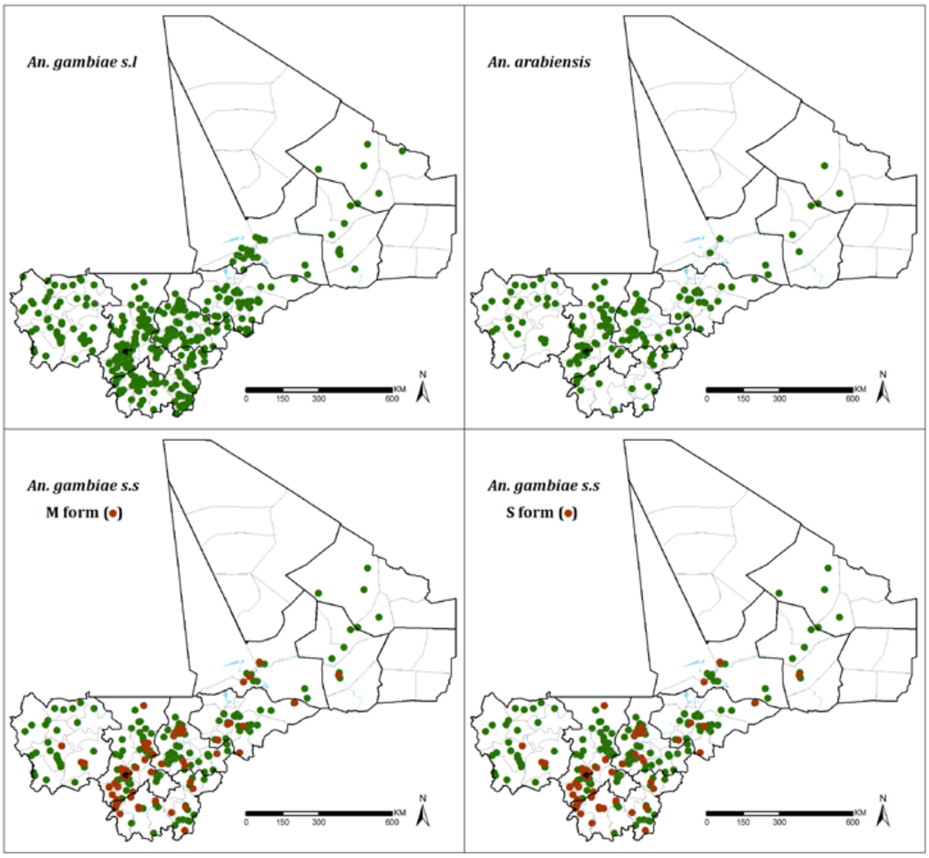


Figure 35 Distribution of members of *An. gambiae* complex

Only a few members of *An. rivulorum* and *An. leesoni* have been described, while there are no records for *An. funestus s.s. An. nili* has been recorded only in the central southern part of Mali, where it is considered as a dominant vector species (Figure 38). *An. pharoensis, An. squamosus, An. rufipes* and *An. coustani s.l.* have also been described in the central and southern areas and are considered as secondary vectors of malaria (Figure 35, Figure 36). *An. moucheti* has never been described in Mali.

Figure 36 Location of members of *An. funestus* group and *An. coustani* group

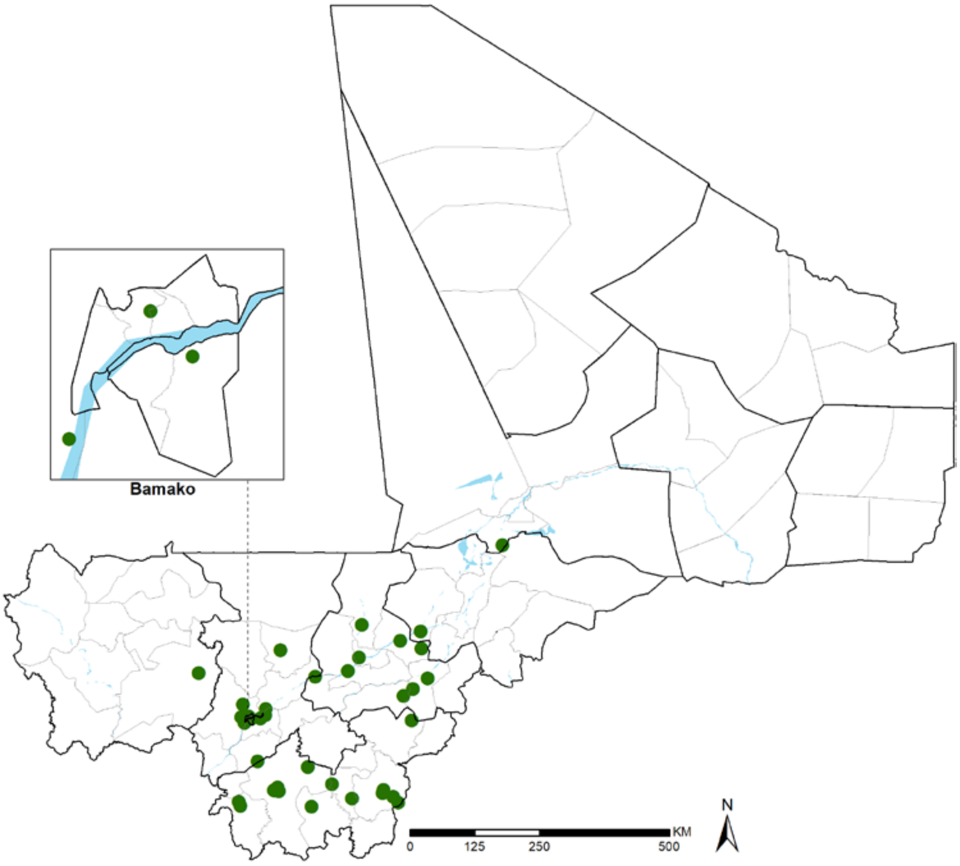


Figure 37 Distribution of documented *An. nili s.l.* (n=36)

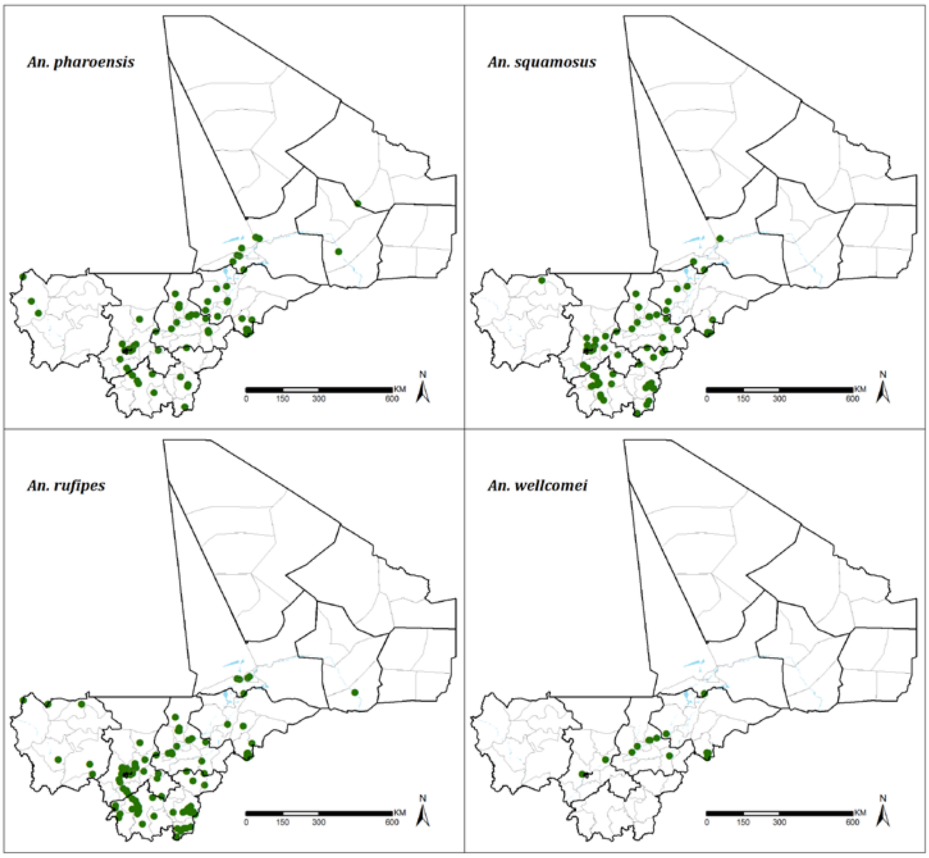


Figure 38 Location of other potential secondary vectors

Other anophelines reported in Mali since 1906 but not implicated in malaria transmission include: *An. brohieri, An. brunnipes, An. domicolus, An. flavicosta, An. hancocki, An. longipalpis, An. macmahoni, An. maculipalpis, An. obscurus, An. paludis, An. pretoriensis, An. rhodesiensis and An. ziemanni.*

Taxonomy

Anopheles gambiae s.l.:The *Anopheles gambiae* complex has undergone numerous transitions in taxonomy over time. The earliest descriptions of the *An. gambiae* complex referred to a single species, *An. costalis*, during the first decade of the last century. Following the Liverpool School visit to the Gambia in 1902, this species was named *An. gambiensis* Giles. In the 1940s, *An. melas* (West Africa) and *An. merus* (East Africa) were confirmed as sibling species of the *An. gambiae* complex through observations on salinity tolerance and slight morphological variations. In the 1950s and 1960s, the innovation of new hybridisation methods (cross-mating) made it possible to distinguish three fresh-water breeding species of *An. gambiae* (A-C). At around the same time, a morphologically unique sibling [Species D] was identified in the mineral springs of the Semliki National Park, Bwamba district, Uganda, and later named *An. bwambae* White.[121–123] Chromosomal investigations of species A and B were undertaken in the late 1960s and this led to the ability to distinguish between *An. gambiae sensu stricto* and *An. arabiensis*, respectively.[124] The zoophilic *An. quadriannulatus* A and *An. quadriannulatus* B were described as sibling-species of the *An. gambiae* complex (previously species C) in the early 1980s but not regarded as vectors of malaria within their geographic ranges of southern Africa and Ethiopia.[125,126] *An. quadriannulatus* B from Ethiopia was later renamed *An. amharicus* Hunt, Wilkerson & Coetzee sp. n. while the name *An. quadriannulatus* was retained for the southern African form.[5,127]

In the early 2000s, *An. gambiae s.s* was genetically distinguished as *An. gambiae* s.s. S form (Savanna/Bamako) and M form (Mopti).[128,129] In 2013, the "M form" was re-named *An. coluzzii* Coetzee & Wilkerson sp. n while the "S form" retained the name *An. gambiae s.s.* [5]

All the records of *An. gambies s.s* species (or Species A) before the invention of genetic tools referred to either the M or S forms or both, but not solely the S form, as is now defined. For this reason, that the name "*An. gambiae s.s"* was retained to include both species that formerly belonged to the *sensu stricto and* only indicated the S form when specifically recorded as so

An. melas, An. merus, An. amharicus and *An. bwambe* have not been described in Mali. Given that the majority of the data pre-date effective taxonomy between the sibling species of the complex the relative contributions of *An. gambiae s.s.* and *An. arabiensis* cannot be established. However, recent molecular studies of *An. gambiae s.l* suggest that *An. gambiae s.s.* predominates and while M and S forms have been detected, the S form is dominant.[130,131]

Understanding whether *An. gambiae*, which is a major malaria vector in the Sahelian regions, aestivates (lies in dormant state to allow for extended longevity during the summer) is critical to explaining the patterns of rapid establishment of mosquito populations soon after the rains following a period of four to eight months of dryness. A recent study that used a mark release–recapture experiment from the end of one wet season to the beginning of the next in Sahelian villages in Mali provides strong evidence of aestivation by the *An. gambiae* during the summer.[132] During the dry season, *An. gambiae* was largely absent in the study villages. However, a ten-fold increase in mosquito populations was observed within five days after the first rain and before a new generation of adults could be produced in support of this conclusion.

Anopheles gambiae s.s.: *An. gambiae s.s.* larvae typically inhabit sunlit, shallow, temporary bodies of fresh water such as round depressions, puddles, pools and hoof prints. This aspect of their bionomics may allow members of the *An. gambiae* complex to avoid most predators and the larvae are able to develop very quickly (circa six days from egg to adult under optimal conditions). *An. gambiae s.s* has been reported from habitats containing floating and submerged algae, emergent grass, rice, or 'short plants' in roadside ditches and from sites devoid of any vegetation. It is considered to be highly anthropophilic, with many studies finding a marked preference for human hosts. This vector typically feeds late at night and is often described as an endophagic and endophilic species, i.e. biting and resting mostly indoors. The species is considered to be one of the most efficient vectors of malaria in the world.

Anopheles arabiensis: *An. arabiensis* is considered a species of dry, savannah environments or sparse woodland. Evidence is growing of a more ubiquitous range of *An. arabiensis* across Africa and the species remains an important vector in Mali. Its larval habitats are generally small, temporary, sunlit, clear and shallow fresh water pools, although *An. arabiensis* is able to utilise a variety of habitats including slow flowing, partially shaded streams, large and small natural and man-made habitats, turbid waters and brackish habitats. *An. arabiensis* is described as a zoophilic, exophagic and exophilic species but has a wide range of feeding and resting patterns, depending on geographical location. This behavioural plasticity allows *An. arabiensis* to adapt quickly to counter IRS control, indicating behavioural avoidance of sprayed surfaces depending on the type of insecticide used. Blood feeding times also vary in frequency; peak evening biting times are reported to begin between the early evening (19:00) and early morning (03:00). This species usually has a greater tendency than *An. gambiae s.s.* to bite animals and to rest outdoors.

Anopheles funestus: The exact composition of the *An. funestus* complex (*An. funestus s.s., An. parensis, An. vaneedeni and An. rivulorum*) remains unclear without molecular identification. Only *An. funestus s.s*. is implicated in transmission of *Plasmodium*, while sibling species have either no role or only limited roles in transmission. It is assumed that reports of *An. funestus* are all *sensu stricto*. A typical *An. funestus* larval habitat is a large, permanent or semi-permanent body of fresh water with emergent vegetation, such as a swamp, a large pond and or lake edges. *An. funestus* is a highly adaptable species, allowing it to occupy and maintain its wide distribution and utilise and conform to the many habitats and climatic conditions. *An. funestus* is considered to be highly anthropophilic with a late-night biting pattern (after 22.00). Endophilic resting and endophagic feeding behaviours are also commonly reported and these characteristics are responsible for rapid disappearance of this vector following expanded IRS and ITN use. Compared to other dominant vector species in Africa, *An. funestus* shows fairly consistent behaviour (generally anthropophilic, endophagic and endophilic) throughout its range. In the absence of insecticide use, the endophilic resting behaviour of *An. funestus* combined with a relatively high longevity, makes it as good a vector, or better in some areas, as *An. gambiae s.s.*

Anopheles nili: The *An. nili* complex includes *An. carnevalei*, *An. nili s.s.*, *An. ovengensis* and *An. somalicus*. *An. nili s.s.* is among the most important malaria vectors in sub-Saharan Africa. It has a wide geographic distribution range spreading across most of West, Central and East Africa mainly populating humid savannahs and degraded rainforest areas. In Mali, the complex appears to have a distinctive genetic structure.[133] It is considered to be strongly anthropophilic, and will readily feed both indoors and outdoors.[134–143] It is sometimes found biting outdoors in the early evening when people are socialising and then continues to bite indoors once people move inside, with peak feeding occurring before midnight. Despite feeding preferentially on humans, this mosquito can be highly zoophilic.[140,141] *An. nili* is usually responsible for transmission in villages close to rivers, but its abundance rapidly decreases within a few kilometres of the breeding sites.[143] It is also present at the periphery of urban areas. Larvae thrive at the sunny edge of fast running streams and rivers, where floating vegetation and debris provide suitable shelters. The prevalence of *Plasmodium* infections in wild females typically ranges between 1% and 3% and transmission rate reaching 200 infective bites/human/year have been reported in the literature for *An. nili.*[139,140,144]

Anopheles coustani: *An. coustani* is widespread across much of Africa although not described in Mauritania or Niger. In West and Central Africa, the *ziemanni* form is exclusively found along the coast and coexists with the *typicus* form [Hamon, 1951]. Larvae are found in extremely varied locations: swamps, ponds, edges of lakes and rivers, rice fields, temporary grassy pools and hollow rocks, and can also proliferate in manmade habitats. They can tolerate a slight salinity (*An. coustani ziemanni*) and develop in those habitats where the water temperature drops to 4°C overnight (*An. coustani typicus*).[134] Adults are exophilic over most of their range and it is known to enter lighted tents probably for the purpose of resting.[123] *An. coustani ziemanni* is thought to be an aggressive outdoor biting vector, especially during the early hours of the evening at the edges of rivers.[145] *An. coustani s.l.* has been shown to display both exophagic tendencies, along with early evening foraging behaviour in Zambia, Nigeria, Mozambique and Ethiopia.[145–148] *An. coustani* displays peak biting outdoors before 21:00, being most active from 20:00 to 21:00 with biting activity steadily declining throughout the night. The combination of outdoor and early evening foraging behaviour for this species could increase its potential as a secondary vector in areas where indoor control measures such as IRS or ITNs are employed. The *An. coustani* complex in Macha, Southern Zambia, has demonstrated unexpectedly high anthropophily.

Anopheles pharoensis: *An. pharoensis* is primarily a species of large vegetated swamps. It is also found along lakeshores and among floating plants, reservoirs, rice fields, streams, ditches and overgrown wells. *An. pharoensis* is largely a swamp breeder throughout its range, found in very large numbers associated with the aquatic weed *Ceratophyllum demersumIt*.[149] It is a variable species both in morphology and bionomics, with adults have varying behaviours dependent upon the region in which they are found; sometimes anthropophilic, sometimes zoophilic, sometimes endophilic or exophilic.[150–152] *An. pharoensis* bites humans and animals indoors or outdoors and rests outdoors after feeding.[152] It feeds from dusk to dawn with a peak at about 01:00. *An. pharoensis* is peculiar in that it may occur in very large numbers for several nights and then disappear for long periods from a particular area. It is the major vector of malaria in Egypt, but its role as a malaria vector is minor elsewhere. Studies on *Plasmodium falciparum* infection rates in *An. pharoensis* range from 0.5% in Senegal to 1.3% in Kenya.[153,154]

Anopheles rufipes: *An. rufipes* is a predominantly savannah mosquito and breeding sires are varied, usually sunny or in light shade.[95,155–157] It is of three forms, including *ingrami*, *seneveti* and *brucechwatti.*[158] [Edward 1929; Hamon et al 1961b]. *An. rufipes* is exophagic and partially endophilic and has also been reported in small bodies of water such as puddles located in riverbeds and even hoof prints of animals.[95] [Holstein et al 1961]. This vector was observed in several areas in Mali (including Bamako) and present in large numbers in homes, rivers, ponds, rice paddies, swamps, irrigated crops, ponds, hollow rocks and residual stream [Holstein et al 1961]. In a study in neighbouring Burkina Faso, almost 12% of mosquitoes captured in a savannah village were *An. rufipes* with an estimated infectivity rate of 1.2%.[159] While the extent of its contribution to malaria transmission is unclear, *An. rufipes* is likely to an important malaria vector in the Sahelian region given its frequency, especially during the dry season.

Figure 40 depicts the distribution of recorded species across all surveys by region.

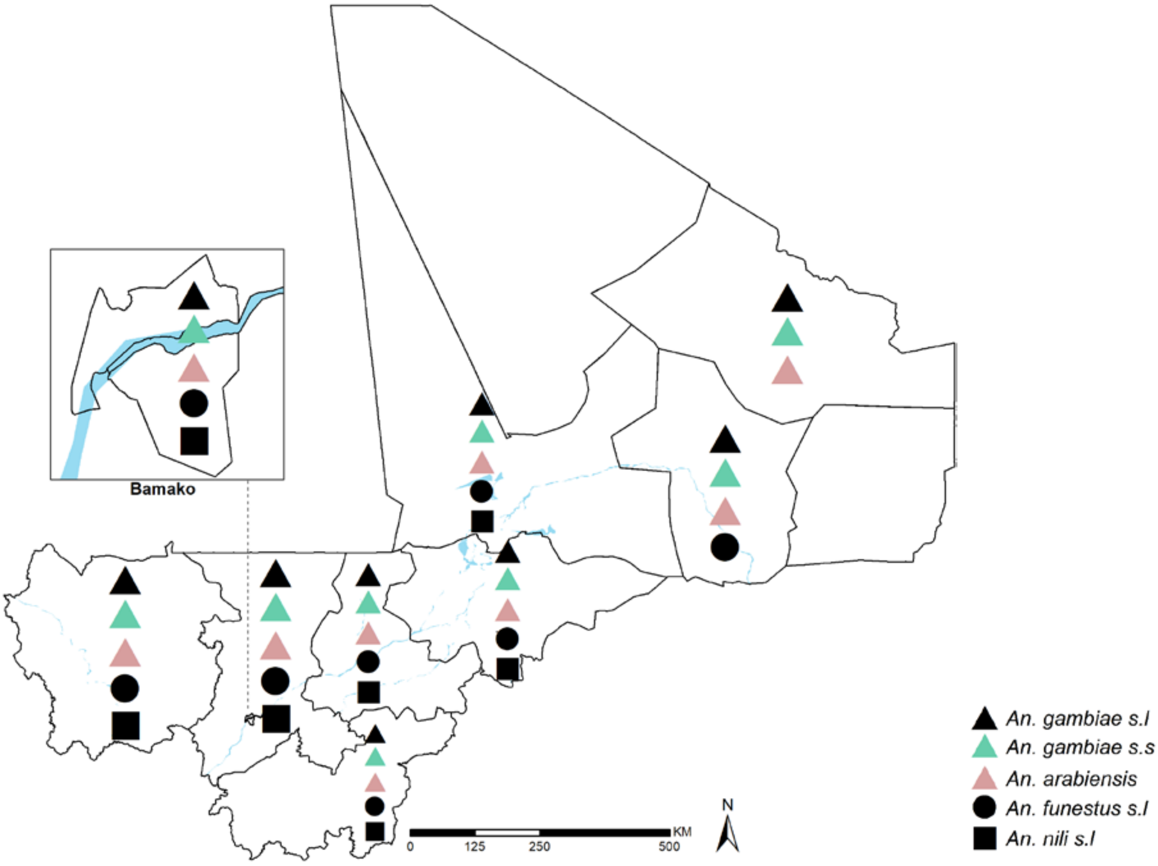


Figure 39 Recorded species identification across all surveys by region

Malaria vector control

1.17 Indoor Residual Spraying

Spraying with insecticides has a long history in Mali although the intervention was never implemented at large-scale at national level. As early as 1904, environmental interventions through the 'hygiène prophylactique' began to decrease mosquito populations in European and African settlements.[160] These were primarily carried out in urban areas such as Bamako and Kayes.[160,161] These efforts were built upon when the Office du Niger was initiated by the French to construct dams and canals to irrigate land north of the Niger River for cotton and rice cultivation.[160,162] In addition to chemoprophylaxis, spraying of breeding sites during household visits was the main intervention in Mali in the 1940s.[77,164] Household spraying with DDT began in 1950 and continued for seven years.[160,164,165] However, by 1978, vertical programmes were phased out and malaria became embedded in the primary healthcare system. Presumptive treatment of patients became the primary approach to controlling malaria throughout the country.[104]

By the time the PNLP was established in Mali, there were no operational programmes for IRS in Mali despite it being recommended in epidemic-prone areas by the national malaria strategy. In 2008, PMI began to support IRS scale-up in Bla and Koulikoro districts in conjunction with PNLP larvicide efforts. These two districts had an estimated population of 405,936 people in 87,198 households.[166] The pyrethroid lambda-cyhalothrin (ICON-CS©) was selected as the primary insecticide for IRS.[166]

Operational research in 2010 concerning larviciding in combination with IRS identified differences in resting densities, biting rates, EIR and sporozoite rates.[3] In 2011, Baraouelli became the third district supported for IRS by PMI, yielding an intervention coverage of 836,568 persons in the three districts by 2014.[167]

Due to the associated costs with transitioning to organophosphate insecticides, the number of districts covered was reduced to two in 2015. However, with the added assistance of the UNITAID Next Generation Indoor Residual Spraying (NGenIRS) project in 2016, the project campaign was expanded to include the 2015 targets of Baraoueli, Fana and Koulikoro.[3] Coverage was most recently shifted to four districts in Mopti Region in 2017, with additional support allowing for improved trainings, commodity and personal protective equipment purchasing, M&E and supervision. This change was based on 2015 MIS findings of high prevalence in Mopti Region, and the completion of IRS in Baraoueli, Fana and Koulikoro. This is anticipated to achieve a coverage of approximately 150,000 structures for the protection of 650,000 people.[3] All eligible structures in Badiagara, Bankass, Djenne and Mopti districts will be covered under this approach, with post-IRS resurgences monitored by PMI and the PNLP. Due to the degree of surveillance being carried out in the region, it is aimed to target IRS as low as the health area rather than the district level in the medium-to-long term.[3]

IRS is often used in the private sector as well, with at least five mining companies in Mali providing such a service in residence sites and neighbouring villages.[3]

According to the Plan Strategique de Lutte contre le Paludisme 2018–2022, 91% of the population at risk in targeted areas were protected by IRS in 2017. This exceeds the goal of the 2013–2017 strategy to provide 80% protection in targeted zones. IRS is now carried out in Mali following community campaigns involving radio broadcasts, household visits and distributions of printed materials.[3] Monitoring is carried out in the IRS sites of Mopti, as well as in three of the former IRS sites to monitor withdrawal effects.[3]

1.18 Distribution of ITNs and LLINs

ITN distribution 2000 – 2014

By 2002, the use of ITNs was seen as a key preventative tool for malaria control in Mali. In the 1990s, the NetMark project was established with funding from USAID and other partners to support the availability of ITNs through social marketing and Mali was selected as one of the first countries in Africa to be supported. Between 2003 and 2006, substantial reductions in unit cost of ITNs were made evident in the commercial retail sector through the NetMark project, which in turn increased the availability of nets in the private sector by working with large net manufacturers and a voucher scheme in one district. In addition, the Malian government accepted the removal of taxes on ITNs. Over 300,000 ITNs had been distributed in Mali when the project closed in December 2006.[168]

ITN distribution 2014 to present

ITNs are freely provided through mass household distributions or routinely through ANC and EPI clinics, with the first free distribution taking place in 2007.[3] The Plan Strategique de Lutte contre le Paludisme 2018–2022 stipulates that all pregnant women must receive a free LLIN at their first ANC visit, with a goal to ensure that 80% of pregnant women are using an LLIN by 2022. Net use by pregnant women is to be encouraged through sensitisation campaigns conducted both in person and over the radio.

The PNLP has reported the distribution of 12,226,202 LLINs as of 2018 through nine mass distribution campaigns.[1] Reported routine distributions to pregnant women and newborns have varied, with 1,436,163 in 2013; 1,466,265 in 2013; 1,997,451 in 2015; 1,400,000 in 2016; and 1,249,950 in 2017. In 2013, the PNLP was disrupted regarding LLIN distribution due to the socio-political crisis which in turn resulted in the suspension of the Global Fund grant and partner activity.[1]

In 2015, 39% of households had at least one LLIN for every two persons in 2015 and that 68% of all persons at risk slept under an LLIN the night before the same survey.[169] During the same period, 71% of under 5s were reported to have slept under an LLIN the night before being surveyed, as did 78% of pregnant women. This is fairly close to the 2013–2017 strategy goal of 80% of the population at risk of malaria using ITNs.

Pregnant women and LLIN use differed slightly according to location, with 77.4% of pregnant women in urban areas using a net as opposed to 80.6% in rural. Ninety-five percent of households owned a net regardless of its treatment status or urban/rural status.[1]

ITN mapping

Typically, national household surveys are designed to be precise at national and regional levels and rarely at lower levels such as districts. Therefore, simply aggregating survey data to provide district level estimates of an outcome of interest will lead to values of low precision. SAE methods handle the problem of making reliable estimates of a variable at these areal units under conditions where the information available for the variable, on its own, is not sufficient to make valid estimates.[170] The geo-coded household data from the 2010, 2012/2013 and 2015 national sample surveys has been used to provide information on coverage and reported LLIN use for 63 districts using Small Area Estimation (SAE) methods. Hierarchical Bayesian spatial and temporal SAE techniques have been used below using a geo-additive regression approach.[171,172] This method uses survey data from a health district and neighbourhood information from adjacent districts to smooth values at the health district. Importantly, quantities were predicted among all age groups, as this now represents the important indicator for universal coverage and necessary when computing likely impacts on malaria transmission.[173,174] In addition, WHO recommended targets for universal coverage have been defined as at least 2 people per LLIN per household and shown for each national survey year.

Using these methods, Figure 40 presents the percent of households with universal coverage of ITNs, defined here as at least one ITN for every two people. By 2015, 13 of the districts had achieved more than 20% of coverage, compared to three in 2010 and 15 in 2012/2013.

Additionally, maps of net utilisation through the proportion of the population sleeping under an ITN have been provided. Again, the maps produced through the modelling exercise of household data (Figure 41) indicate that there were country-wide improvements in net use by district. In 2010, 20 districts reported more than 60% of the population were sleeping under an ITN. By 2015, three had achieved 80% or greater coverage.

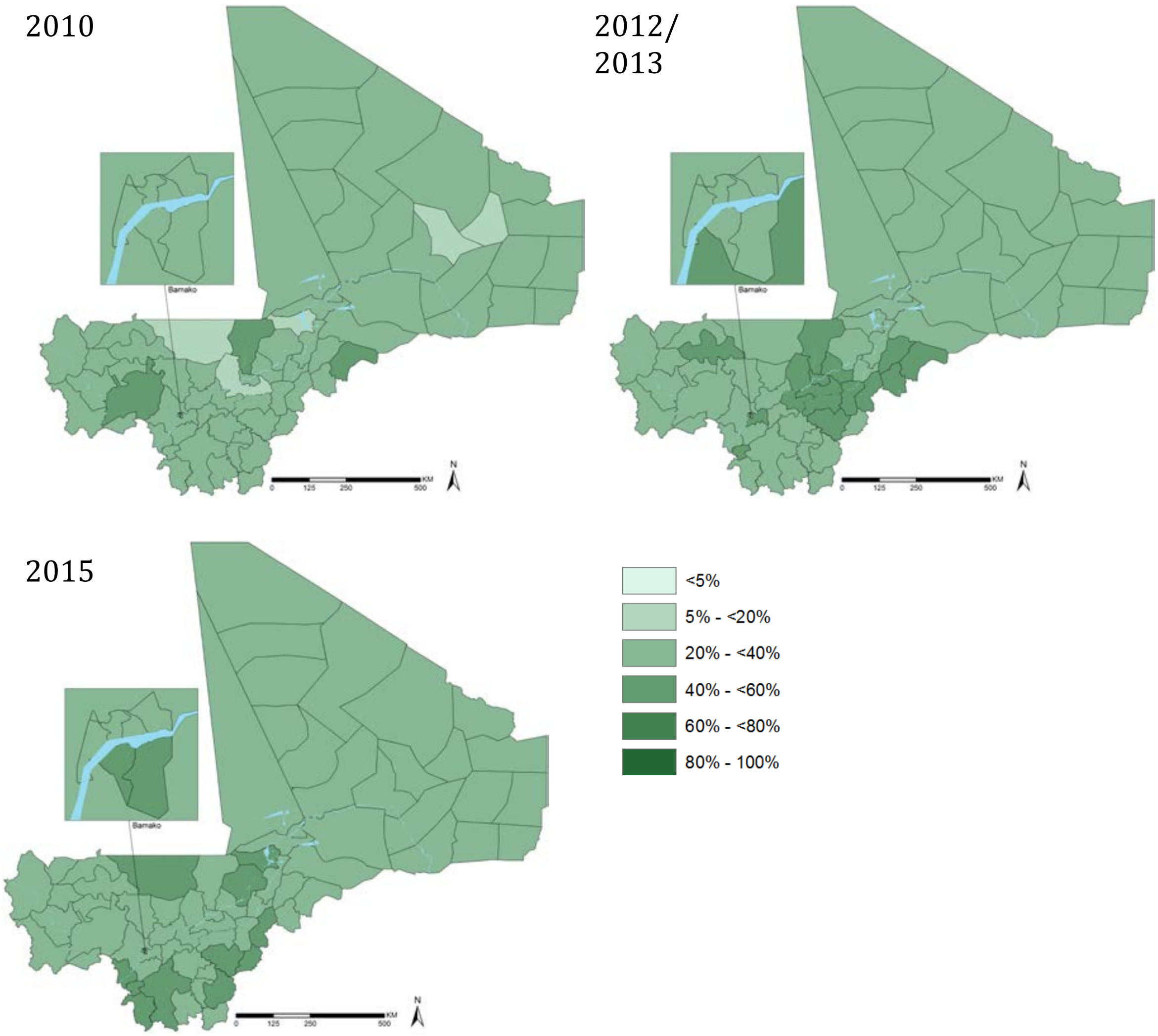


Figure 40 Percentage of households with at least one ITN for every two persons in 2010, 2012/2013 and 2015

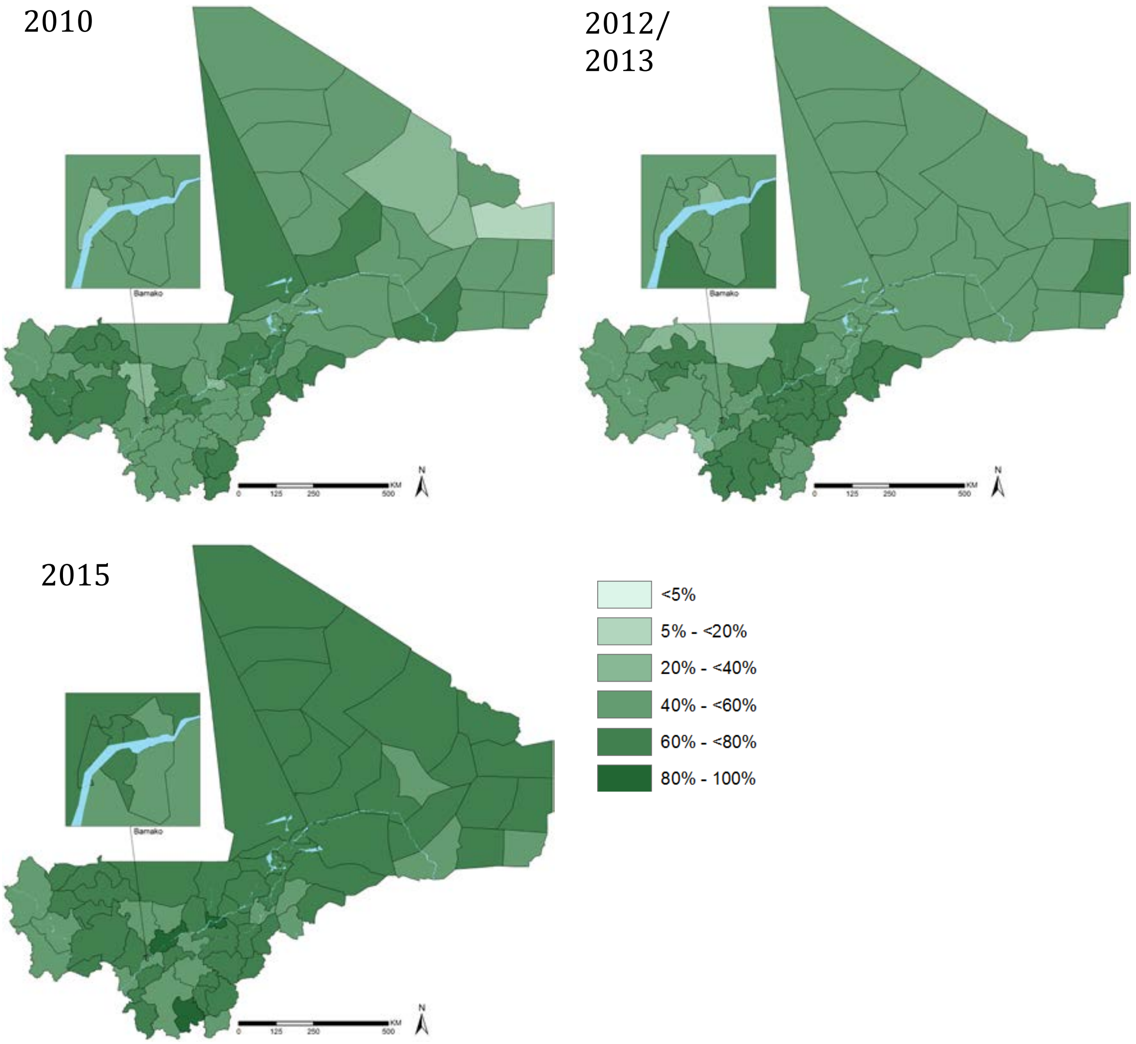


Figure 41 Percentage of households sleeping under an ITN in 2010, 2012/2013 and 2015

Interrogation of results

The findings above are to be reviewed and interrogated by the PNLP and partner organisations once the results are disseminated in September 2018.

1.19 Knowledge and research gaps

As identified through the Plan Strategique de Lutte contre le Paludisme 2018–2022, the first LINK profile, and through the challenges encountered while collecting data for the revised profile, several gaps exist in Mali regarding malaria knowledge and research. Mali inherently and most notably struggles with research gaps due to the ongoing conflict in the northern regions of the country. Programme disruptions have implicated health priorities, such as immunisation schedules, HIV/AIDS management, and Guinea worm, tuberculosis and malaria diagnostics and treatment. Similarly, epidemiological data relevant to malaria control has suffered in transmission to the central level, either due to lacking infrastructure to do so or insufficient health facility numbers.

The mobile population within Mali requires additional attention regarding malariometric data, as populations from the north are particularly at risk for severe malaria and likely to be or have been displaced due to ongoing conflict. The capture of relevant data may serve to improve disease control planning and liaisons between the different sectors of health and agriculture, as they are populations that are particularly vulnerable to droughts, malnutrition and violence. Further study of urban areas of Mali may also prove enlightening as the urban population is rapidly increasing and opportunities for control may be identified.

The northern regions of Mali are often not captured by large surveys and require a reliance upon the strength of data from other regions or past surveys and diminish the overall precision of predictions. However, these regions have large areas of aridity or semi-aridity which are sparsely populated and are of generally low malaria transmission.

As outlined by the PNLP in the Plan Strategique de Lutte contre le Paludisme 2018–2022, continued monitoring of the indicators in the associated M&E plan will be essential to ensure that progress is made through intervention delivery. These will ideally be facilitated by engagement with the private sector and advocacy among target populations.

Annex A: Health administrative unit mapping

The health administrative units shapefile used for mapping (75 districts) was provided by Ousmane Toure (obtoure@gmail.com) of the IMO Cluster Santé to Nicholas Dellasanta of the LINK programme (nicholas.dellasanta1@lshtm.ac.uk). The units used had not yet been validated by the Geographical Institute of Mali when provided, as they included the two new regions of Taoudenit (formerly in Tombouctou region) including six districts and Menaka region (formerly in Gao region) including four districts. However, the Ministère de la Santé et de l'Hygiène Publique utilised the 75 districts in the 29 April 2018 *Bulletin Epidemiologique Hebdomadaire*, which justified their use as future planning boundaries. These were confirmed again during a midterm meeting with the PNLP and partners in July 2018.

The shapefile provided contained 80 districts, however, five sliver polygons were identified after careful cleaning and comparisons to other shapefiles. The sliver polygons duplicated the names of five districts.

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