An Epidemiological Profile of Malaria in Mali

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Contents

1. Introduction

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 from the mid-1950s. Data included epidemiological descriptions of transmission, vectors, topography and climate. There was a recognition over 50 years ago that one important source of planning data was infection prevalence among children aged 2-10 years (*Pf*PR_{2-10}), used to define categories of endemic risk designed to guide and monitor progress toward malaria elimination targets [Metselaar and van Thiel, 1959; Macdonald and Göeckel, 1964; Lysenko and Semashko, 1968].

The skills necessary to design malaria control based on an understanding of the spatial epidemiology diminished during the 1970s when the agenda for malaria control fell under a less specialized, integrated primary care mandate focused on managing fevers. In 1996, there was a renewed plea for better malaria cartography to guide malaria control in Africa [Snow et al., 1996] and over the last decade there has been a growth in spatial data on malaria and populations not available to malariologists or programme control managers 60 years ago. The growth in data has been accompanied by the development of statistical approaches to model and map risk and intervention access in space and in time using Model Based Geo-Statistics (MBG) [Diggle and Ribeiro, 2007].

At the launch of the Roll Back Malaria (RBM) initiative, calls for universal coverage of all available interventions was probably an appropriate response to the epidemic that affected most of sub-Saharan Africa during the mid-late 1990s [WHO, 2000; Snow et al., 2012]. At a time when 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 will require 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 intervention, assess the impact of current investment and, equally important, demonstrate what might happen should funding and intervention coverage decline.

In 2011, the WHO Office for the Africa Region (AFRO) developed a manual to assist countries in developing their National Malaria Strategic (NMS) plans including, as a prelude, the undertaking of a National Malaria Programme Performance Review (MPR) [WHO-AFRO, 2012]. 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 the Mali in 2011, states the need to ensure 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)*" [PNLP, 2012].

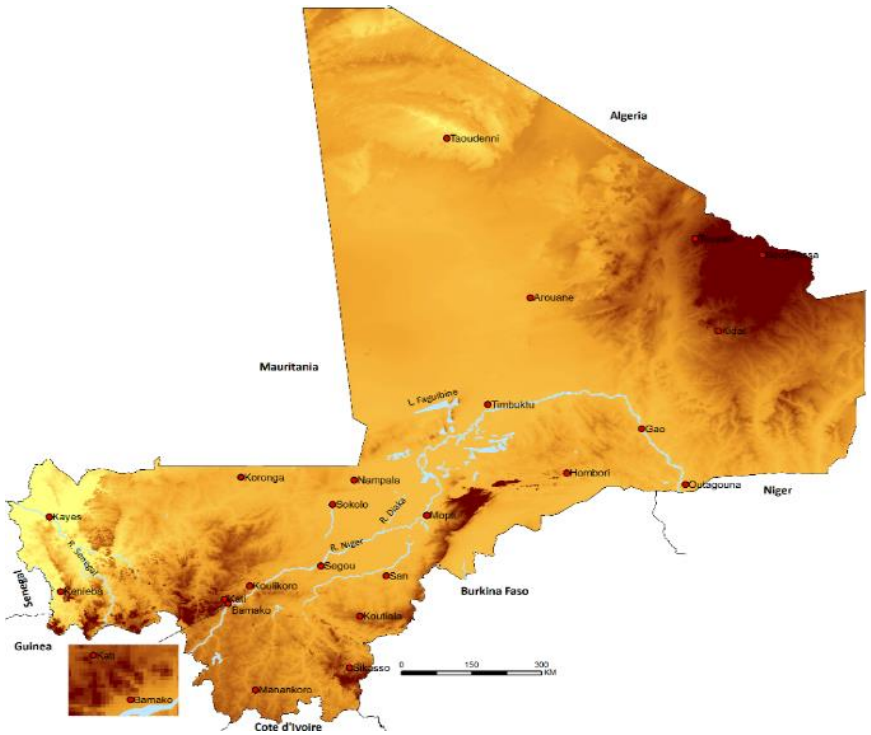
This epidemiological profile attempts to assemble the epidemiological evidence base for tracking progress and for a more targeted approach to malaria control in the Mali. It draws together historical and current evidence of parasite transmission risk, data on the distribution of dominant vector species and available data on insecticide resistance and distribution of health facilities.

2. Country context

2.1. Location and geographical features

The Republic of Mali, originally part the Empire of Mali (1312-1337), French Soudan (1892-1959), Mali Federation with Senegal (1959) and Mali after the dissolution of the Federation (1960 onwards) is Africa's eighth largest country covering an area of approximately 1.24 million km^2 [http://en.wikipedia.org/wiki/History_of_Mali; http://lcweb2.loc.gov/frd/cs/profiles/Mali.pdf]. It is located in the northern hemisphere in West Africa and neighbours Mauritania to the east, Senegal and Guinea to the south-west, Cote d'Ivoire to the south, Niger and Burkina Faso to the south-east and Algeria to the north (Figure 2.1). Mali is a landlocked country with Bamako City as its capital.

Figure 2.1 Map of major relief features showing elevation[1], rivers and lakes,[2] and major cities.



Mali's terrain is mostly flat and comprises the northern sandy plains, the southern savanna and the rugged hills in northeast (Figure 2.1). The lowest point in the country is the Senegal River which is 23 m above mean sea level (amsl) and the highest is the Hombori Tondo (1155 amsl). The two main geological regions of the country are the Keniéba and Bougounu regional geologies

[1] The Digital Elevation Models (DEM) with a resolution of 90m at the equator was developed form Shuttle Radar Topography Mission (SRTM) and is available at [http://www.diva-gis.org/gdata].

[2] Data for Mali's water body was downloaded in shapefile format from the digital chart of the world (DCW) which is hosted at [http://www.diva-gis.com]. The shapefile contained a total of 1878 perennial and non-perennial water features categorized as lakes, rivers and swamps or land subject to inundation. We eliminated all the non-perennial and swampy features (n=1401) from the shapefile. Majority of the remaining water features did not have names (n=392), these were mainly tributaries and ponds and thus were eliminated. We then removed duplicates by using the dissolve tool in ArcGIS so that our final shapefile contained 85 named permanent inland water features, these we considered to represent major inland waters in Mali.

[Chirico et al., 2010]. The Keneiba regional geology covers most of southern parts of the country and includes the Tamaoura escarpment that rises to up to 500 m above mean sea level. The Bougounu regional geology covers the Bougouni, Koulikoro, Yanfoliba and Kangaba areas in the south west and extends to Guinea.

The most prominent drainage features are the Niger River, the third longest in Africa, which originates from Guinea and forms a fertile inland delta in Mali before emptying into the Gulf of Guinea. Of the 4180 km of the Niger River, 1693 km(40.5%) are in Mali. Described as the country's lifeblood, the Niger River is the main source of water for domestic consumption, farming and irrigation and transportation for riverine population [http://en.wikipedia.org/wiki/List_of_rivers_of_Mali]. Other important rivers in Mali include the Senegal River (1790 km) which flows from the Atlantic Ocean and passes through Senegal, Mauritania and Mali, the Bani River (1100 km) which forms a drainage basin in the regions of Sikasso and Mopti, the Bafing River (1006 km) which passes through the Koulikoro region in Mali into Guinea and the Faleme River (650 km) which also flows from the Atlantic Ocean (Figure 2.1) [http://en.wikipedia.org/wiki/List_of_rivers_of_Mali].

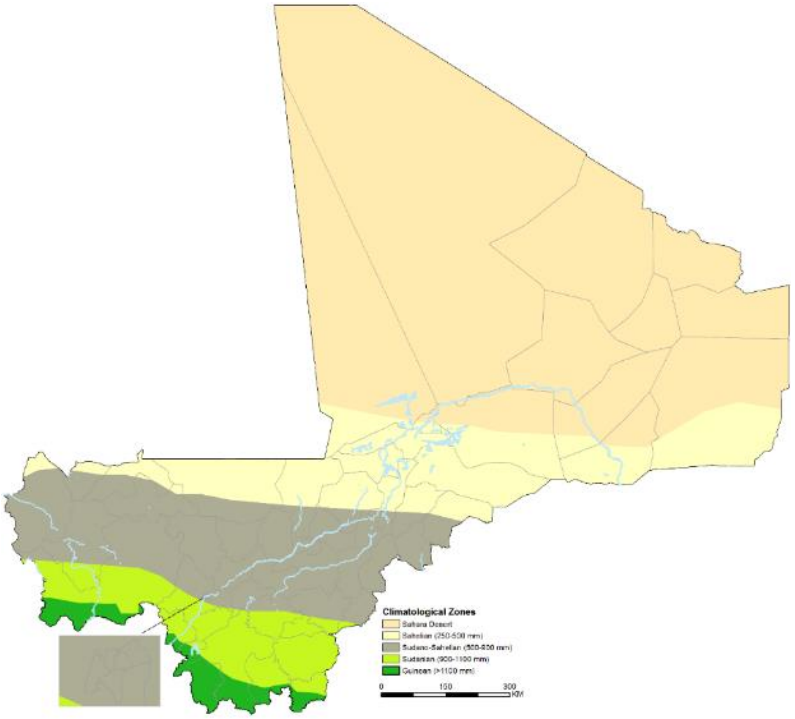
2.2. Climate

The country has four climatic zones with most of the south covered by the Sudanese and Guinean zones which are the main agricultural areas. To the north are the central semi-arid Sahelian and northern arid Saharan zone (Figure 2.2 and 2.3). Approximately 65% of the country is covered by semi-desert and desert areas. The rainy seasons in Mali are modulated by the movement of the Inter-Tropical Conversion Zone (ITCZ) which oscillates from north to south tropics over the course of the year. When in the northern part of the tropics, the ITCZ brings rain to Mali between June-October with a peak in August. The average monthly rainfall in the south reach about 300mm (Figure 2.3a). The hot and dry season is from February to June and the December to February the weather is cool and dry [Sweeney et al., 2010; http://country-profiles.geog.ox.ac.uk].

Variations in latitudinal oscillations in the ITCZ result in large inter-annual variations in rainfall. Consequently, Mali is prone to frequent droughts which have led to high levels of malnutrition and socio-economic disruptions [http://country-profiles.geog.ox.ac.uk; Sweeney et al., 2010]. The country is also hot with mean temperatures of 27-30 ^{o}C but vary in the mountainous ranges at 25-27 ^{o}C and in the northern areas at 27-35 ^{o}C. Winter day temperatures get as low as 15 ^{o}C. During the dry month of February the harmattan wind blows in a northeasterly direction [http://www.atlapedia.com/online/countries/mali.htm].

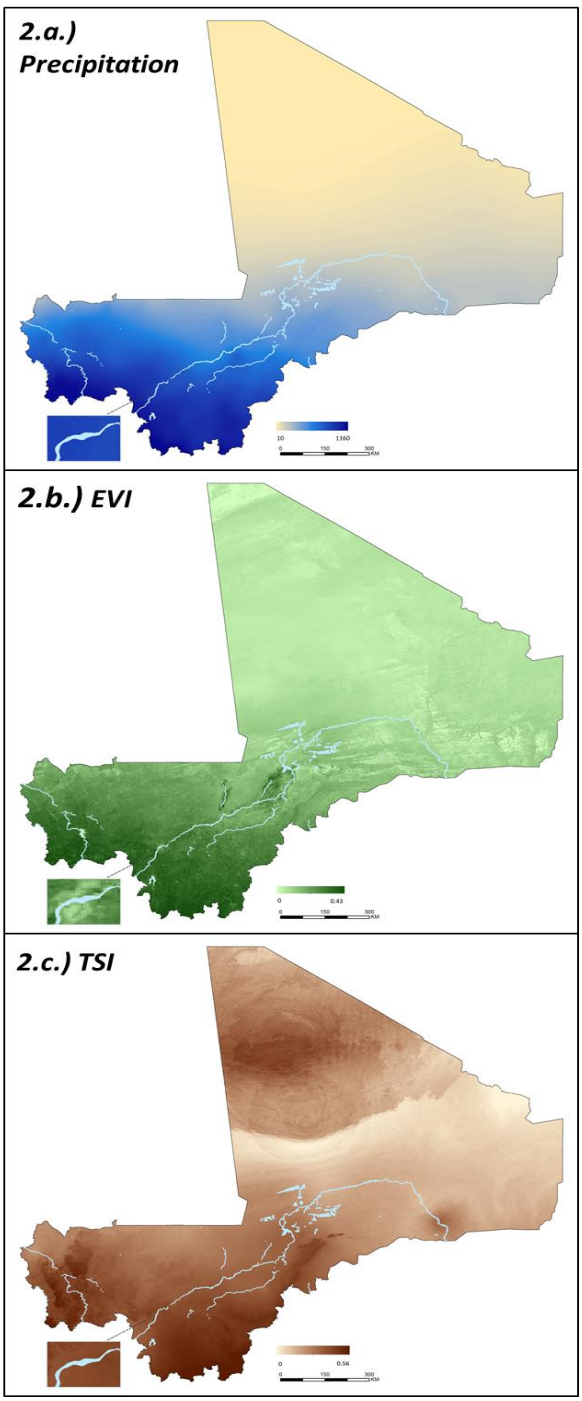
Countries in the Sahelian region, including Mali, face environmental challenges such as droughts, desertification, soil erosion and reducing water supplies [Shanahan et al., 2009]. Drought in the Sahel have been reported as early as the 17th Century and in most decades since 1900 [Batterbury 2001; African Environmental Outlook 2014].

Figure 2.2 Map of eco-climatic zone in Mali [Source: http://www.fao.org/docrep/006/J2517e/J2517e00.htm]



One of the worst droughts in recorded history in the Sahel occurred from 1972–84 in which an estimated 100 000 people died, and by 1974 more than 750 000 people in Mali, Niger and Mauritania were wholly dependent on food aid [Wijkman and Timberlake 1984]. Power shortages also occurred Benin, Chad, Mali, and Nigeria because of water shortages in hydroelectric dams [African Environmental Outlook 2014]. In August 2010, a famine struck the Sahel resulting in crop failure in several countries amid record temperatures and almost complete failure of the rains. This led not only to widespread food shortage and starvation but also reports of rise disease related to poor nutrition, sanitation and pollution.

Figure 2.3 Climate features of Mali a) Long-term annual precipitation; b) Enhanced Vegetation Index (EVI); and c) Temperature Suitability Index (TSI) for sporogony in dominant vectors



Rainfall is a major determinant of vector abundance. Monthly rainfall surfaces are produced from global weather station records gathered from a variety of sources for the period 1950-2000 and interpolated using a thin-plate smoothing spline algorithm to produce a continuous global surface [Hijmans et al., 2005] and monthly average rainfall raster surfaces at 1×1 km resolution available from the WorldClim website (http://www.worldclim.org/download.html). Data shown here are mean annual rainfall in mm

For vegetation, Fourier–processed EVI, derived from the MODerate-resolution Imaging Spectroradiometer (MODIS) sensor imagery and available at approx. 1×1 km spatial resolution [Scharlemann et al., 2008] was used to develop an annual mean EVI surface. EVI is an index of intensity of photosynthetic activity and ranges from 0 (no vegetation) to 1 (complete vegetation)

Temperature suitability index (TSI) has been developed at a spatial resolution of 1×1 km [Gething et al., 2011a]. The TSI model uses a biological framework based on survival of vectors and the fluctuating monthly ambient temperature effects on the duration of sporogony that must be completed within the lifetime of a single generation of Anophelines and constructed using monthly temperature time series [Hijmans et al., 2005]. On a scale of increasing transmission suitability, TSI ranges from 0 (unsuitable) to 1 (most suitable). Unsuitable areas represented by a TSI value of 0 are classified as

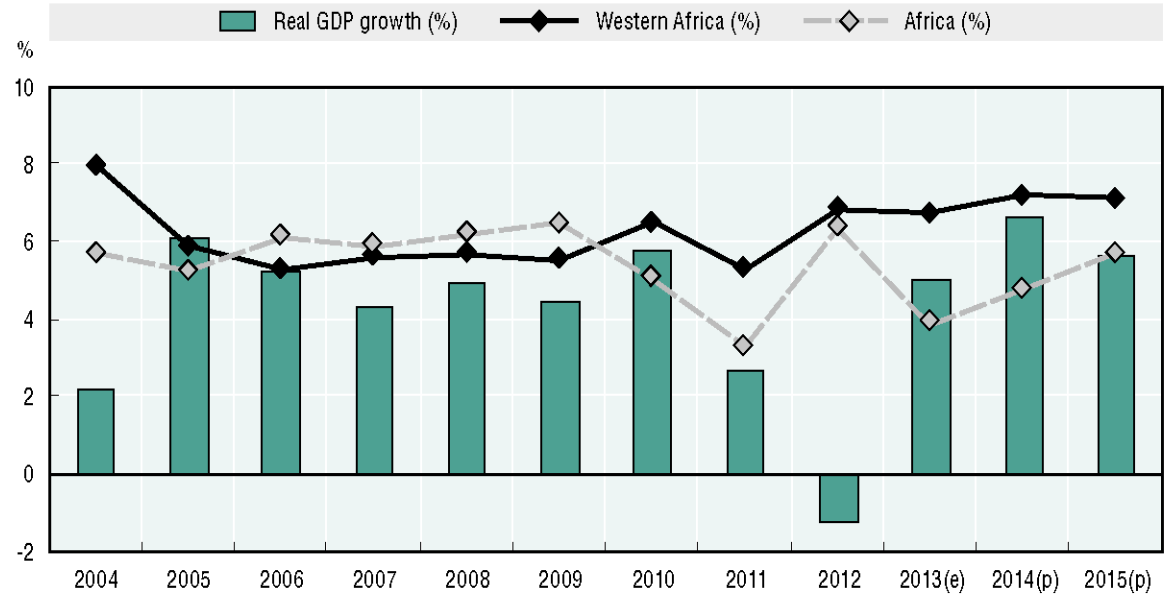
2.3. Economy, natural resources and poverty

Agriculture is the main economic activity in the country making up almost 40% of the GDP and employing approximately 70% of the labour force [African Economic Outlook, 2014; CIA World Fact Book]. The main agricultural activities are the production of rice, sorghum and livestock. Fishing, particularly along the Niger River is an important source of nutrition and revenue for the riverine communities although production has been declining in the past few decades. The most important non-agricultural foreign exchange earner in the country is mining with gold accounting for most of the mineral exports and 75% of the country exports. Due to the large dependence on

the primary sector such as agriculture which is mainly rain-fed, the country's economy is vulnerable to weather patterns such as droughts and floods.

Economic reform in Mali has gone through several phases beginning with the influence of socialist approaches in the early years after independence with Russian and later Chinese influences [http://africanhistory.about.com/od/mali/p/MaliHist1.htm; African Economic Outlook, 2014]. In the period 1992 to 1995 the country implemented tough IMF supported structural adjustments programmes which eventually improved economic growth and reduced imbalances. Despite these improvements, Mali remains one of the top ten poorest countries in the world with poverty incidence of 42% and is among the most highly indebted [African Economic Outlook, 2014]. In 2012, the country registered a negative GDP growth of -1.2 coinciding with a period of conflict although this rebounded to 5% in 2013 and is expected to rise to 6.7% in 2014 [African Economic Outlook, 2014].

Figure 2.3 Real GDP growth and projections for the period 2004-2015 in Mali. GDP growth is compared to patterns in Western Africa (solid black line) and the all of Africa (dashed grey line). [Source: Africa Economic Outlook 2014].

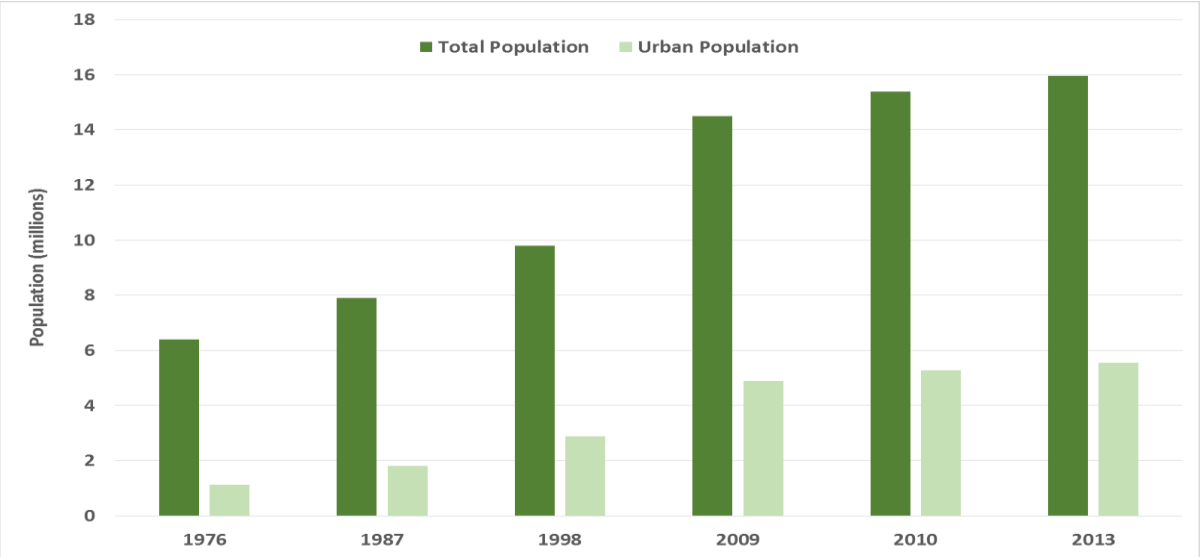


2.4. Population distribution

Since independence there have been four national population censuses undertaken in Mali in 1976, 1987, 1998 and 2009 [http://www.geohive.com/cntry/mali.aspx; INS 2010]. Figure 2.4 shows the population numbers at each census rising from approximately 6.4 million in 1976 to 14.5 million in 2009. It is projected that by 2013 population would have risen to almost 16 million [http://www.indexmundi.com/mali/demographics_profile.html].

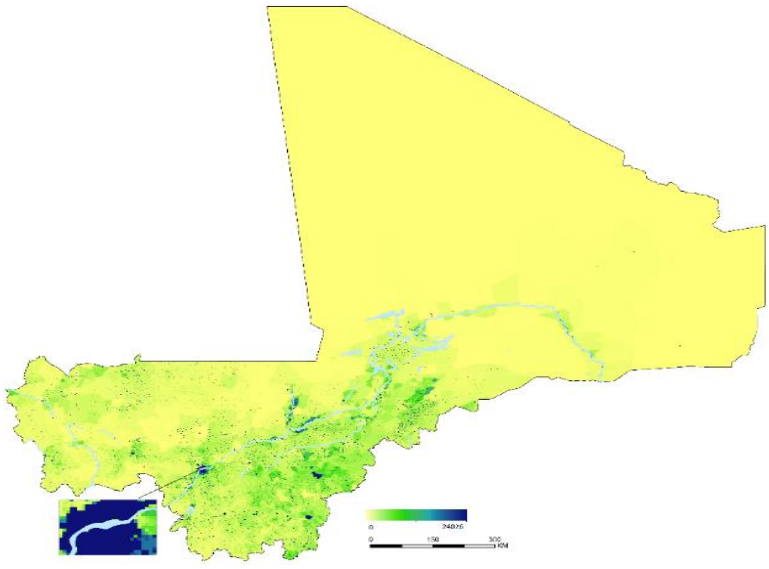
In 1976, urban population in Mali was 17.5% (1.1 million) living mainly in Bamako City and a few other main urban areas such as Ségou, Sikasso, Mopti, and Koutiala, Kayes, Timbuktu, Gao, and Kati. By 2009 these had risen to 33.6% (4.9 million) and 34.7% (5.5 million) in 2013 (Figure 2.4).

Figure 2.4 Total and urban population counts in Mali in the census years of 1976, 1987, 1998 and 2009 and projections to 2010 and 2013.



For disease mapping purposes, high spatial resolution population distribution maps are required. Recently, spatial modelling techniques for the reallocation of populations within census units have been developed in an attempt to overcome the difficulties caused by input census data of varying, and often low, spatial resolution [Linard et al., 2012]. The resulting population density map for Mali is shown in Figure 2.5 updated with the 2009 census data and projected to 2013.

Figure 2.5 Modelled population density projected to 2013[3] represented by increasing density as shown in legend ranging from zero to around 74,000 per km^2 in Bamako.



[3] A dasymetric modelling technique [Mennis, 2009] was used to redistribute population counts within 687 enumeration regions used during the 2009 census and adjusted for total populations presented across 8 census regions and the district of Bamako assisted by land cover data sets and satellite imagery. A different population weight was assigned to each land cover class in order to shift populations away from unlikely populated areas, such as protected areas, forest cover 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 the adjusted using rural and urban growth rates provided by the UN [UN, 2011].

2.5. Conflict and refugee populations

In January 2012, the National Movement for the Liberation of Azawad (MNLA) began an insurgency against government in the northern regions of Timbuktu, Gao and Kidal [http://www.unhcr.org/pages/49e484e66.html]. This conflict led to significant deterioration of security in these regions and displacements of large populations. The MNLA remained in control of these regions until April 2013 following the intervention of the French government army in January 2013 to help the Malian government forces to reclaim control of the north. In July 2013 the United Nations Multidimensional Integrated Stabilization Mission in Mali (MINUSMA) was deployed. Since then, the security situation has improved, although the region of Timbuktu and Gao are still considered of high risk with frequent skirmishes between the insurgents of government forces.

This conflict led to flight of the local population to neighbouring countries and to the southern areas in the country. Currently there are about 300,000 internally displaced populations (IDPs) in the country. In addition the country is grappling with the problem of refugees who had fled to neighbouring countries and are now returning after the stabilization [http://www.unhcr.org/pages/49e484e66.html]. Many of these IDPs are from the almost malaria free northern desert regions and therefore mostly non-immune have settlement in areas in the south, mainly in Bamako with the potential for malaria epidemics arising.

2.6. Health indicators

A summary of key health indicators for Mali are shown in Figure 2.5a, 2.5b and 2.6. Although Mali has achieved significant progress in health and large reduction in child and infant mortality rates, the country still has some of the poorest indicators globally. Infant and child remain high at 128 and 80 per 1000 live births respectively. Maternal mortality was estimated to be 460 per 100,000 births in 2012 [http://www.unicef.org/infobycountry/mali_statistics.html]. The 2012-2013 DHS estimated maternal mortality at 360 per 100,000 population [DHS 2013]. Mali also faces major nutritional challenges with low birth weight rates at 18% over the period 2008-2012, and proportion of children who were underweight or stunted were 19% and 28% respectively reaching the thresholds classified as severe by the WHO.

Figure 2.5 Basic health indicators in Mali: a) child and maternal mortality rate; b) malnutrition among children under the age of five years [http://www.unicef.org/infobycountry/mali_statistics.html]

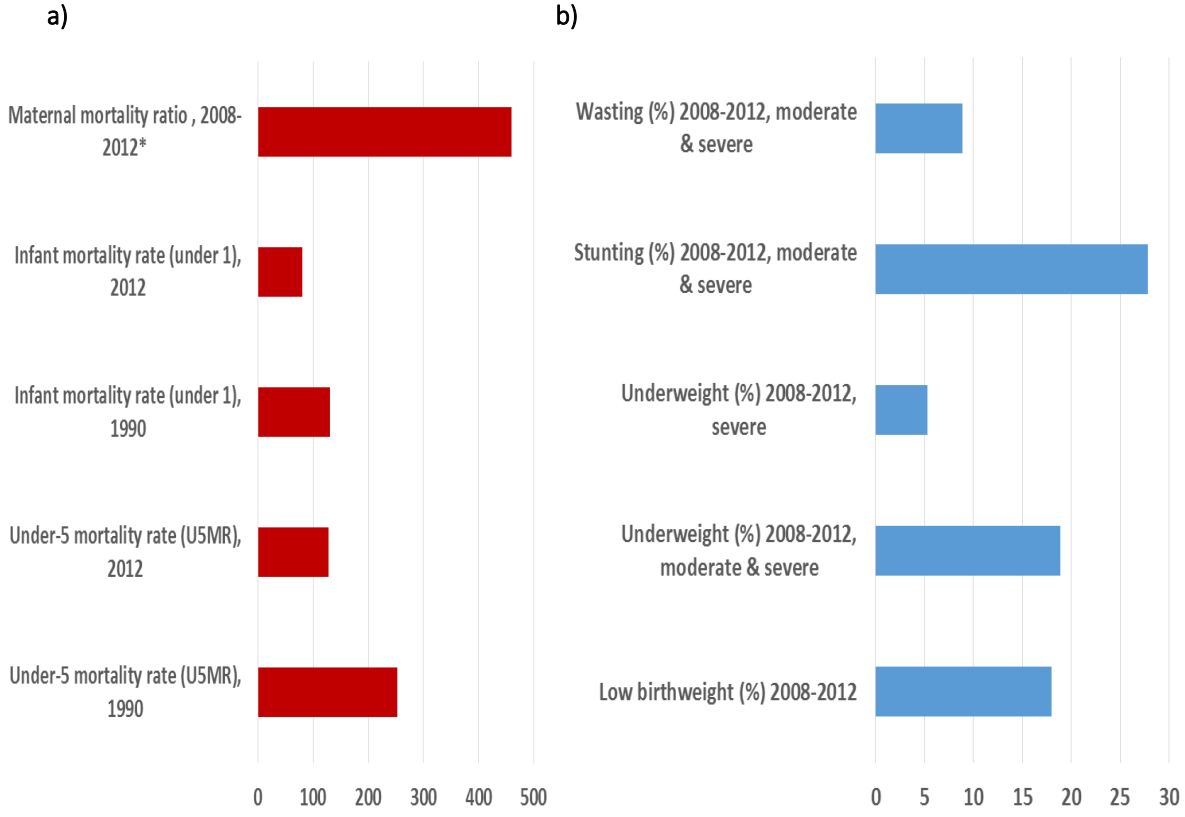
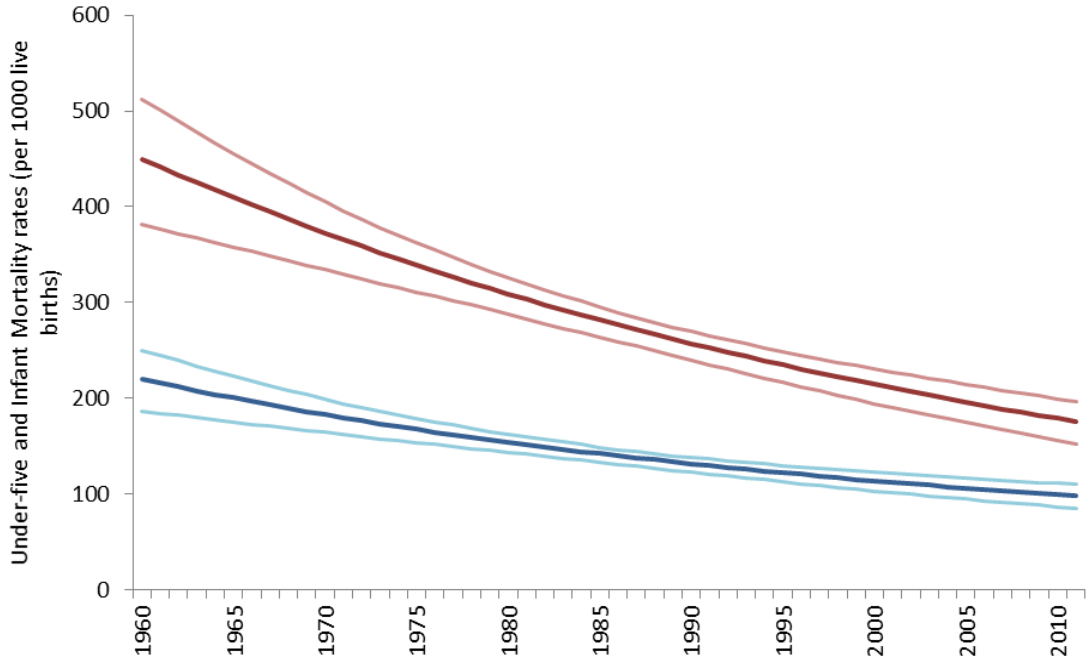


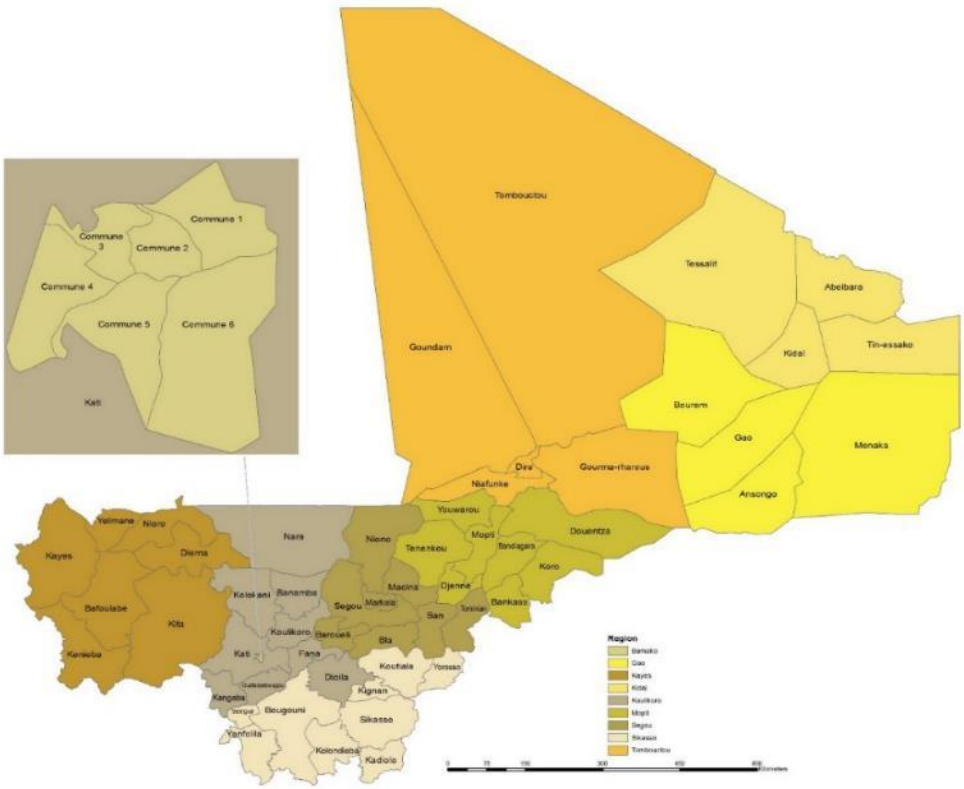
Figure 2.6 Under-five mortality rates (red) and Infant mortality rate (blue) per 1000 live births for Mali, 1959 to 2011. All rates are defined as per 1000 live births [UNICEF-IGME, 2011]. For IMR and U5MR, a country-specific local log-linear regression model is fitted to observations for one of the two indicators, within a model life table. Projections have been adjusted for projected mother-to-child HIV infection risks [You et al., 2009; Hill et al., 2012; UNICEF-IGME, 2011]. Observations are collected from censuses, DHS surveys, and Multiple Indicator Cluster Surveys and World Fertility surveys [Hill et al., 2012]. A loess line is produced with an uncertainty range (shown as boundaries to dark line in the graph).



2.7. Decentralized planning

Defining the exact boundaries of health administrative units used by a country is central to resolving health information for planning and disease burden estimation. Without congruence to accepted national health decision making units the value of the cartographic information of risk is diminished. Decentralization of government functions such as health as policy began as early as 1992 in Mali when it was enshrined in the constitution but only became a reality in 1999 with the formation of elected local governments [http://www.afro.who.int/fr/mali/profil-de-sante-du-pays.html; Diarra et al., 2004].

Figure 2.7 Nine administrative provinces and 60 districts used in the malaria risk mapping in Mali (Section 4.3; all codes are provided in accompanying Excel file)[4]



Administratively the country is divided into 8 regions and the Capital City of Bamako. Collectively these 9 regions have 60 districts (*cercles*) administered by commandants (*prefets*) (Figure 2.7) [Connel, 2008]. The districts are further sub-divided into communes which are made up of villages or quarters. Currently there are 703 communes in Mali [Lodenstein and Dao 2011]. Local government and commune leaders are elected through universal suffrage and are responsible for collecting local revenues. The central government provides a large proportion of budgetary support to local governments.

[4] Several sources were consulted to develop the current 60 health districts. First we scanned and digitized hardcopy map from the ministry, this contained 49 districts. We then compared the list of the districts to that contained in the health facility (HF) list provided by Dr. Massambou Sacko, Mali WHO Coordinateur du Cluster Santé, to Prof. Bob Snow via email. The deficit of 11 health districts (communes 1-6, Fana, Ouelessebougou, Markala, Kignan, and Selingue) were obtained by merging and or splitting, in ArcGIS, 3rd level communes and 2nd level admins from UNOCHA with the HF list of districts as our point of reference. The resultant shapefile containing 60 health districts was aligned to match the external boundaries of global administrative unit layer (GAUL) admin 0.

2.8. Health delivery structure and facility mapping

Healthcare in Mali is mainly provided by the public sector as private care providers were not allowed after independence in 1960 although they were permitted later in 1985 but restricted to urban areas [Balique 1998]. Traditional healers are registered under Federation of Malian Traditional Healers (FEMAT). FEMAT collaborates with the Traditional Medicine Department at the Ministry of Health to foster interaction between traditional and modern medicine [IIF 2004]. Other healthcare providers include parastatal health centers, those belonging enterprises (CMIE) or the army, insurance companies, public and private schools, pharmacies, and NGOs [SIDA, 2006].

Mali Ministry of Health (MoH) developed a national health policy in 1991 that aimed at promoting community involvement in healthcare through decentralization of healthcare services to within 15 km radius of the population [Schmid *et al*, 2008; Lodenstein and Dao 2011]. The National Health Directorate is charged with the responsibility of implementing health policy, through the Regional Health Directorates. The healthcare delivery system is organized into pyramidal structure as shown in Figure 2.8 [IIF 2004; Lodenstein and Dao 2011].

Figure 2.8 The health service provision pyramid in Mali

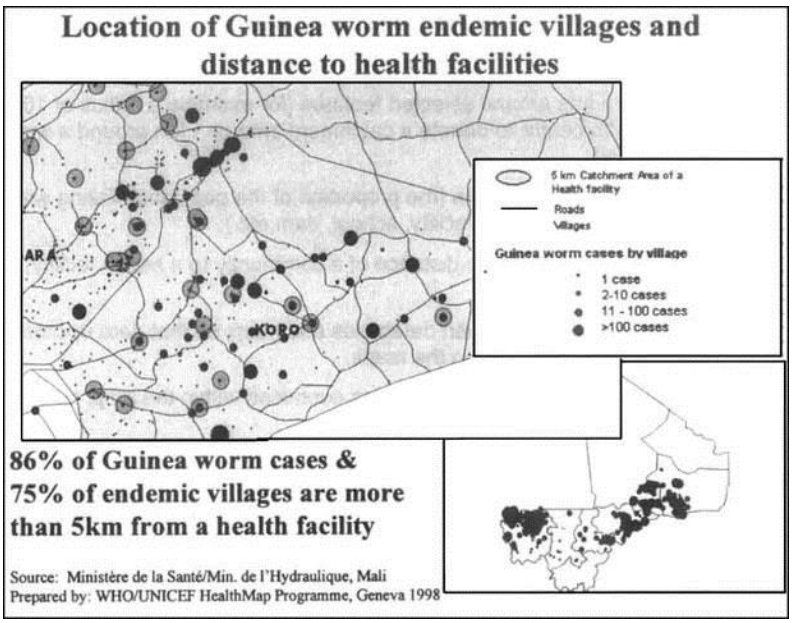
At the very top are the third (tertiary) referral hospitals located mainly in Bamako followed by a hospital for each of the 8 regions which act as second level referral hospitals. Below this are the Referral Health Centers (CSRef) and Polyclinics. CSRefs are linked to Regional Health Directorates and are present in each district. CSRefs offer first reference care including emergencies, obstetrics, surgical operations due to its advanced medical equipment, and they also act as link between Centre de Santé Communautaire (CSCom) and the hospitals. CSRefs are primarily financed by government and donors, and supplemented by user fees. Clinics are also classified under second level with capability of providing in-patient care, however, they do not offer advanced surgical operations like CSRefs and Polyclinics.

At first level of contact are the CSComs which provide basic preventive, promotional and curative health services with most having capabilities for maternal and child health [Lodenstein and Dao 2011]. The services are rendered by staff members who include nurse, midwife, and someone to

deal with drugs. CSComs are mainly created and managed by communities through an Association for community Health (ASACO) consisting of a Board of directors (representatives of the village, the commune and the health staff) and a management committee. Financial and technical support for CSCom is provided by the government and its technical partners. The state through the Ministry of Health also provides CSCom with initial supply of essential materials, equipment, and medications, in-service training and supervision of the technical staff to deliver the national minimum package of primary health care services. The ASACO recruits staff and manages income generated by the clinic to pay staff salaries, renew the stocks of medications and supplies, and maintain the facility. The ASACO also oversees the day-to-day management of the CSCom and its links with the community.

The location of clinical service providers is critical for planning the future health sector requirements [Noor et al 2004]. During the Guinea worm eradication project, maps of health facilities have been useful in planning interventions [Figure 2.9].

Figure 2.9 Location of health facilities with 5 km buffers used during the Guinea worm eradication project in Mali [Source: http://helid.digicollection.org/documents/who46e/p156.jpg].



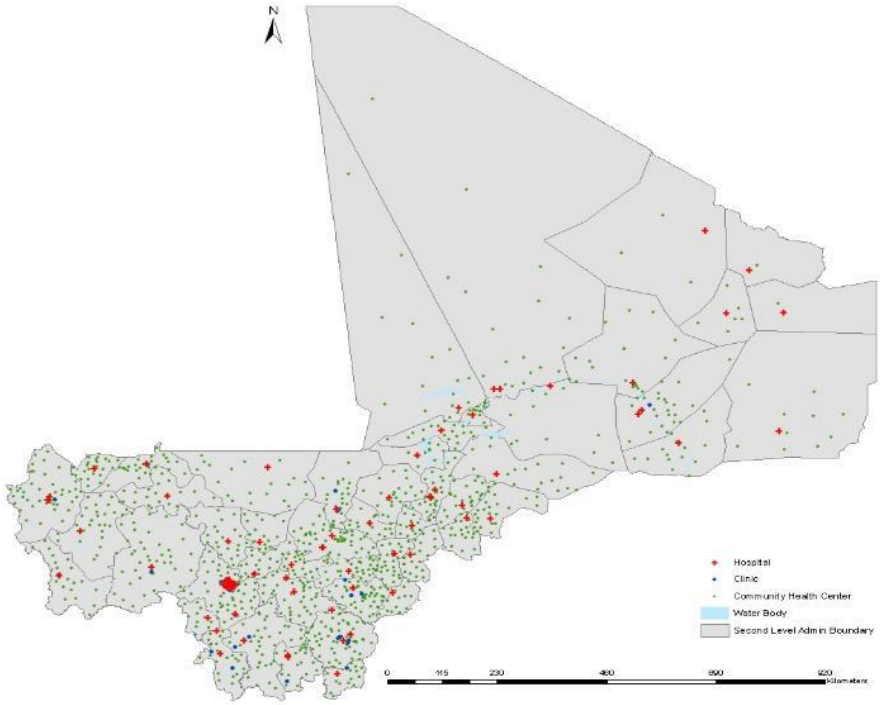
To map the health facilities in Mali, a list was first obtained from the Health facility list used to support United Nations Office of Humanitarian Affairs (UNOCHA) operations in Mali. This list contained the following: Cabinet (332), Centre de Recherche (6), clinic (102), Centre Médico-Inter Entreprise-CMIE (25), Confessionnel (25), CSCOM (1,147), CSRef (60), Ecoles de formation en santé (72), Hôpital (15), Imagerie Médicale (4), Infirmerie de Garnison (19), Laboratoire d'analyses médicales (8), Officine de Pharmacie (500), Polyclinique (11), and Tradithérapeute (20).

The following changes were made during the cleaning process: 330 facilities with facility type as Cabinet were assumed equivalent to private and thus moved to private category; Research Centers/CMIE/Confessionnel/Medical Training Schools/ Imagerie Médicale/Infirmerie de garnison/ Medical Laboratory/ Officine de Pharmacie/Traditional Healers – 679 facilities were assumed to be providing care to specialized group or was performing other tasks other than treatment like labs, these facilities were removed from the health facility database. The remaining

public facilities were checked again to remove facilities providing maternal or other forms of specialized care.

At the end, there were 1,326 facilities classified as public offering general care under four main types (Hospital, CSRef, Polyclinics, Clinics, and CSCom). The public facility types were re-coded to three main levels of operation based on functionality. The three re-coded levels included: Hospitals (combined CSRefs, Polyclinics, and Hospitals) ; Clinics – capable of providing inpatient care and classified as level 2; and finally CSComs. Some duplication was found in the data either as repeated names and similar coordinates for two or more different health facilities. Duplicate names were removed and where coordinates for multiple facilities were similar new coordinates were generated using Google Earth, GeoNames, and Encarta. Two public health facilities could not be geolocated using any of the available data sources. The final list of contained 1325 public health facilities made up of 85 hospitals (hospitals, clinics and referral health centres), 95 clinics and 1145 CSComs (Figure 2.10).

Figure 2.10 Location of health facilities[5] by hospitals (red cross- includes hospitals, clinics and referral health centres), clinics (blue cross) and community health centres (CSCom - green dot).



[5] Health facility list used to support United Nations Office of Humanitarian Affairs (UNOCHA) operations in Mali was provided by Dr Massambou Sacko. The database contained 2344 entries of health facilities indexed by health district and regions. Facilities that were labelled duplicates, pharmacies, research centres, medical laboratory, medical training schools, traditional healers and other specialised facilities (n=687) were removed as these do not provide routine curative care. Private facilities (n=332) were also removed as these are accessible to few people and often do not feature in malariometric surveys. The remaining 1325 public facilities were assigned facility codes by matching names and location to another health facility file provided by Dr. Massambou on 1st May, 2013. We were able to assign all public facilities with a facility code. Though most of the facilities and centres were provided with GPS coordinates (n=2342), we corrected for obvious errors in the coordinates such as duplicated coordinates using methods described in section 2.8.

3. 100 years of malaria control

In this section we provide an overview of the evolution of malaria control in the Mali from the period before independence, through the era of the Global Malaria Eradication Programme (GMEP), from the abandonment of elimination to the present Roll Back Malaria (RBM) control period. This chapter is motivated by a need to: a) capture a historical perspective of control to be applied to today's control ambitions; and b) maintain an institutional memory of the last few decades of malaria control in the Mali. The work is laid out as a timeline highlighting the major events, data and locations of activities and resistance emergence.

1904

The 'hygiène prophylactique' began as a set of environmental interventions to reduce mosquito populations in European and Africa settlements in mainly urban areas such as Bamako and Kayes. In addition this campaign advocated for limiting the contact between non-immune European and 'infectious' African populations [Le Masle 1904; Giles-Vernick 2008].

1906-1908

The earliest detailed species description of mosquitoes in the French Soudan was undertaken by Le Moal (1906) and Bouffard (1908).

1920-1934

A large irrigation scheme, Office du Niger, was initiated by the French to tap water through a system of dams and canals to irrigate land on the north of Niger for rice and cotton production [van Beusekom 2002, Echenberg and Filipovitch 1986; Giles-Vernick 2008]. Work on this project continued all the way to the time of independence. The scheme led to the rapid increase of population in the affected areas and rise of the mosquito density leading to increase in malaria transmission. Consequently the Office du Niger set up health services across the scheme including a hospital in Segou [Giles-Vernick 2008].

1940-1949

Efforts against malaria continued throughout the French Soudan focusing mainly of household visits to eradicate mosquito breeding sites and using chemoprophylaxis to prevent infections among inhabitants [Service de Santé 1949].

1950-1957

DDT spraying began in Bamako in 1950, once a year in most households but up to four times a year in areas which high density of mosquitoes. By 1957, DDT spraying had been expanded to five zones including the Office du Niger [Service de Santé 1950; Colonie du Soudan Francais 1957; Giles-Vernick 2008].

1960-1980

During this period insecticide spraying of houses and their environs together with chemoprophylaxis were the main interventions used to control malaria in Mali. Although the campaigns were well structured they did not achieve their stated objective of interrupting malaria transmission in Mali [PNLP 2001]. By 1978 the vertical programmes were beginning to unwind and malaria became embedded in the primary health care system. Presumptive treatment of febrile patients became the main approach to controlling malaria in the country [PNLP 2001].

1977

Early description of malaria and anemia in pregnancy among Malian women. The study showed a strong contribution of malaria to anemia among the women and recommended chemoprophylaxis from the second trimester [Rougemont 1977].

1981

A study named KBK survey was funded by the World Bank through the International Association for Development (IDA, Nº P.108 Mali) and implemented by the National school of Medicine and Pharmacy (ENMP) was undertaken. The study aimed to assess the health problems and required actions and to measure the levels of health in 3 districts of Kayes region, Bafoulabé, Kéniéba and Kati. The study showed a point prevalence of 80.6% for *P. falciparum,* 18.5% for *P. malariae* and 0.9% for *P. ovale* in May . In December, the point prevalence for malaria parasites species were 86.2% for *Plasmodium falciparum*, 11.4% *P. malariae* and 2.4% for *P. ovalae*. Globally gametocytes index was 7.3% in May and 9.6% in December.

1987

In September, the Bamako Initiative was adopted by the African Heads of States as a formal agreement to increase availability of essential drugs and other healthcare services in sub-Saharan African countries. The agreement was signed in Bamako, Mali as a joint initiative between WHO and UNICEF. Decentralization of health service provision was a key aspect of this initiative [http://www.unicef.org/media/media_11991.html].

1988

At study was published by Chabasse et al., showing the presence of chloroquine resistant *P. falciparum* in a single case of congenital malaria [Chabasse et al., 1988].

1991

A paper on the epidemiology of malaria in Mali was published based on data from 9 locations surveyed from August to September 1988 in Mali [Doumbo et al., 1991a]. This paper remain the main reference for the epidemiology of malaria in Mali that has been used to in national policy documents since 1993.

Results from an experimental study undertaken from May 1989 to June 1990 in two villages (Tiénéguébougou amd Kambila) of hyperendemic malaria in the Malian Savannah was published [Doumbo et al., 1991b]. The study showed that the impregnated curtains were accepted by the population but the blankets were not accepted well. Large reduction in entomological indices were observed.

By this year parasite resistance levels to CQ had reached almost 30% [Plowe et al., 2001].

1992

Malaria Research and Training Centre (MRTC) was created to undertake malaria research in Mali to provide the necessary evidence for malaria control in Mali and the African continent [http://www.sante.gov.ml/]. The center has grown by developing collaborations with several universities and research institutions worldwide. The MRTC was situated within the Department of Epidemiology of Parasitical Diseases at the University of Mali (now the University of Bamako).

It was established as a partnership between the Faculty of Medicine, Pharmacy and Dentistry, National Institutes of Health of the United States, the University of Rome (La Sapienza), the Rockefeller Foundation and the World Health Organization (WHO). The MRTC has since published a large body of work through basic and epidemiological research in Mali and has been at the forefront of generating high quality evidence for malaria in the region. The MRTC has since worked with Programme National de Lutte contre le Paludisme (PNLP) in areas of evidence for policy, research translation, community awareness and policy development and training [Saade 2005].

1993

The Programme National de Lutte contre le Paludisme (PNLP) was set up following the Amsterdam Conference which the Mali government had participated. The PNLP developed the implementation of the Five-Year Action Plan 1993-1997 [PNLP 2007].

1996

A study was published showing high rates of resistance to pyrimethamine among residents in two villages using sulphadoxine-pyrimethamine (SP) for the treatment of *P. falciparum* malaria [Plowe et al., 1996].

1997

Results from a multi-phase study looking at seasonality, malaria and in the impact of chemoprophylaxis with proguanil and chloroquine in Bougoula village of Sikasso region were published. The first paper concluded the significant role malaria played in the in anemia in pregnancy in the village [Bouvier et al., 1997a]. In the second paper, a strong seasonal effect was shown in the likelihood of mother giving birth to underweight children with a higher risk among infants of first and second pregnancies. Parasiteamia during pregnancy was associated with low brithweight and the when taken for 20 weeks or more the drugs suppressed the effects seasonal variations and parity on birth weight [Bouvier et al., 1997b]. The third paper looked at the association of parasite density and fever showing a variable relation with age and season but a generally weak association between levels of parasiteamia and fever [Bouvier et al., 1997c].

1998

The government of Mali launched the Ten-Year Health and Social Development Plan 1998-2009 (PRODESS II). The plan was to be implemented as two Five-Year Health and Social Development Programmes in 1998-2003 as well as 2004-2009 [http://webapps01.un.org/nvp/indpolicy.action?id=1422]. In the same year the PNLP developed 'the accelerated fight against malaria plan 1998' which built on the achievements and lessons land from the Five-Year Action Plan 1993-1997 [PNLP 2007].

Djimbe and colleagues published a study on the use of antimalarials in Mali. The study showed high use of non-recommended antimalarials, poor dosing regimen and poor adherence. This appeared to happen even when prescriptions were made by well-trained health workers [Djimde et al., 1998].

1999

The USAID-Netmark-PSI project for promotion of commercial distribution of insecticide treated nets started [http://www.esc-pau.fr/ppp/documents/featured_projects/mali.pdf]. Mali was selected as one of the first countries for this project.

2000

Soon after the Abuja Declaration, the first national strategic plan 2001-2005 for Mali was launched. The main control strategies were coverage of vulnerable populations (children under the age of five years and pregnant women) with insecticide treated nets, intermittent preventive treatment of pregnant women with SP in the second and third trimester and case management. First line treatment for uncomplicated malaria was changed from CQ to AQ+SP [PNLP 2001].

2001

Taxes on bed nets and insecticides used to treat them were abolished in April 2001 to facilitate access to this essential tool for prevention throughout the country [PNLP 2007].

A national integrated strategy for the promotion of ITNs was developed. The aim was to increase availability and use of malaria prevention measures for pregnant women and children under 5 years. For this objective, the program was to build on existing efforts by targeting free distribution of a long-lasting insecticide-treated bed net for every woman seen for antenatal consultation, and one ITN for every child coming to the EPI for anti-measles vaccination.

A study was published showing an association between the pfcrt T76 mutation in *P. falciparum* and the development of chloroquine resistance during the treatment of malaria malaria [Djimde et al., 2001]. This study provided an approach to more precise assessement of chloroquine efficacy in Mali and other African countries.

2003

Global Fund R1 grant of about 2.6 million USD was approved for malaria control activities with the Ministry of Health as the principal recipient [http://portfolio.theglobalfund.org/en/Grant/Index/MAL-102-G01-M-00].

Later in the year, a study was published showing that in Bandiagara district of Mali which was endemic for malaria, the malaria-attributable fraction of fever cases was 33.6% during the rainy season and 23.3% during the dry season [Dicko et al., 2003].

2004

Mali received the first disbursement for malaria from the Global Fund as part of the R1 proposal. The total disbursed was at this time as 678,620 USD [http://portfolio.theglobalfund.org/en/Country/Index/MLI].

2005

MSF introduced a pilot project to provide free ACTs (AS+AQ) after confirmation with RDTs in Kangaba district of Mali [Ponsar et al., 2011]. The project continued to 2010. The study showed a significant rise in the use of health services for the treatment of malaria in children under the age of five years and recommended the removal of user fees for health for vulnerable groups in Mali.

In December Mali was selected as one of the countries to be funded under the United States Presidential Initiative American Fight against Malaria (PMI) [PMI Mali Report 2008].

2006

Mali changed its first line antimalarial drug policy from chloroquine (CQ) to an artemisinin combination therapy *artesunate+ amodiaquine* (AS+AQ). An MOH Circular Letter of April 21 2006 relating to free distribution of insecticide- treated bed nets to children under 5 and to pregnant women was released [NSP 2007].

2007

In July 18, 2007, the PNLP was transformed into a Directorate of Programme National de Lutte contre le Paludisme which was ratified through an Ordinance No. 07-022/PRM ratified by Law No. 07-060 of 30 November 2007 as the lead agency for the fight against malaria.

In the same year, the first five-year (2007-2011) national strategic plan which was an update of the 2001-2005 plan for malaria was launched. This is the first strategy to recommend the use of AS+AQ as the first line treatment for uncomplicated malaria while a recommendation of parasitological testing of suspected malaria cases before treatment was made [NSP 2007-2013].

Global Fund R4 grant of about 2.76 million USD was approved for malaria control activities with the Ministry of Health as the principal recipient [http://portfolio.theglobalfund.org/en/Grant/Index/MAL-607-G04-M].

Another grant was signed under R4 worth about 10.3 million USD for malaria control with Groupe Pivot Sante Population, an NGO, as the principal recipient [http://portfolio.theglobalfund.org/en/Grant/Index/MAL-607-G05-M].

4.5 million USD was provided by PMI for various malaria control initiatives primariliy in the distribution LLINs nationally and indoor residual spraying (IRS) in Bla and Koulikoro districts districts [http://www.pmi.gov/docs/default-source/default-document-library/country-profiles/mali_profile.pdf?sfvrsn=8].

The Department of Medical Entomology and Vector Ecology (DMEVE) of the MRTC with support from the WHO/TDR set up the African Center for Training in Functional Genomics of Insect vectors of Human Disease (AFRO VECTGEN) program to train regional scientists genome research for sequencing on insect vectors of human disease [Doumbia et al 2007].

A paper was published looking at the high resolution spatial distributions of *Anopheles gambiae sensu stricto* and *An. Arabiensis* [Sogoba et al., 2007] showing the various ecological niches for the these two main vectors of malaria in Mali. Another paper was published indicating a high burden of malaria in pregnancy in Mali [Kayentao et al., 2007].

2008

PMI provided an 14.9 million USD for malaria control activities in Mali [PMI Mali Report 2009].
The scale up malaria rapid diagnostic tests nationally began [PNLP 2007].

2009

Following the global call for universal coverage of malaria interventions, Mali formulated a road map for achieving this goal in September 2009. PMI supported the programme with 15.4 million USD in this fiscal year [PMI Mali Report 2010].

A study in Mali showed that the combination of AQ+SP provided a potentially low cost alternative for treatment of uncomplicated *P. falciparum* infection in Mali and appears to have the added value of longer protective effect against new infection [Kayentao et al., 2009]. As the same time another study demonstrated that SP and AQ were appropriate partner drugs that could be associated with artemisinin derivatives in an artemisinin-based combination therapy [Tekete et al., 2009].

2010

PMI provided Mali with 28 million USD for malaria control activities. Management of two malaria GF grants (R6 and R10) were transferred to Plan International as principal recipient for the Global Fund following an accounts audit [PMI Mali Report 2011; 2014]

In October a randomized control trial study on the impact of malaria interventions among school children started in 80 schools in the Sikasso region. The study was led by the Save the Children in partnership with the PNLP, the London School of Hygiene and Tropical Medicine, the French National Center for Scientific Research [Save the Children 2013]. The study looked at two main interventions: malaria prevention education combined with distribution of LLINs; and treatment with a 3 day treatment with AS+SP of all children at the beginning of the term regardless of infection status. The study showed significant positive impact of the intervention of ITN use behavior, infection prevalence and anemia among school children. The study ended in May 2012.

In 2010, Mali adopted the integrated community case management (iCCM) package to be offered by community health workers (Agents de Santé Communautaires [ASCs]). The ASCs were to provide free treatment for uncomplicated malaria, acute respiratory infections, diarrhea, micronutrient supplementation and primary care to newborns and family planning for eligible families. ASCs were to receive financial incentive from the local government and different partners for their services, provide [PMI Mali Report 2014].

A study showed no increase in the frequency of molecular markers of SP resistance in areas where IPTi with SP was implemented for one year [Dicko et al., 2010]. A study produced a molecular map of chloroquine [Djimde et al., 2010].

2011

PMI provided Mali with 26.9 million USD for malaria control activities [PMI Mali Report 2012].

A study in three localities in Kati, Mali, showed that intermittent preventive treatment of malaria in children (IPTc) with AS+AQ targeting the transmission season showed that it provided substantial protection against *P. falciparum* malaria illness, infection, and anaemia in children between 3-59 months using an LLIN [Dicko et al., 2011].

Another study showed that adding a third dose of SP for IPTp halved the risk of placental malaria, low birth weight, and preterm births in all gravidae, compared with the standard 2-dose regimen, in this area of highly seasonal transmission with low levels of SP resistance [Diakite et al., 2011].

2012

The 2007-2011 NMCP Strategic Plan[6] was reviewed in early 2012 and a new five-year plan (2013-2017) was developed by the NMCP and partners in 2013 [PMI Mali Report 2014]. PMI provided Mali with 27 million USD for malaria control activities.

In March 2012 WHO recommended the scale up of seasonal malaria chemoprevention (SMC) in children 3-59 months in areas where more than 60% of cases of seasonal malaria transmission occur during a period of up to four months or where 60% or more of the annual rainfall occurred in 3 consecutive months [WHO 2012]. The PNLP the adopted SMC into the national malaria strategy [PNLP 2012].

Consequently, the MSF Mali and the PNLP began an SMC implementation pilot project in Koutiala health district in Sikasso region covering an area of 42 health treatment centres and 26 villages [http://www.msf.fr/sites/www.msf.fr/files/201307_smc_mali_-eng.pdf]. The first round started in August 2012 using door-to-door and fixed site distribution approaches. There were distributions every four weeks ending October 2012. The study showed huge reductions in pediatric uncomplicated malaria cases, hospitalizations and deaths compared to estimates a four weeks preceding the intervention. Average cost of intervention was estimated to be 4.5 Euros per child for four rounds.

A study was published that showed 30% of malaria confirmed cases in five health facilities in Goundam, Tombouctou, Gao, Bourem and Kidal were *Plasmodium vivax* [Bernabeu et al 2012]. The study recommended policy attention regarding the burden, diagnosis and treatment of vivax malaria cases in Mali.

2013

PMI provided Mali with 25 million USD for malaria control activities [PMI Mali Report 2014]. In addition in April the Global Fund approved its largest malaria grant to the country to date with signing of almost 59 million USD worth of support for malaria control under Round 10 [http://portfolio.theglobalfund.org/en/Country/Index/MLI]. This time Population Services International (PSI) was the principal recipient [http://portfolio.theglobalfund.org/en/Grant/Index/MAL-M-PSI].

2014

PMI provided Mali with 25 million USD for malaria control activities. By this year total PMI support for malaria control in Mali stood at 166.7 million USD [PMI Mali Report 2014].

[6] The 2013-2017 NMCP Strategic Plan [PNLP 2012] aims to achieve the following targets by 2015: Reduce malaria mortality to near zero; Reduce malaria morbidity by at least 75% as compared to 2000 levels; and Reinforce/strengthen the NMCP coordination and management capacity. The targets for the period 2013-2017 are: At least 80% of the population at risk of malaria is using LLINs including pregnant women and children under five years old; At least 80% of pregnant women have received three sulfadoxine-pyrimethamine (SP) doses as intermittent preventive treatment of pregnant women (IPTp) during their pregnancy; At least 80% of children under five received the four full courses of seasonal malaria chemoprevention (SMC) in selected zones; At least 90% of suspected malaria cases are confirmed using microscopy or RDTs before treatment, at all levels of the health system including the CHW level; At least 90% of confirmed malaria cases receive appropriate malaria treatment both for severe and uncomplicated cases as indicated in the national guidelines; At least 80% of the population is protected by indoor residual spraying (IRS) in IRS target zones; At least 80% of the general population knows what tools are on recommended to prevent malaria. ; At least 90% of emergency cases and malaria epidemics.

4. Mapping the epidemiology of malaria transmission

4.1. 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 vector [Le Moal 1906; Bouffard 1908l; Joyeux et al., 1939; Holstein 1949; Hamon 1961]. These studies confirmed the predominance of the *Anopheles gambiae* complex [Holstein 1949; Hamon 1961]. Another specie, *An. funestus,* was also shown to be widespread (see Chapter 5 for more details). Early French researchers also described the ecological niches inhabited by the mosquitoes using the broad climatic categorization [Holstein 1949; Hamon 1961] which have been adopted to describe the contemporary malaria ecology in Mali [Doumbo 1991a; Traore et al., 1983]. These zones were: the Saharan zone (the Sahara desert area); the Sahelian zone (mean annual rainfall of 250-500mm); the Sudano-Sahelian zone (also the known us 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) (see Figure 2.2). On several occasions reference is made to the various combinations of these zones either as Sahara-Sahelian or Sudano-Guinean zones.

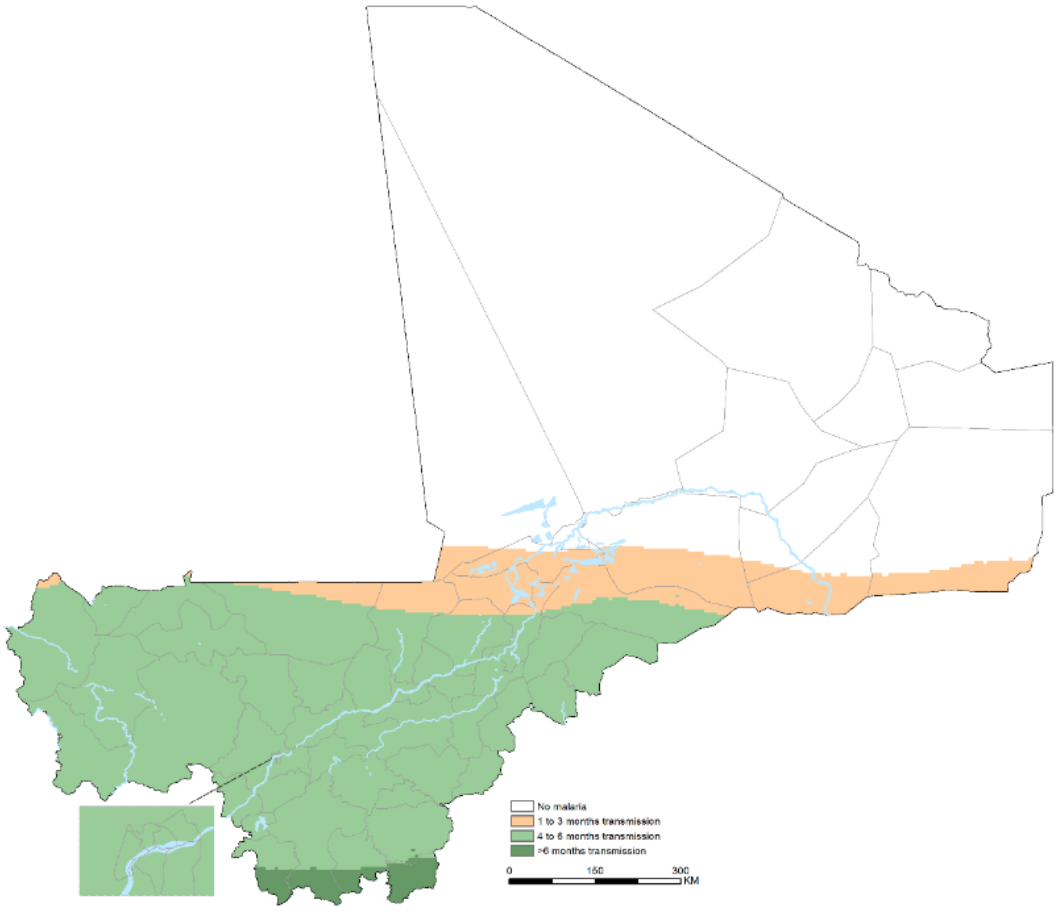
Within these climatic ecologies, epidemiological studies on the levels of malaria infection rates in humans started in the early 1900s and were initially concentrated in Bamako. In 1909 *P. falciparum* prevalence of 33% in one location and 33% and 20% in two locations in 1914 were reported [Leger 1914]. A much higher prevalence among a smaller sample size of about 78% in 1922 was reported in an area of Bamako [Gambier 1922]. 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% [Sautet and Marneffe 1943]. Perhaps the largest maliometric 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 [Escudie and Hamon, 1956]. Surveys were undertaken in 358 villages with *P. falciparum* prevalence of greater than 50% reported in locations 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 of very low transmission and epidemic prone, to the Guinean where transmission was hyperndemic to holoendemic [Doumbo 1991a]. The frequency and size of the parasitological studies increased substantially after the establishment of the MRTC in 1992.

4.2. Malaria risk stratification 2000-2013

By 2000 a map of the length of the malaria transmission season in Africa was developed under the Mapping Malaria Risk in Africa (MARA) project [Craig et al., 1999; Tanser et al., 2003; http://www.mara.org.za/] (Figure 4.1[7]).

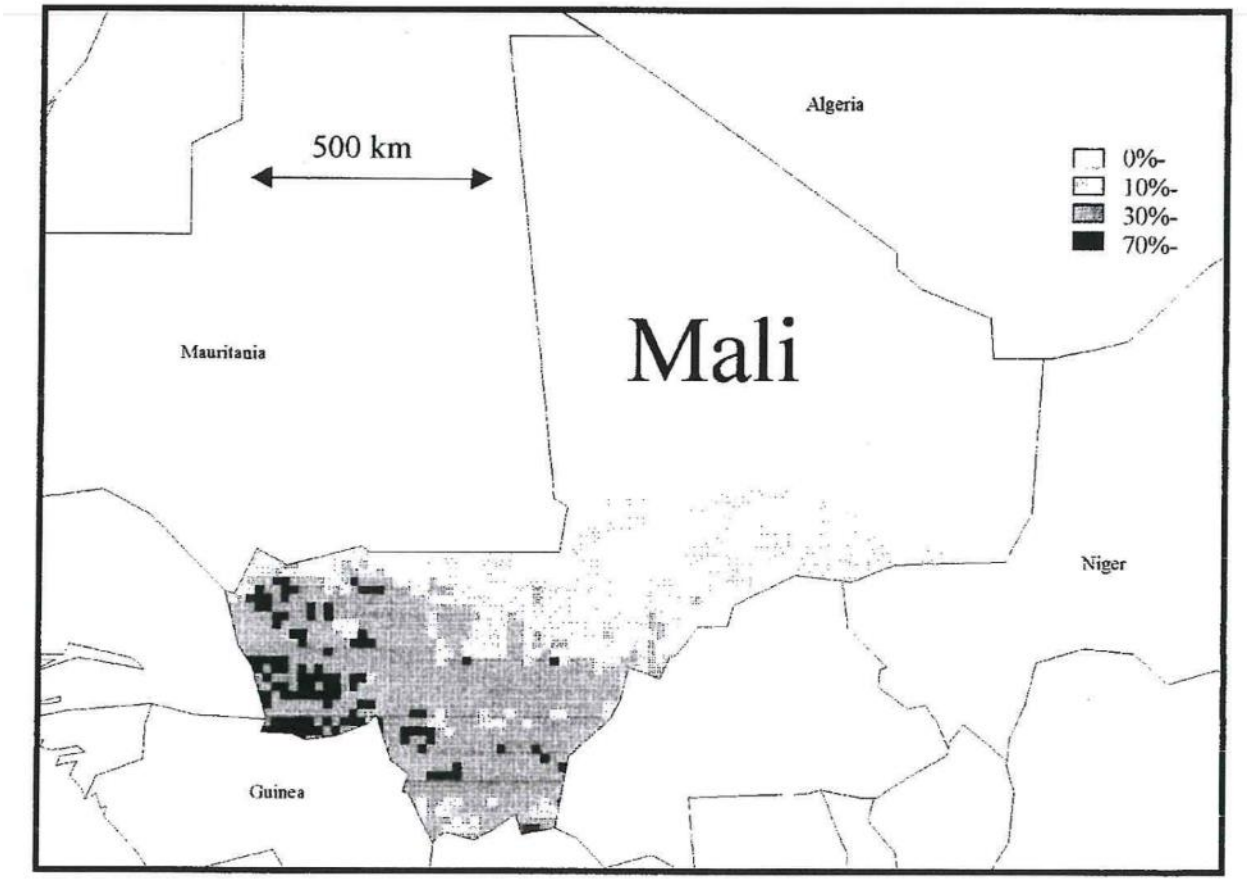
Figure 4.1: MARA climate malaria seasons map [http://www.mara.org.za/]



In 2000 the first geostatistical prevalence based malaria risk map of Mali was developed using parasite rate data in children under 10 years age from 101 survey locations from 1960-2000 [Kleinschmidt et al., 2000]. This map was developed by combining the parasite rate data with climatic, topographic and population data within a regression plus Kriging approach (Figure 4.2).

[7] 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^{o}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^{0}C and rainfall > 60 mm within a 3-month moving window and at least one month of highly suitable conditions (> 22^{0}C, > 80 mm) occurred as a catalyst month. For areas considered "stable" the equivalent values were 19.5^{0}C and 80 mm with no requirement for a catalyst month.

Figure 4.2 Map malaria risk in Mali in 2000 predicted using regression plus Kriging approach [Source: Kleinschmidt et al 2000]



By the time the first national strategic plan for malaria control 2001-2005 was launched after the start of the Roll Back Malaria (RBM) initiative [PNLP, 2001], a map (Figure 4.3) was developed that combined the information on climatic zones (Figure 2.2), levels of infection prevalence reported in various studies and a length of transmission season shown in Figure 4.1. This map was developed through a collaboration between the MRTC and the PNLP and classified malaria risk in Mali into the five zones (Figure 4.3).

Also in 2001 Kleinschmidt and colleagues also another malaria risk map (Figure 4.4) but covering the whole of West Africa [Kleinschmidt et al., 2001]. The map used 450 survey data points from the period 1970-2001 with at least a minimum sample of 50 persons examined. Prediction was undertaken separately within the main climatic zones (Sudano-Sahel, Guinean and Forest zones) ad standardised to the age range 2 to < 10 years. 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 the areas in the Sudano-Guinean zone had predicted *P. falciparum* rates in children 2-10 years of age of >30% (Figure 4.4) in which 67% of the population lived in 2001.

Figure 4.3: Map of malaria risk zones[8] in Mali developed using semi-quantitative combination of climatic zones, infection prevalence and length of transmission season [PNLP 2007].

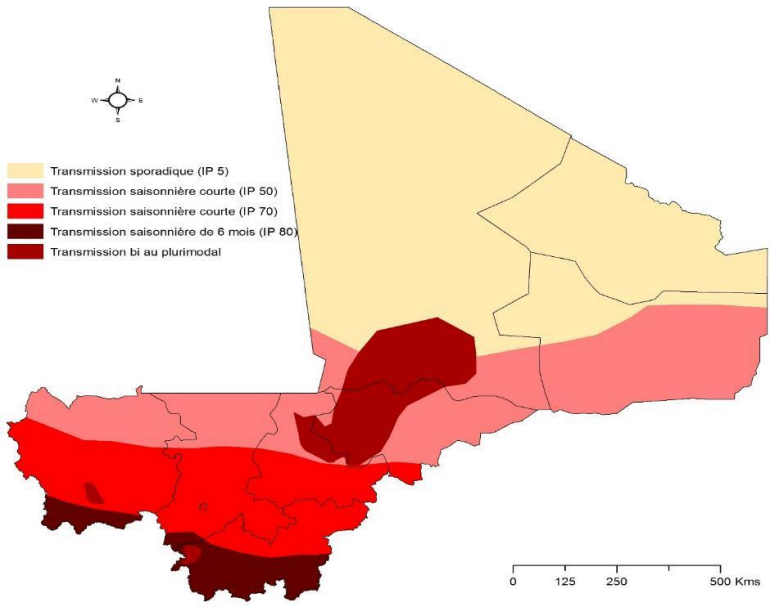
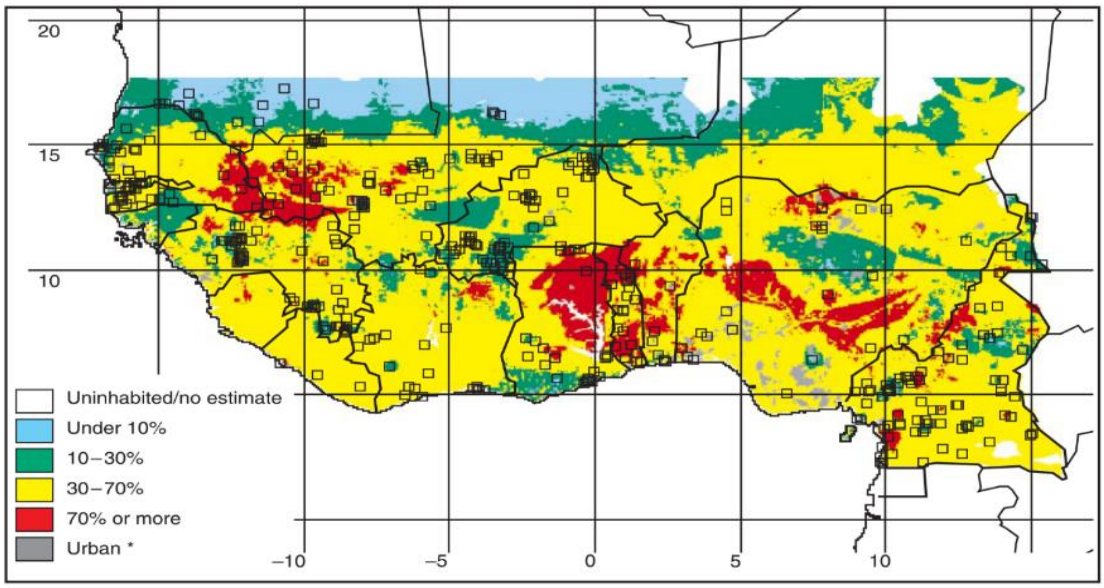


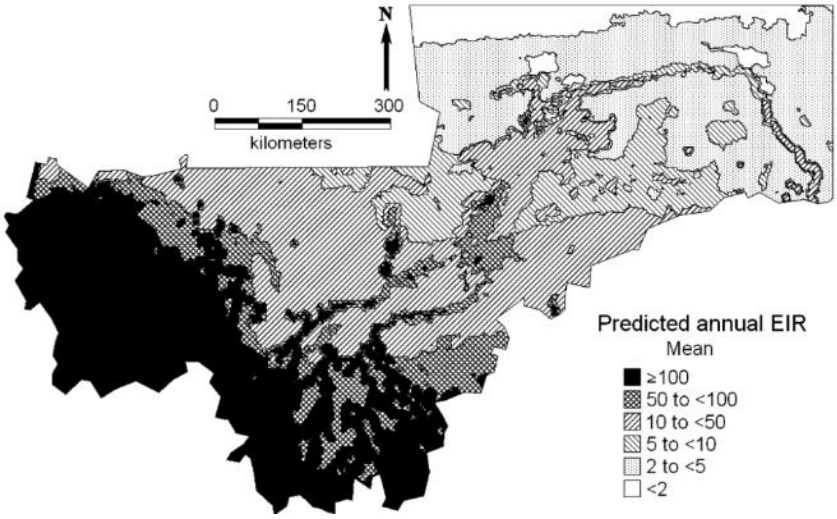
Figure 4.4 Predicted prevalence of *P. falciparum* parasite rate in children aged 2-10 years in West Africa predicted using 450 parasite survey data with a minimum sample 50 persons examined from the period 1970-2001. Prediction was implemented using Bayesian geostatistical models [Source: Kleinschmidt et al., 2001].



[8] 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 5-6 years. Sudanian zone: transmission is seasonal and normally ≤ 3 months. In this area, parasite rate in children is between 50-70%. The status of acquired immunity is rarely achieved before the age of 9-10 years. Sudano-Sahelian zone: Areas of bi-or multimodal including the inland delta of the Niger River and the areas of dam and transmission rice: Niono Sélingué Manatali and Markala. The parasite rate among children is between 40-50%. Anemia remains a significant clinical phenotype. Sahara-Sahelian zone: An area of sporadic or epidemic transmission corresponding to the northern regions and some areas of Koulikoro and Kayes (Nara, Nioro Diéma, Yélimané, Kayes). 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: The very conducive to malaria infection especially 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 exposed to severe and complicated malaria.

In 2006, a map of entomological inoculation rates (EIR) in Mali was developed using 164 survey data from the 1965-1998 assembled through the MARA project [Gemperli et al., 2006]. EIR estimates were first derived by fitting the Garki model [Dietz et al 1974] to the parasite prevalence data (Figure 4.5).

Figure 4.5 Spatial prediction of the mean annual entomological inoculation rate in Mali using 164 survey data at 147 locations from the 1965-1998 collected by MARA and modelled using Bayesian geostatistcal models. The map does not show most of the northern areas that coincide with the Sahara Desert [Source: Gemperli et al., 2006]



Spatial modelling of EIR was implemented using Bayesian geostistical methods. The same climatic variable used by Kleinschmidt *et al* 2000 were used in estimating EIR. These estimates were then transformed back to age-specific (<5 years and 2 to <10 years) predictions of parasite prevalence (Figure 4.6). The parasite maps showed that parasite rate among both age groups was greater than 20% across Mali below the Sahara desert with rates >80% in most of the Sudano-Guinean zone.

Although based only on 89 data points from the period 1977-1995 Gosoniu and colleagues developed a map of *P. falciparum* prevalence in children 1 to 10 years of age in Mali comparing the results of stationary and non-stationary models [Gosoniu et al., 2007]. Length of season, vegetation, temperature, rainfall and proximity to water bodies were used as covariates in the model. The analysis showed that the non-stationary models, which assumes directional heterogeneity in parasite rates, performed better. The maps that most of the Sudano-Guinean had parasite prevalences of >50% and most of Sahelian region had predicted prevalence of <20% (Figure 4.7).

Figure 4.6 Spatial prediction of the age-specific parasite rate 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 [Source: Gemperli et al., 2006]

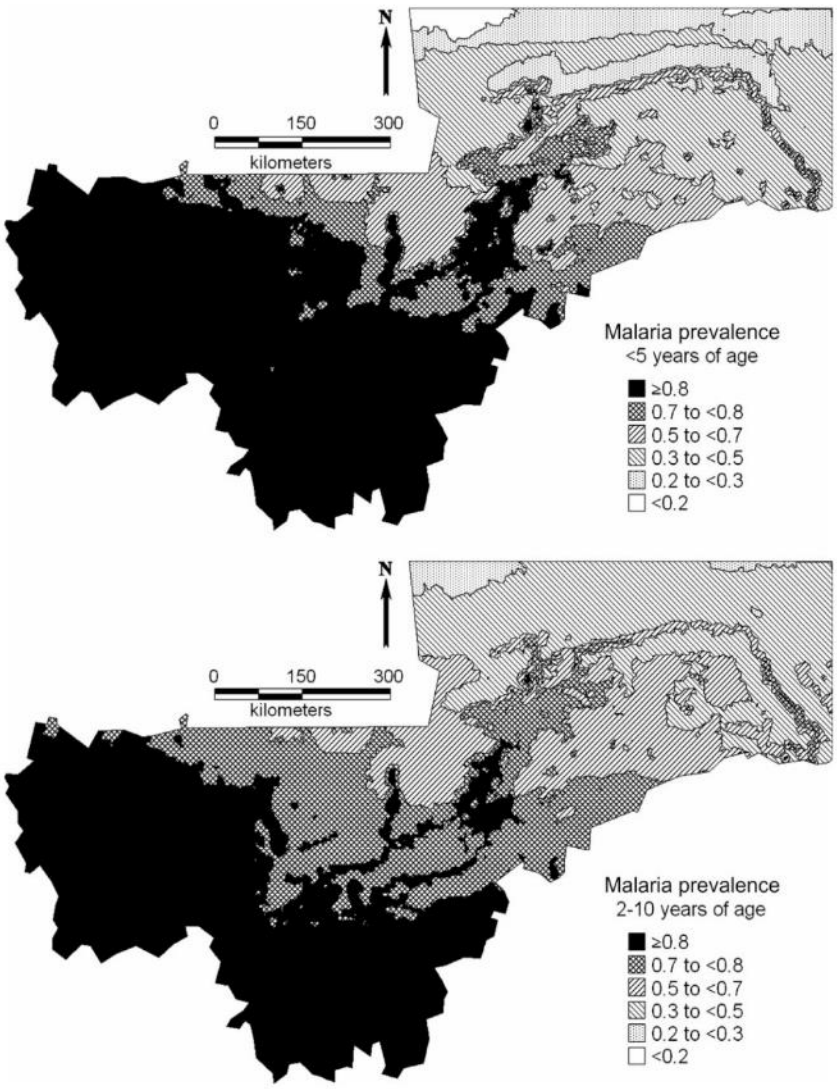
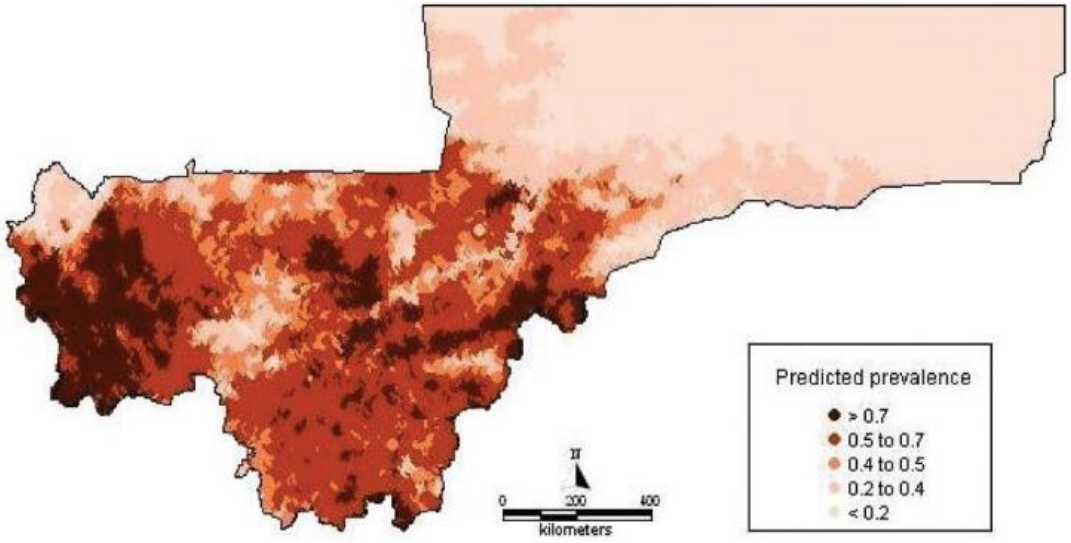
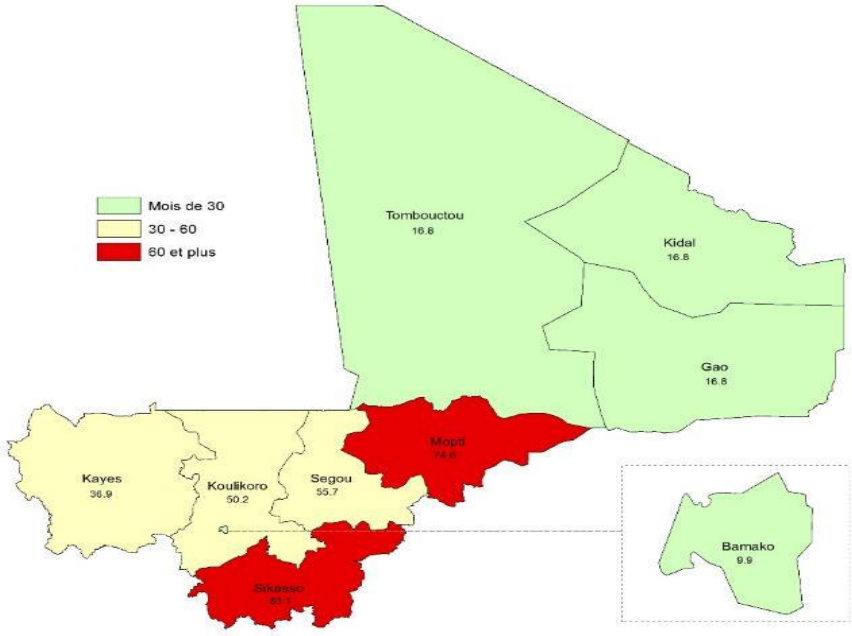


Figure 4.7 Spatial prediction of parasite rate in children 1-10 years in Mali derived from 89 data points from the period 1977-1995. The maps do not show most of the northern areas that coincide with the Sahara Desert [Source: Gosoniu et al., 2007]



A recently completed map of malaria transmission intensity was included in the updated national strategic plan for malaria 2013-2017 [PNLP 2013]. The map was based on the results of the national anemia and prevalence survey among children in 2010 [Traoré et al., 2010] in 114 clusters and the malaria module of the Demographic and Health Survey (DHS) 2012 in 413 clusters [DHS 2013]. The map was simply a summary of the proportion of children under the age of five years sampled during and who tested positive for *P. falciparum* malaria (Figure 4.8). The survey results were summaries at regional level and classified into three strata: <30% parasite prevalence (Bamako, Tombouctou, Gao and Kidal); 30% to 59% (Kayes, Koulikoro, Segou); and ≥60% (Mopti and Sikasso).

Figure 4.8 Malaria strata based on parasite prevalence among children under the age of five years surveyed during the national household surveys of 2010 and 2013 [Traoré et al., 2010; DHS 2013].



4.3. Revised malaria risk maps

4.3.1. Background

There was a recognition over 50 years ago that one important source of planning data was infection prevalence among children aged 2-10 years (*Pf*PR_{2-10}), used to define categories of endemic risk designed to guide and monitor progress toward malaria elimination targets [Metselaar and van Thiel, 1959; Macdonald and Göeckel, 1964; Lysenko and Semashko, 1968]. There is a growing body of evidence that the clinical epidemiology [Snow and Marsh, 2002], the impact of vector control [Killeen et al., 2007; Smith et al., 2009; Griffin et al., 2010], cost-effectiveness of treatment and prevention interventions [Okell et al., 2012] and timelines to malaria elimination [Cohen et al., 2010] are all dependent on pre-control, parasite transmission intensity.

A wealth of parasite survey data was collected after independence in Mali (Annex A.1). As described in Section 4.2, most contemporary maps of malaria risk in Mali have so far depended on the very few data points. Here we have developed a more comprehensive inventory of geo-coded parasite prevalence data and have applied rigorous Bayesian, model-based geo-statistical methods to interpolate estimates of *Pf*PR_{2-10} across the Mali in 2000, 2010 and 2013 and derived quantities of population-adjusted risk per *cercle* (district).

4.3.2. Assembling empirical data on malaria infection prevalence

We have identified and assembled parasite prevalence survey reports through combinations of on-line published journal searches, investigations of archive material in Geneva and Brazzaville, Institut Pasteur library in Paris and contacts with national academics and research groups for unpublished data (details provided in Annex A.1). We located 649 estimates of malaria infection prevalence over the interval 1980 to 2013. Twenty-four surveys that sampled less than 10 individuals were excluded. The temporal distribution of the remaining 625 surveys is shown in Figure 4.9. 121 (19.4%) of all data were from surveys undertaken before 2000, 45 (7.2%) from surveys undertaken between 2000 and 2005, and 459 (73.4%) surveys were undertaken over the from 2006-2013. These data included those from the Anaemia and Parasiteamia survey of 2006 and the Demographic and Health Survey of 2012-2013 [http://dhsprogram.com/data/available-datasets.cfm].

The surveys sampled varying age-groups at each sampled site, including young children to adults aged over 15 years. To make any meaningful comparisons in time and space we have adapted catalytic conversion models to standardize all survey data to one age group, children aged 2-10 years, *Pf*PR_{2-10} [Smith et al., 2007]. The mean overall trends in averaged *Pf*PR_{2-10} suggest that risks of *P. falciparum* infection are marginally higher over the last decade compared to prevalence reported before 1999 (Figure 4.10). However, caution is required in interpreting these data, as survey sites will not have been the same within each decadal period. We approach this using modeled data within different time-periods to highlight long-term change more precisely in Section 4.3.3.

Figure 4.9: Number of *P. falciparum* infection prevalence surveys (Y-axis, n=625) by year 1980-2013 (X-Axis)

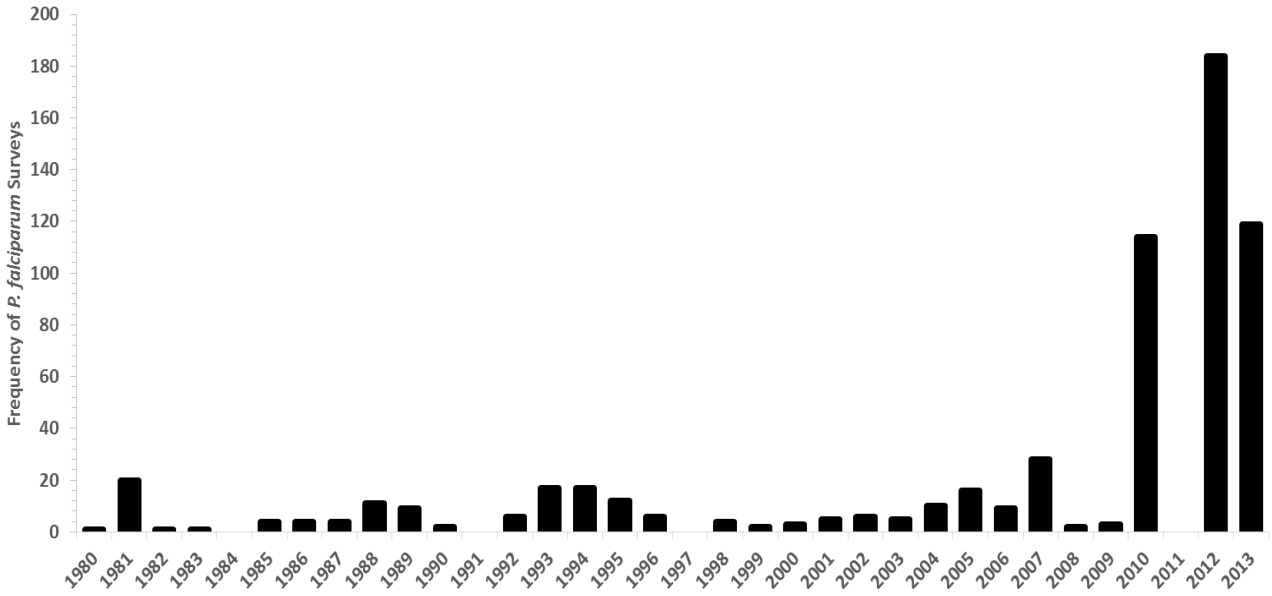
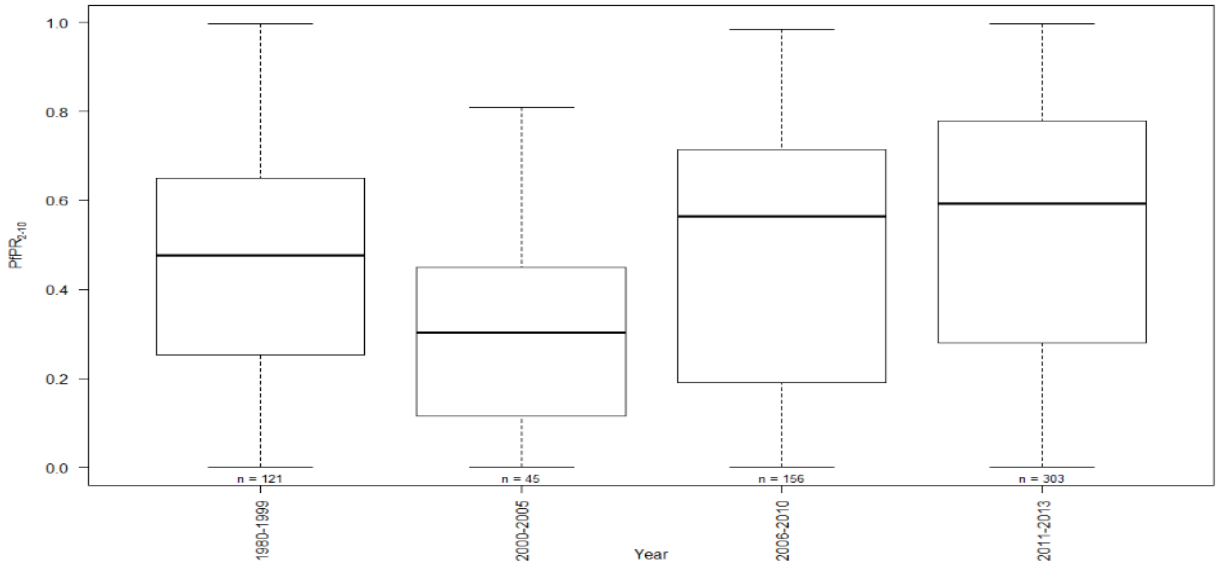


Figure 4.10: Box and Whisker plot of *P. falciparum* infection prevalence surveys by five years (the thick middle line in the box is the median, the upper and lower bounds of the box show the 75th and 25th percentiles, the upper and lower bounds of the whiskers show the maximum and minimum values excluding the outliers)



4.3.3. Modeling $PfPR_{2-10}$ in space and in time

The empirical prevalence survey data were non-randomly over-dispersed in time and in space. The spatial and temporal dependencies of the data within the country, however, allow for the application of model-based geo-statistical (MBG) methods[9] that interpolate from data at known

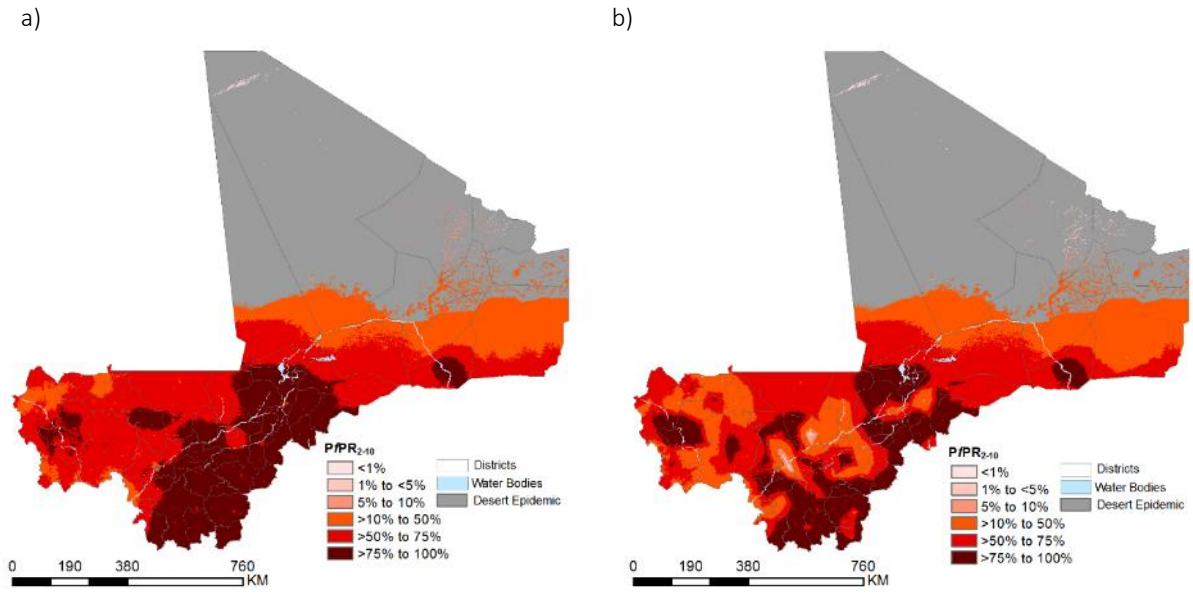
[9] MBG methods use the basic principles that the values of more proximal information (either in time or space) are more similar than more distal points in space or in time [Tobler, 1970]

locations and time to provide predictions of quantities and estimates of their uncertainty at locations and times where data do not exist [Diggle and Ribero, 2007].

We have used information from the available age-corrected survey data (sample size and numbers positive) at known locations (longitude and latitude) and times (year) with a minimal set of conservative, long-term covariates traditionally used in vector-borne disease mapping. In statistical modelling, a set of independent environmental covariates of the main outcome measure is often used to improve the model fit and increase the precision of predicted estimates.

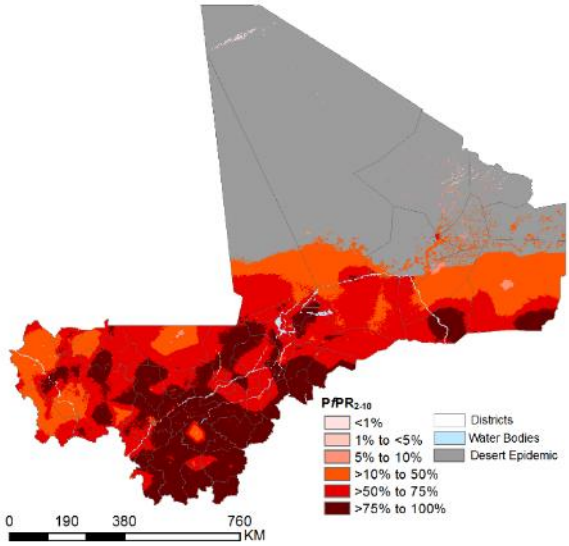
A Bayesian hierarchical space-time model was implemented through Stochastic Partial Differential Equations (SPDE) using Integrated Nested Laplace Approximations (INLA) for inference. The covariates used together with the parasite rate data to predict malaria risk were temperature suitability index (TSI), precipitation, enhanced vegetation index (EVI) and urbanization. See Annex A.2 for full model details, covariate selection, model outputs and model precision metrics. Analysis was limited to areas with data south of Sahara Desert[10]. In the desert areas transmission is highly constrained by aridity and disease manifests in the form of epidemics following unusually high rainfall analysis. The sparsely populated northern arid areas where they were barely any parasite rate data across the period 1990-2013 were defined as epidemic prone and malarious near water consistent with national strategy.

Figure 4.11 The *Pf*PR$_{2-10}$ malaria endemicity classes at 1x1 km spatial resolution derived from the continuous predictions of the mean *Pf*PR$_{2-10}$ in Mali in a) 2000; b) 2010; c) 2013. The area shaded grey represents the Sahara Desert region and are classified to have very malaria risk which manifest as epidemics.



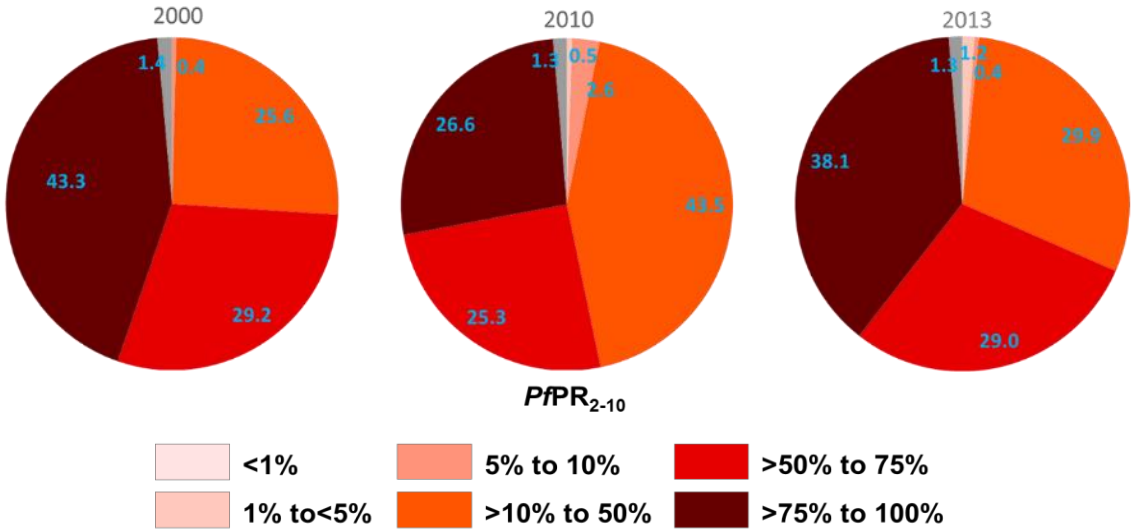
[10] To define aridity enhanced vegetation index (EVI) at 1×1 km resolution processed from earth orbiting satellite imagery was used. Data from 12 monthly surfaces were used to classify areas of the Republic into those likely to support transmission, defined by an EVI of >0.1 for any two consecutive months and areas without two or more consecutive months of an EVI >0.1 as unable to support transmission [Noor et al., 2012; Snow et al., 2012]

c)



Continuous maps of *Pf*PR$_{2-10}$ Maps of predicted 1 × 1 km grid were generated (Annex A) and these were classified into various endemicity ranges (Figure 4.11). The modeled and the population density grids (Figure 2.5), projected to 2000, 2010 and 2013, were then used to extract populations at risk by district at each 1 × 1 km *Pf*PR$_{2-10}$ grid location using the *Zonal Statistics* function in ArcGIS 10.1. These population were then classified by *Pf*PR$_{2-10}$ endemicity class by year to demonstrated the changing risk in Mali from 2000-2013 (Figure 4.13).

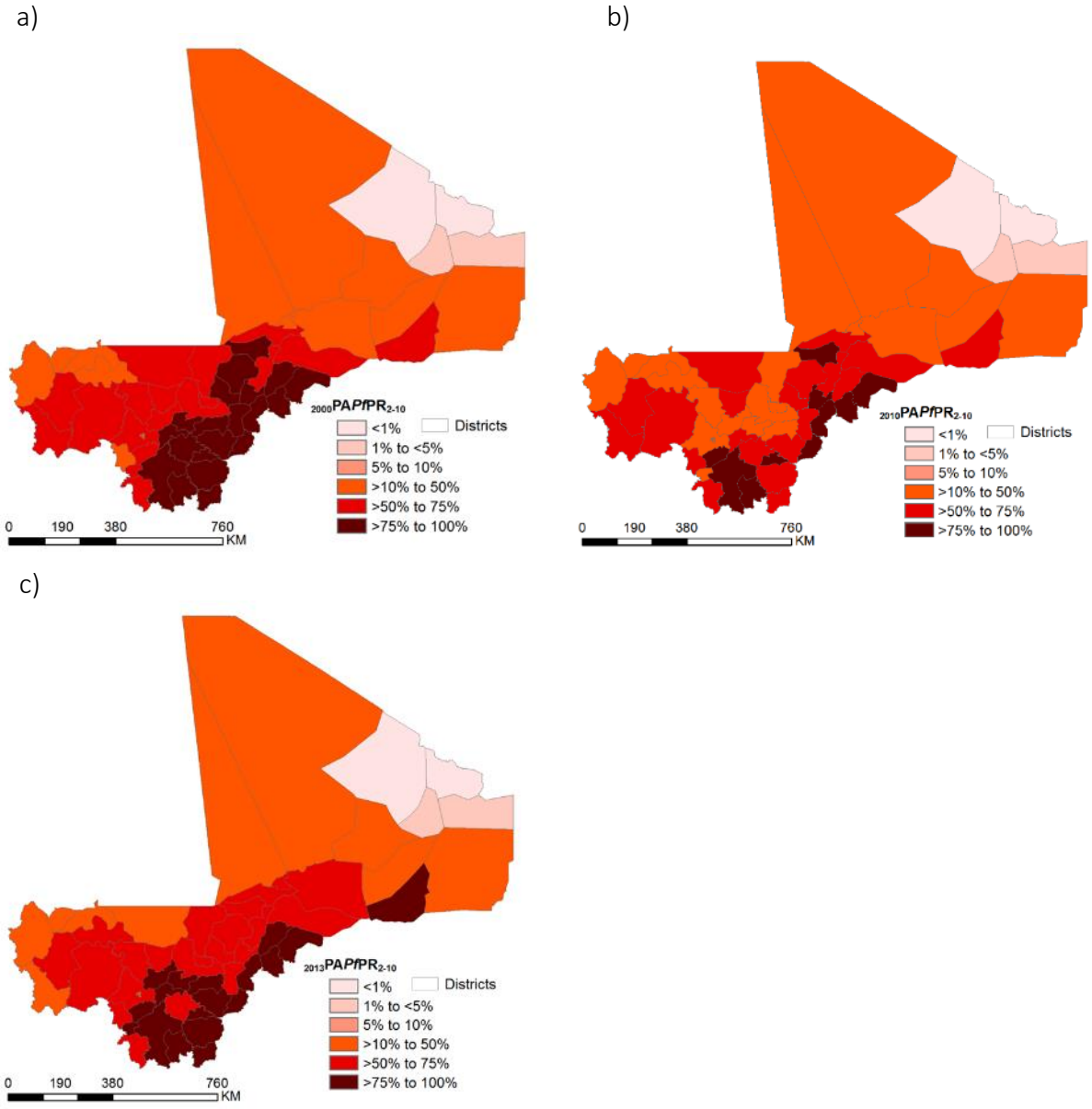
Figure 4.12: Proportion of the population in Mali living in areas of varying predicted *Pf*PR$_{2-10}$ malaria endemicity classes in 2000, 2010 and 2013



The results indicate that by 2000 approximately 72.5% (8.2 million) of the population of Mali lived in areas where *Pf*PR$_{2-10}$ was >50% among and most of the rest (25.6%, 3.9 million) were in areas where *Pf*PR$_{2-10}$ was >10% to 50% (Figure 4.12). By 2010, the percentage of the population at risk in the hyper-to holoendemic areas had reduced to about 52% (8.0 million) with most transitioning to mesoendemic risk areas. By 2013, the trend appears to have been reversed with population in the two highest risk classes increasing to 65.6% (11.0 million).

Matching population density to malaria risk allows for the calculation of Population-Adjusted *Pf*PR$_{2-10}$ (PA*Pf*PR$_{2-10}$) within each of the districts for each prediction year (Figure 4.13). For the estimates of population at risk and PA*Pf*PR$_{2-10}$ by district please see accompanying MS Excel file. Between 2000-2013, the general endemicity levels have remained the same in most of the districts of Tomboctou, Kidal and Gao regions with transmission largely hypoendemic in Kidal and mesoendemic in the two other regions (Figure 4.13). Areas of hyper-endemic and holo-endemic transmission were concentrated throughout in the districts of southern regions of Sikasso, Segou, Koulikoro and Kayes. By 2010, the number of districts under holoendemic risk reduced from 20 out of 60 to 10 but rose to back 18 in 2013 and were mainly in Segou and Sikasso regions. In the six communes of Bamako, transmission levels ranged from 35% to 45% PA*Pf*PR$_{2-10}$ in 2000, reduced to between 18% to 35% in 2010 and went back to almost the 2000 transmission in 2013 of 35% to 46%.

Figure 4.13 The population adjusted 1939 *Pf*PR$_{2-10}$ (PA*Pf*PR$_{2-10}$) by health district (n=60) in Mali in: a) 2000; b) 2010; and c) 2013.



4.4. Other malaria parasites

According to the national malaria strategic and planning documents *P. falciparum* remains the dominant parasite across all regions of Mali while *P. malariae* accounts for between 10% to 14% of the malaria infections while 1% are due to *P. ovale* [PNLP 2007]. These documents do not mention the presence of *P. vivax*, in line with the belief that this parasite is absent in most West African countries to the largely Duffy negative populations. However, several studies show the presence of multiple parasite species, including *P. vivax*, in various parts of Mali.

In a study of 9 locations surveyed from August to September 1988 in Mali among 2185 individuals only one *P. vivax* infection and one co-infection of *P. falciparum* and *P. malariae* were found while all remaining cases were *P. falciparum*. None of the persons tested showed infection with *P. ovale* [Doumbo et al 1991a]. In 2001 in Mandela, a settlement located in the southern part of Mali where malaria is hyper- to holoendemic, investigations among children aged 0-14 years old showed the presence of the malaria parasite in 64.1% in May and 72.3% in October. In May, the predominant parasite species was *P. falciparum* at 87.4%, followed by *P. malariae* at 5.6%, and for *P. ovale* was at 1%, with the remainder of samples showing a mixture of *P. falciparum* and *P. malariae* with a similar pattern in October [Guindo 2004]. A study conducted in Mopti region, the prevalence was *P. falciparum* 95%, *Plasmodium malariae* 4%, *Pf* + *Pm*=1% in children aged 0 to 9 years [Arama 2002]. In October 2001 in Missira, a rural town with Sudanese zone, a cross-sectional survey showed malaria prevalence of 48.5%. The predominant parasite species was *Pl. falciparum* 94%, followed by *P. malariae* 5% and *P. ovale* 1% [Darrar 2004]. However, a cross sectional study undertaken in Maneka district in northeastern Mali to examine the seasonality of malaria parasite prevalence during dry hot (May 2004) and cold (February 2005) seasons showed a significant presence of *P. vivax* [Koita et al 2012]. In May prevalence and morbidity were: *P. falciparum* = 74.1%, *P. malariae* = 9.4%, *P.ovale* = 3.1%, *P. vivax* 7.8%, *P.falciparum* + *P. malariae* = 1.5%. In February the prevalence and morbidity were: *P. falciparum* = 63.7%, *P.malariae* = 22.5%, *P.ovale* = 2.1% (n=97), *P. vivax* 10.3%, *P.falciparum* + *P. malariae*= 7.2% and *P. vivax* = 1.03%.

In another study in five cities (Goundam,Tombouctou, Gao, Bourem and Kidal) in northern Sahelian and Saharan Mali showed close to 30% of cases from health care facilities were positive for *P. vivax* [Bernabeu et al 2012]. To confirm the presence of this parasite, Giemsa/field-stained smears and nested-PCR and DNA-sequence analyses of selected samples was undertaken. In a study in the district of Menaka on the edge of the Sahara Desert a study conducted in May 2004 (hot dry season) and February 2005 (cold dry season) among 1328 persons showed that although *Plasmodium falciparum* was the most prevalent at 74.1% and 63.7% at the beginning and end of the study, *P. malariae* was 9.4% to 22.5% and the prevalence of *P. vivax* was higher 10.3% without seasonal variation.

5. Dominant vectors and bionomics

5.1. Background

All national malaria strategies across sub-Saharan Africa implement interventions aimed at reducing human exposure to infectious malaria vectors. These include insecticide treated nets, applications of residual insecticides on household walls, or the targeting of larval stages of vectors to reduce vector abundance, survival and/or human-feeding frequency. However, the distribution of vector compositions linked to their intrinsic behavioural bionomics and their resistance to insecticides remains largely unknown or under-emphasized when planning vector control at national scales.

Vector resistance to insecticides and behavioural adaptive changes accompanied by changing vector biodiversity pose real challenges to the future effectiveness of current vector control [Ferguson et al., 2010; Gatton et al., 2013; Pates and Curtis, 2005; Ranson et al., 2011]. A lack of reliable entomological monitoring systems limit the capacity of malaria control programs to manage on-going vector control efforts by adapting to changes in vector behaviour and insecticide susceptibility [Govella et al., 2013].

Since 1996, there has been a renaissance in the assembly of spatially defined databases of vector species occurrence, following the launch of the Mapping Malaria Risk in Africa collaboration [Snow et al., 1996; Coetzee et al., 2000]. There are six on-line databases that now provide useful information on the location of the major dominant vector species in Africa[11]. However, these databases do not capture all published observations, exclude much unpublished work and do not cover the entire species diversity within each country. Here we attempt to update the anopheline inventory for Mali from the early 1900s to the present day.

5.2. Historical studies on malaria entomology in Mali

Mali has a rich history of malaria entomological research dating back to the pre-independence period and the establishment of the Office du Niger. By 1913 *An. gambiae* was reported in the Bamako area and between 1938 and 1939 *An. gambiae*, *An. pharoenesis*, *An. coustani*, *An. rufipes* and *An. squamosus* were all recorded in Segou [Senevet and Ethes, 1939]. Around the Office du Niger studies showed the widespread distribution of *An. gambiae*, *An. pharoenesis*, *An. coustani* and limited presence of *An. funestus* in the project area [Joyeux, Sicé and Sautet, 1932]. In the 1960s, a nationwide entomological study was undertaken in over 270 locations showed the abundance of the *An. gambiae* complex followed by *An. funsetus* [Hamon et al 1961]. There was also considerable presence of *An. rufipes, An. coustani* and *An. pharaonesis*. Further descriptions especially of the genetic composition and distribution of the dominant *An. gambiae sl* and *An. funsetus* in Mali were published extensively [Toure et al., 1983; 1994; 1998]. These studies showed that the main vectors of malaria in Mali were The main malaria vectors are *An. gambiae s.l.* and *An. funestus*. The *An. gambiae s.l.* is composed of *An. arabiensis* and three chromosomal forms of *An. gambiae s.s.* named Bamako, Mopti and Savannah [Toure et al., 1983]. Using

[11]MARA/ARMA collaboration [https://www.mara.org.za]; AnoBase [http://skonops.imbb.forth.gr/]; VectorBase [https://www.vectorbase.org]; MAP [http://www.map.ox.ac.uk]; Disease Vectors database [https://www.diseasevectors.org]; Walter Reed Biosystematics Unit Mosquito Catalog [http://www.mosquitocatalog.org]

published and unpublished data from the MRTC an empirical map of the spatial distribution of these main vectors was developed indicating that *An. arabiensis* was concentrated in the drier savannah areas, while *An. gambiae s.s.* was predominant in the southern savannah and along the rivers [Songoba et al 2007]. This map, however, was based on data from 90 locations from the period 1981 – 2004. In a related study, the spatial distribution of the chromosomal forms of *An. gambiae* in Mali was mapped [et al., 2008] using data from 79 rural sites the variable ecological niches preferred by the different forms. The Mopti form ingabuts the dryer northern Savanna and Sahel or the flooded and irrigated areas of the Niger River Delta. The Savanna form favours the Sudan savannah areas, particularly the South and South-Eastern parts of the country in Kayes and Sikasso regions. The Bamako form is restricted to the Sudan savanna areas in urban Bamako areas and the Western Sikasso region. The hybrids/recombinants are found mainly in the Western part of the country (Kayes region) bordering the Republic of Guinea Conakry. [Songoba et al., 2008]. In 2010, the Malaria Atlas Project (MAP) published a map of dominant vectors in Africa and for Mali only 160 data points were used [Sinka et al., 2010].

5.3. Data assembly

We first ran on-line searches of medical literature databases including PubMed, Google Scholar and Web of Science using search terms “Anopheles AND Mali“ and "Anopheles AND French Soudan" for all study publications after January 1964 and post the last searches undertaken by MAP [Sinka et al. 2010]. We searched all on-line publications on malaria in the MALI from the historical archive maintained by the library services of the Institute of Tropical Medicine, Antwerp [http://lib.itg.be/], the Wellcome Trust Library in London [https://catalogue.wellcomelibrary.org/] and the Institute Pasteur, Paris [http://www.pasteur.fr]. The Antwerp library service proved to be an invaluable resource allowing remote access to all volumes of the *Annales de la Société Belge de Médecine Tropicale* since 1920. In addition, we made manual searches of unpublished archive material held at the Tropical Institute in Antwerp, Institute Pasteur in Paris and all unpublished archive material held WHO libraries in Geneva and Brazzaville.

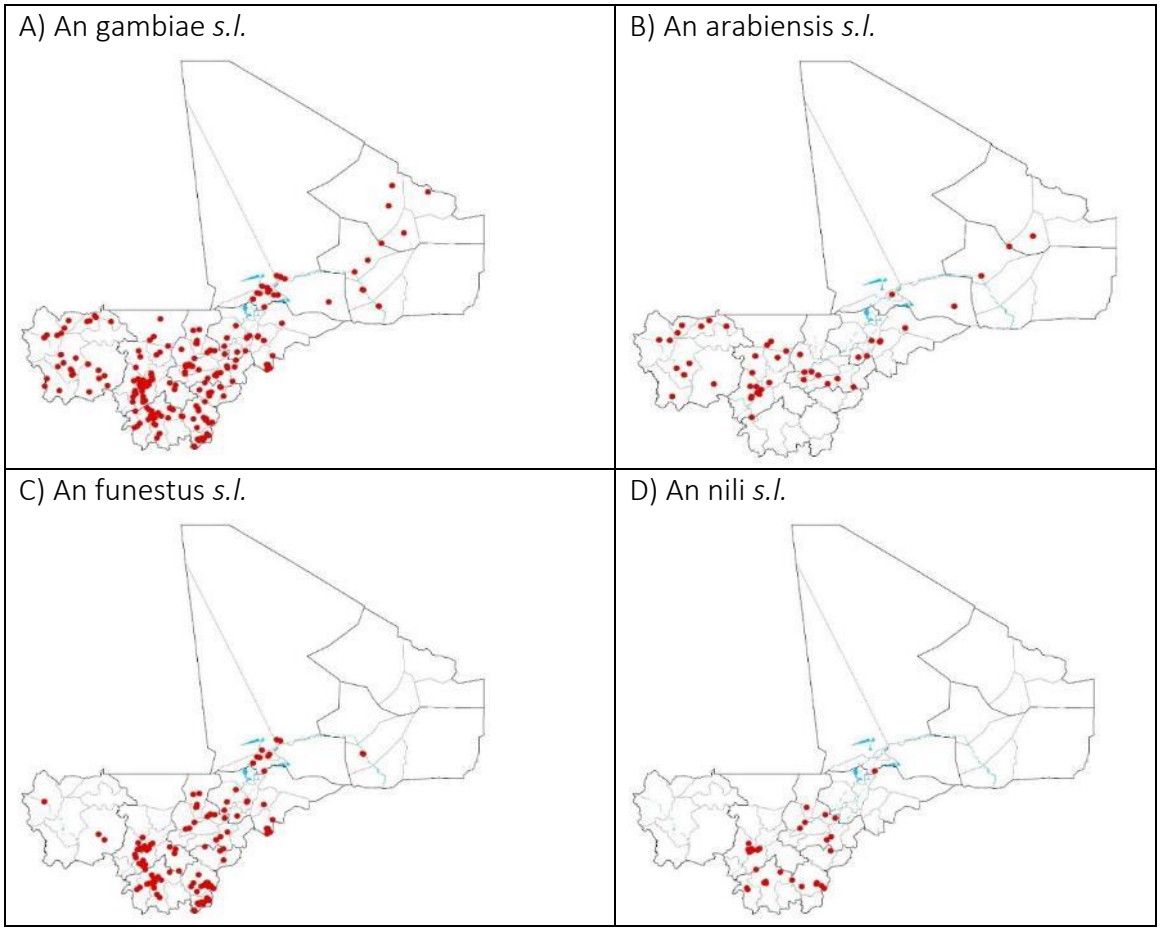
Each study site was geo-coded using methods described in Annex A.1.3. Data abstracted from each report included the start and end of the entomological survey, species identified at complex or species levels, whether adults or larvae were collected, methods of sampling (animal bait catches, bed net traps, CDC light traps, human landing catches, indoor resting searches, pyrethrum spray catches, exit traps, larval searches), methods of species detection (morphological keys, Polymerase Chain Reaction (PCR), Chromosome Banding Sequences (CBS), DNA probes or enzyme electrophoresis) and the full citation source. All species and sibling species names were recorded whether implicated in transmission or not. Care was taken to ensure that sites that were reported several times by the same or different authors in different reports were collapsed to single site records with multiple citations. Records at the same site were included multiple times only when separated by at least three years. A complete database is provided with this report.

5.4. The Anopheles distribution database

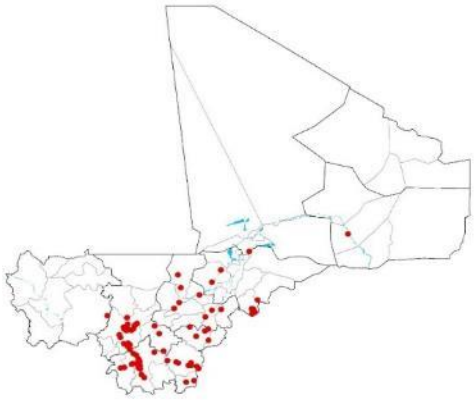
The final database contained 358 site/time specific reports of anopheline malaria vector occurrence between 1906 and 2007. A total of 222 (62%) sites were investigated before independence in 1960 and the rest between 1960 and 2007. The distribution of the vectors whose presence has been described (figure 5.1) in Mali are as follows:

An. coustani coustani Laveran, 1900
An. coustani tenebrosus Donitz, 1900
An. coustani ziemanni Grünberg, 1902
An. funestus Giles, 1902
An. gambiae Giles, 1902
An. hancocki Edwards, 1929
An. leesoni Evans, 1931
An. longipalpis Theobald, 1903
An. maculipalpis Giles, 1902
An. nili Theobald, 1904
An. obscurus Grunberg, 1905
An. paludis Theobald, 1900
An. pharoensis Theobald, 1901
An. pretoriensis Theobald, 1903
An. rhodesiensis Theobald, 1901
An. rivulorum Leeson, 1935
An. rufipes Gough, 1910
An. squamosus Theobald, 1901
An. wellcomei Theobald, 1904
An. ziemanni Grunberg, 1902

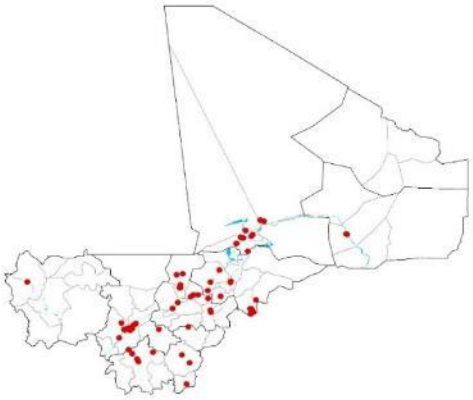
Figure 5.1: Spatial distribution of reported observations from 1906 – 2007 of adult or larval stages of a) *An gambiae* s.l.; b) *An arabiensis* s.l, c). *An funestus* s.l., d) *An nili* s.l., e) *An coustani*, f) *An pharoensis,* , g) *An rufipes.*



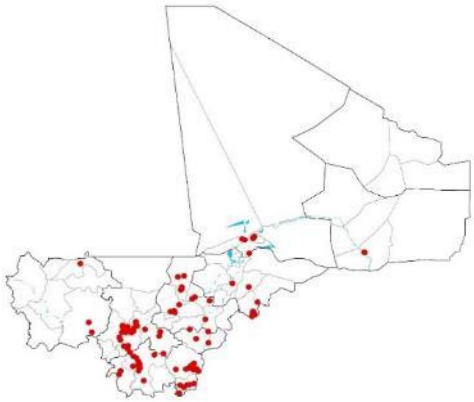
E) An coustani



F) An pharoensis



G) An rufipes



Anopheles gambiae s.l. (Figure 5.1.a and b; 284 site-time identifications): For older survey data it is recognized that there is a degree of taxonomic ambiguity. The *Anopheles gambiae* complex was only fully categorised in 1998 following the genetic distinction of *An. quadriannulatus* species B and designated a separate species after this date [Hunt et al., 1998; Harbach, 2004]; recently named *An. amharicus* [Coetzee et al., 2013]. The *Anopheles gambiae* complex comprises eight members of which *An. gambiae*, *An. coluzzii* and *An. arabiensis* are major malaria vectors, *An. merus*, *An. melas* and *An. bwambae* are minor/localised vectors, and *An. quadriannulatus* and *An. amharicus* are not known to transmit malaria. *An. melas, An. merus*, *An. amharicus* and *An. bwambe* have not been described in the Mali. Given that the majority of the data pre-date effective taxonomy between the sibling species of the complex [Marneffe & Sautate 1944 a,b] 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 Mali [Toure et al 1998; et al 2008]. Understanding whether the *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 period 4-8 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 [Lehmann et al 2010]. 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 supporting this conclusion.

Anopheles 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* 6 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 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 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 utilize a variety of habitats including slow flowing, partially shaded streams, large and small natural and man-made habitats, turbid waters and there are reports of larval identification in 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 indoor residual spraying control showing 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.

In the Sahelian zones of Mali, a study using a mark-release-recapture method showed that *An. gambiae* aestivates during the dry season [Lehmann et al., 2010]. Within five days of rains and before new mosquitoes could breed the mosquito population had dramatically risen several fold. Some of the mosquitoes that were marked at the beginning of the dry season were among those recaptured during the rains. This phenomenon is now considered to behind sudden upsurge in malaria cases after the rains in the acutely Sahelian belt.

Anopheles funestus (Figure 5.1.c: 153 site-time identifications): The exact composition of the *An. funestus* complex (*An. funestus* s.s., *An. parensis*, *An. vaneedeni* and *An. rivulorum*) remains unclear without molecular identification techniques. Only *An. funestus* s.s. is implicated in transmission, while other sibling species have either no role or only limited roles in transmission. We have assumed that reports of *An. funestus* were 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 swamps, large ponds and 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 hours). Endophilic resting and endophagic feeding behaviours are also commonly reported, and these characteristics are responsible for rapid disappearance of this vector following expanded indoor residual spraying and insecticide-treated nets. 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 (Figure 5.1.d: 31 site-time identifications): 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 savannas and degraded rainforest areas but the complex in the Mali appears to have a distinctive genetic structure [Ndo et al., 2010]. It is considered to be strongly anthropophilic [Gillies and de Meillon, 1968; Costantini and Diallo, 2001; Awono-Ambene et al., 2004; Dia et al., 2003; Antonio-Nkondjio et al., 2002; 2006], and will readily feed both indoors and outdoors [Carnevale and Zoulani, 1975; Krafsur, 1970; Coene, 1993; Brunhes et al., 1999]. 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 at times highly zoophilic [Carnevale et al., 1975; Krafsur 1970]. *An. nili* is usually responsible for transmission in villages close to rivers, but its abundance rapidly decreases within a few kilometres from the breeding sites [Brunhes et al., 1999]. 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* [Carnevale and Zoulani, 1975; Antonio-Nkondjio et al., 2006; Awono-Ambene et al., 2009].

Anopheles coustani (Figure 5.1.e: 92 site-time identifications): *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 typical form [Hamon, 1951]. Larvae are found in extremely varied locations: swamps, ponds, edges of lakes and rivers, rice fields, grassy pools temporary, hollow rock, *etc.* 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 until 4°C overnight (*An. coustani typicus*) [Gilles and De Meillion, 1968]. Adults are exophilic over most of its range and it is known to enter lighted tents probably for the purpose of resting [Haddow, 1945]. *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 [Fornadel et al., 2011]. *An. coustani* s.l. has been shown to display both exophagic tendencies, along with early evening foraging behavior in Zambia [Fornadel et al., 2011], Nigeria [Hanney, 1960], Mozambique [Mendis et al., 2000] and Ethiopia [Taye et al., 2006]. *An. coustani* displays peak biting outdoors before 21:00, being most active from 20:00 to 21:00 with its biting activity steadily declining throughout the night. The combination of outdoor and early evening foraging behavior for this species could increase its potential as a secondary vector in areas where indoor control measures such as indoor residual spraying or ITNs are employed. The *An. coustani* complex in Macha, Southern Zambia, has demonstrated unexpectedly high anthropophily.

Anopheles pharoensis (Figure 5.1.f: 77 site-time identifications): *An. pharoensis* is primarily a species of large vegetated swamps; also found along lakeshores and among floating plants, reservoirs, rice fields, streams, ditches and overgrown wells. Largely a swamp breeder throughout its range; Schwetz (1941) found it in very large numbers associated with the aquatic weed *Ceratophyllum demersumIt*. It is a variable species both in morphology and bionomics, adults have varying behaviors depending on the region in which they are found; sometimes anthropophilic,

sometimes zoophilic, sometimes endophilic or exophilic [Zahar, 1975; 1989; Mouchet et al., 2008]. *An. pharoensis* bites humans and animals indoors or outdoors, and rests outdoors after feeding [Mouchet et al., 2008]. It feeds from dusk to dawn with a peak at about 01:00h. A peculiarity of *An. pharoensis* is 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 [Carrara et al., 1990] to 1.3% in Kenya [Mukiama and Mwangi, 1989].

Anopheles Rufipes (Figure 5.1.g: 144 site-time identifications): This is a predominantly savanna mosquito and breeding sires are varied, usually sunny or in light shade [Holstein 1950, 1951, Hamon and Mouchet 1961; Hamon et al 1961b]. It is of three forms (i*ngrami,* Edward 1929; *seneveti*, Rioux, 1959, and *brucechwatti*) [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 [Hamon et al 1961b; Holstein et al 1961]. In Mali this vector was observed in several areas including Bamako and was present in large numbers in homes, rivers, ponds, rice paddies, swamps, irrigated crops, hollow rocks, and residual stream [Holstein et al 1961]. In a study in neighbouring Burkina Faso, almost 12% of mosquitoes captured in a Savanna village were *An. rufipes* with an estimated infectivity rate of 1.2% [Da et al 2013]. Although it is unclear the extent of its contribution to malaria transmission, given its frequency, especially during the dry season *An. rufipes* is likely to be an important malaria vector in the Sahelian region.

5.5. Insecticide resistance in Mali

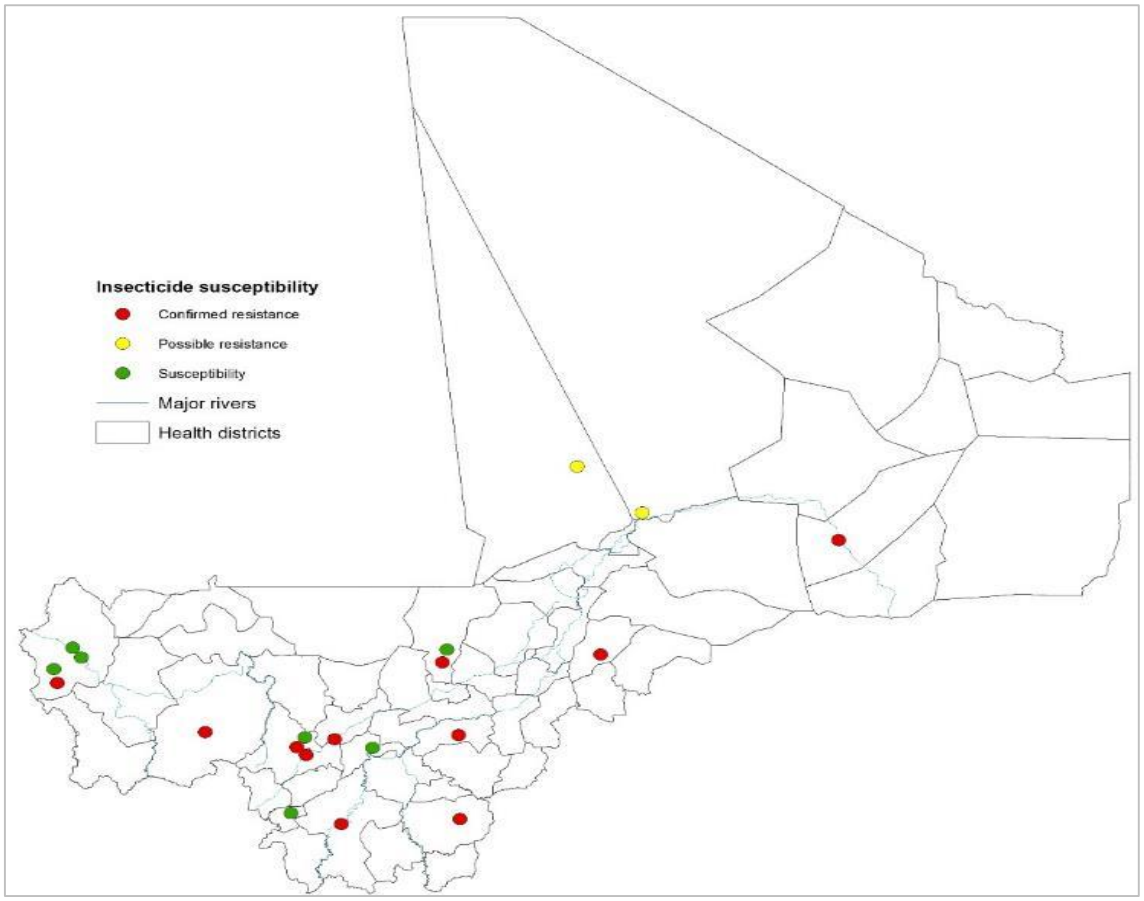
A study around the Selingue hydroelectric dam shows that the *An. gambiae* complex were susceptible to DDT, orgnophosphates (temephos, chlorpyrifos, fenthion, fenitrothion and malathion) but resistant to dieldrin [Toure 1984]. The presence of pyrethroid resistance of the knock-down resistance (kdr) type were tested in samples collected in Bamako and Sikasso of the *An. arabiensis* and the Mopti, Savanna and Bamako chromosomal forms of *An. gambiae* areas. This study reported that the *kdr* allele was associated with Savanna form and was presented in samples dating back to 1987 [Fanello et al 2003]. A subsequent study, however, showed an increasing frequency of kdr allele and its presence in the Bamako form and absence in the M form of the *An. gambiae* [Tripet et al 2007].

Since early 2000 pyrethroids have been used extensively to impregnate mosquito bed nets and for indoor residual spraying in Africa [WHO 2012]. This pressure on the vector has led to emergence of pyrethroid resistance and the mitigation of its spread is now a WHO priority [WHO 2012]. Between October 2000 – March 2001 a joint mission was undertaken by the entomological team of the MRTC and the PNLP in the hydroelectric dam area of Selingué and in the irrigated rice cultivation area of Niono, Office du Niger, to investigate the susceptibility of the main malaria mosquito vectors to insecticides [PNLP- unpublished data].This mission was part of the technical support framework of the MRTC to the PNLP through a USAID and WHO grant. In Sélingué four villages (Sélinkényi, Binko, Fazan, and Kibarou) were selected. In Niono area, two villages were chosen in each of three zones: the villages of Niessoumana (N6bis) and Ténégué (N10) in the Niono zone; the villages of Nionokoroni and Sokourani in the Modolo zone; and the villages of Siengo and Sarango (B4) in the zone of N'Débougou. The WHO-recommended method (WHO/VBC/81.806) was used to test malaria vectors susceptibility to insecticides. The local vector

populations were assayed for the four main insecticides used by the PNLP. The exposure time was one hour, with discriminatory doses of 0.75% for Permethrin; 0.05% for Deltamethrin and Lambdacyhalothrin and 4% for DDT. The species tested were *Anopheles gambiae s.l.* and *An. funestus.* All the *An. gambiae s.l.* at Selinkenyi were susceptible to the four different insecticides. The few Anopheles funestus tested with Permethrin were also susceptible. In Niono area, the *Anopheles funestus* specimens were susceptible to the four different insecticides. *An. gambiae s.l.* were also susceptible to the four different insecticides, but showed a lower mortality to DDT at Siengo, Sarango (B4) and Ténégué.

In 2002 the susceptibility of malaria vectors to permethrin 0.75%, deltamethrin 0.05%, Lambdacyhalothrin 0.05% and DDT 4% insecticides used for impregnating nets the distribution of the mutant gene *kdr* in vector populations in the Selingue rural zone of Mali was evaluated [Diarrassouba 2003]. Susceptibility tests were carried out with *An. gambiae s.l.* and *An. funestus* females in natural conditions. The population of tested *An. gambiae s.l.* were composed of 96% of *An. gambiae s.s.* and 4% of *An. arabiensis*. Remanence tests were carried out with permethrin impregnated bed nets according to the standard WHO method. In a flood zone, the vectors were susceptible to all tested insecticides, but in a drought zone, *An. gambiae s.l.* was resistant to permethrin and to DDT. This vector had a reduced susceptibility to deltamethrin and to lambdacyhalothrin. Knock-down time was shorter in the flood zone than in the drought zone, where a high level of resistance to insecticide was observed. *Kdr* gene was found only at Pimperena (drought zone) and uniquely in the form S of *An. gambiae s.s.* species. The efficacy of impregnated bed nets after six (6) months of use confirmed the high susceptibility of mosquitoes to permethrin in the Selingue rural zone [Diarrassouba 2003]. Another study in two rural sites in Mali showed mosquito mortality rates of about 28% in Koumantou and 52% in Selingue [Fane et al 2012]. In another study of the *An. gambiae s.l.* in 14 sites in Mali showed resistance to DDT in 8/14 sites and to pyrethroids in almost all sites [Vestergaard 2011]. However, the vector was susceptible to fenitrothion and bendiocarb in at least 13 sites. Figure 5.2 show the distribution of study locations and levels of resistance to pyrethroids in the *An. gambiae sl* vector in Mali obtained from the insecticide resistance (IR) mapper (http://www.irmapper.com/). The map indicates widespread resistance to pyrethroid in the dominant malaria transmitting vector in Mali.

Figure 5.2 Map of the distribution of study locations and levels of resistance to pyrethroids in the *An. gambiae sl* vector (Source: http://www.irmapper.com/).



6. ITN and IRS coverage 2000-2013

6.1. Background to insecticide treated net (ITN) distribution 2000-2014

By 2002, the use of insecticide treated mosquito nets (ITNs) was seen as a key preventive tool for malaria control in Mali [PNLP 2005]. 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 early countries in Africa to be supported [NetMark doc]. Between 2003 and 2006 substantial reduction in unit cost of ITNs had been shown in the commercial retail sector through the NetMark project that increased availability of nets in the private sector by working with large net manufacturers and a voucher scheme in one district. In addition the Mali government had accepted the removal of taxes on ITNs. By December 2006 when the project closed, over 300,000 ITNs had been distributed in Mali [PMI 2008 report].

In 2006, the Ministry of Health (MoH) issued a decree that ITNs be provided free-of-charge through public health facilities for children under five years and pregnant women. In addition a second five year decree to remove all national taxes and tariffs on imported LLINs and insecticides for net retreatment was issued by the government. Between the period 2004-2007 a PSI led project distribution over 650,000 net retreatment kits in Mali in both the public and private sectors [PMI 2008 Report].

By December 2007, however, mass free distribution of long lasting insecticidal nets (LLINs) began in Mali through the largest-ever integrated national health campaign in country which also included the delivery of polio and measles vaccines for children under five, vitamin A supplements, and albendazole for deworming, to children under five and their mothers [PMI 2009 report]. Almost 2.3 million LLINs were distributed through this campaign with support from PMI, the Canadian Red Cross, the United Nations Foundation, Malaria No More, WHO, UNICEF, and other organizations. The campaign excluded Tombouctou and Gao regions, which were covered in a subnational campaign in June 2007 in which 220,000 free LLINs were distributed with support from PMI [PMI 2009 Report].

In 2008 universal coverage with LLINs of one net for every 1.8 persons was adopted as a goal in Mali in which free mass campaigns would be implemented together with routine distribution to children and pregnant women at health clinics. These initiative was to be supported primarily by PMI-USAID, the Global Fund, the Government of Mali and to a lesser extent other partners such as the Red Cross, Malaria No More and UNICEF. In 2008, PMI procured 600,000 LLINs targeting pregnant women and children less than one year of age through routine services at health facilities while UNICEF, Global Fund Round 6 and World Bank contributed an additional 500,000 LLINs to support annual routine services [PMI 2010 Report].

In 2009 the NMCP submitted a Global Fund Round 9 application that included a budget for procuring and distributing 13.8 million LLINs between 2010-2013 through two mass campaigns that were planned for 2010 and 2013. However, by 2010, this had not happened. Instead, PMI had procured 570,000 LLINs for distribution by September 2010 through routine services to pregnant women and children less than one year of age attending ANC and EPI clinics [PMI 2011 Report]. In 2011, over 750,000 LLINs were distributed through routine distribution.

A rolling phased campaign began in April 2011 starting with Sikasso Region. As of June 2013, more than 4.4 million LLINs, 3.9 million were provided by PMI were distributed in Sikasso in 2011, Segou in 2012 and Mopti in 2013. In two districts in Koulikoro and Kayes distribution took place in 2013. UNICEF provided 70,000 nets for the three northern regions in 2013. In 2014, 2 million nets were distributed in Sikasso region to replace the nets distributed in 2011. Free mass campaigns are planned in Bamako district and the three northern regions of Gao, Tombouctou, and Kidal and the region of Segou [PMI 2012, 2013, 2014 reports].

6.2. Changing coverage of ITNs nationally

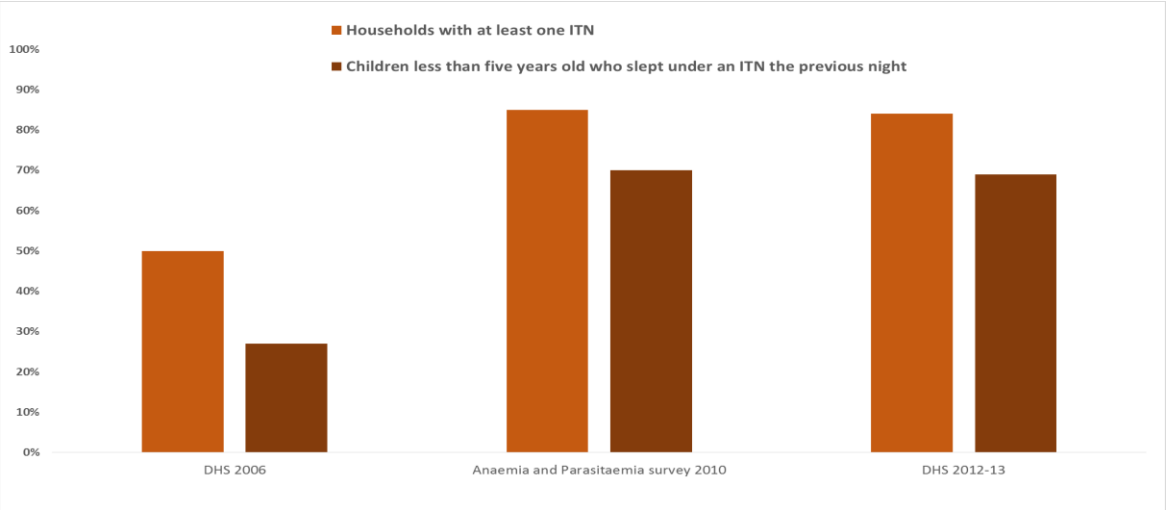
Since 2003, three large scale, national household surveys, with information on the proportion of persons of all ages sleeping under an ITN the night before survey, have been undertaken in Mali (Table 6.1). The details of the survey sampling procedures and sample sizes are provided are found in the MEASURE DHS website [http://dhsprogram.com/data/available-datasets.cfm].

Table 6.1 Summary of large scale household survey data with information on persons sleeping under an ITN the night before survey. The DHS 2012-13 did not include the three northern regions of Tomboctou, Gao and Kidal due to security reasons.

Survey	Clusters	Households	Persons	Age group for ITN coverage information	Source
DHS 2006	410	12,998	71,197	All ages	MEASURE DHS
Anaemia and Parasitemia survey	110	1617	9,624	All ages	MEASURE DHS
DHS 2012-13	415	10,105	57,153	All ages	MEASURE DHS

The results of household ITN ownership and use by residents are summarized in Figure 6.1 indicating that Mali is close to achieving its universal coverage targets for the current national strategy.

Figure 6.1 A national summary of the proportion of households with at least one ITN and the proportion of persons of all ages sleeping under an ITN the night before survey by year. The DHS 2012-13 did not include the three northern regions of Tomboctou, Gao and Kidal due to security reasons. Further details of ownership of ITNs are shown in the survey reports of 2006, 2010 and 2013.



6.4. Modelling spatial aggregates of ITN coverage using Small Area Estimation

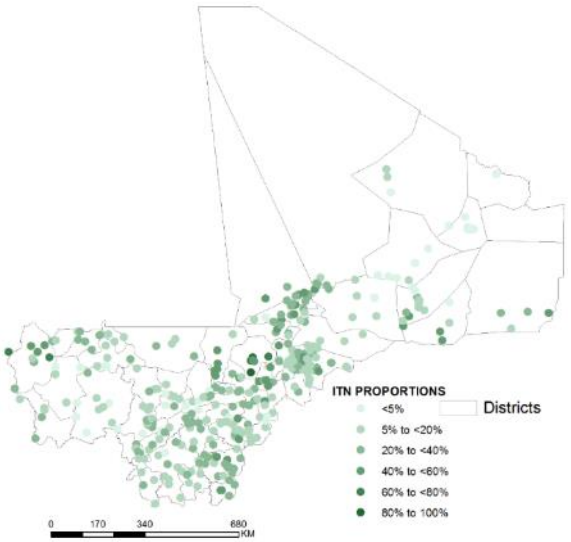
Typically, national household surveys are designed to be precise at national and regional levels and rarely at lower levels such as districts. These surveys are, however, useful at tracking change at national and administrative 1 units. Simply aggregating the survey data to provide district level estimates of an outcome of interest will lead to values of low precision. District level estimates, however, are more important to planners in order to accelerate policy interventions, optimise inputs and improve coverage of health interventions.

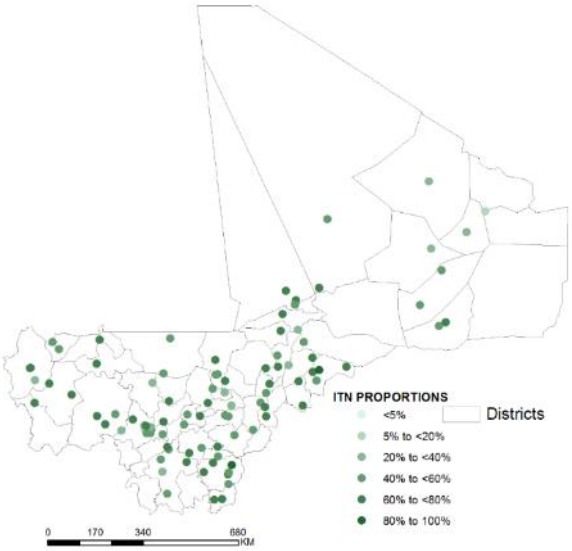
Small Area Estimation (SAE) methods handle the problem of making reliable estimates of a variable at these areal units under conditions where the information available for the variable, on its own, is not sufficient to make valid estimates [Rao et al., 2003; BIAS, 2007]. We have used hierarchical Bayesian spatial and temporal SAE techniques using a geo-additive regression approach [Banerjee et al., 2004; Best et al., 2005; Fahrmeir and Lang 2001; Kamman and Wand 2003] to estimate the ITN coverage by district for the years 2006, 2010 and 2013 using the data from the three national surveys described in section 6.2. The prediction was made for all age groups, as this represents an important indicator for universal coverage and necessary when computing likely impacts on malaria transmission [Smith et al., 2009; Griffin et al., 2010]. Details of model procedures and accuracy metrics are presented in the Annex B. The results are shown in Figure 6.2 with sensitivity of district level predictions shown in Annex Figure B.1 as standard deviations of predicted means.

Data on ITN coverage were first aggregated for each survey cluster and information on the region, health district, year of survey, the number of persons interviewed and the number who slept under an ITN the night before survey (coverage) and the total ITNs in the household were summarized. Each cluster and health district was assigned unique identifiers. These cluster level data were then used to develop small area space-time estimates of ITN coverage at the health district for the years 2006, 2010 and 2013. Data were modelled separately as irregular mass campaigns preceding the surveys and without information on ITN distribution volumes per districts it was difficult to model data within a single space time model.

Figure 6.2 The location of survey clusters showing the observed ITN coverage among sampled populations during the: a) DHS 2006; b) Anemia and parasitaemia survey of 2010; and c) DHS 2012-13. The DHS 2012-13 did not include the three northern regions of Tomboctou, Gao and Kidal due to security reasons.

a) b)


ITN PROPORTIONS
<5%
5% to <20%
20% to <40%
40% to <60%
60% to <80%
80% to 100%
Districts
0 170 340 680
KM


ITN PROPORTIONS
<5%
5% to <20%
20% to <40%
40% to <60%
60% to <80%
80% to 100%
Districts
0 170 340 680
KM

c)

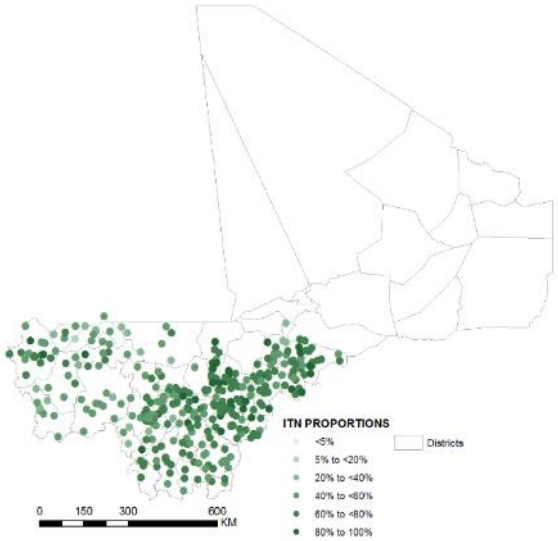
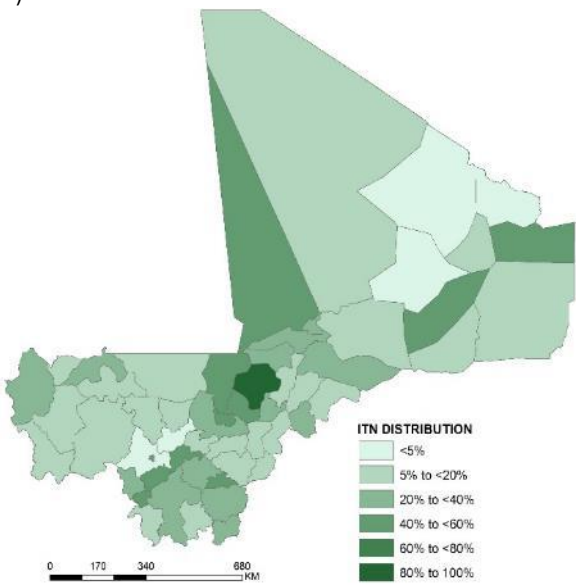
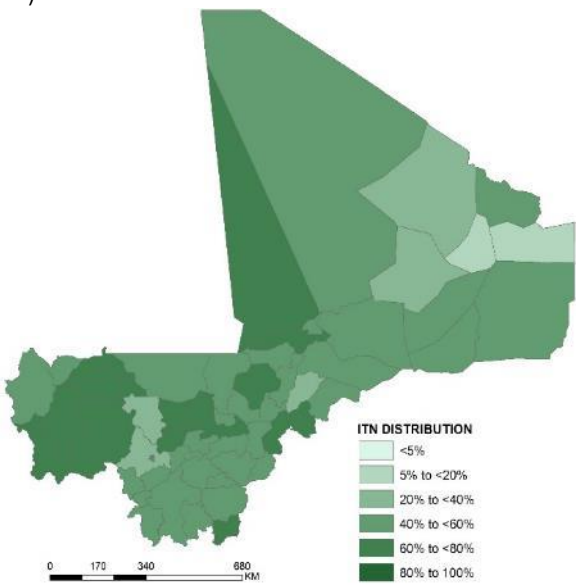

ITN PROPORTIONS
<5%
5% to <20%
20% to <40%
40% to <60%
60% to <80%
80% to 100%
Districts
0 150 300 600
KM

Figure 6.3 The estimated mean ITN coverage among all ages using small-areas estimation methods by health districts using data from the: a) DHS 2006; b) Anemia and parasitaemia survey of 2010; and c) DHS 2012-13. The DHS 2012-13 did not include the three northern regions of Tomboctou, Gao and Kidal due to security reasons (grey) due to security reasons and therefore no ITN coverage estimates are available for 2013.

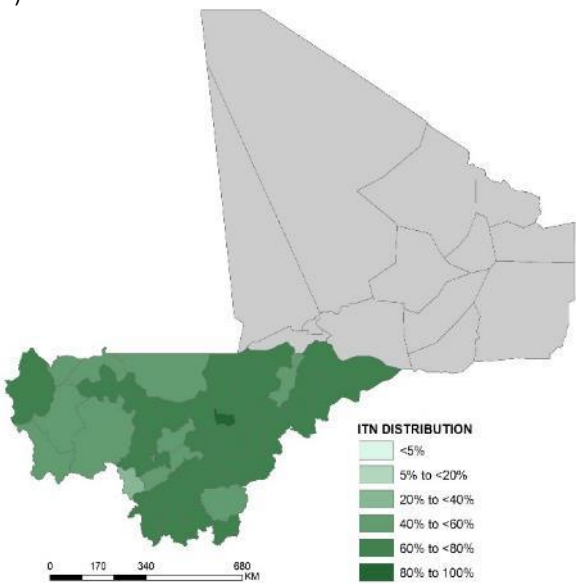
a)



b)



c)



6.5. Indoor Residual Spraying of houses

Spraying with insecticides has a long history in Mali although it was never implemented at large scale nationally. As early as 1904, the 'hygiène prophylactique' began as a set of environmental interventions to reduce mosquito populations in European and Africa settlements in mainly urban areas such as Bamako and Kayes [Le Masle 1904; Giles-Vernick 2008]. These efforts picked up when the Office du Niger was initiated by the French to tap water through a system of dams and canals to irrigate land on the north of Niger for rice and cotton production [van Beusekom 2002,

Echenburg and Filipovitch 1986; Giles-Vernick 2008]. In the 1940s, in addition to chemoprophylaxis, spraying od breeding sites during household visits was the main intervention against malaria in Mali [Colonie du Soudan Francais 1949]. Household spraying with DDT began in 1950 and continued to 1957 [Colonie du Soudan Francais 1950; Colonie du Soudan Francais 1957; Giles-Vernick 2008]. However, by 1978 the vertical programmes were beginning to unwind and malaria became embedded in the primary health care system. Presumptive treatment of febrile patients became the main approach to controlling malaria in the country [PNLP 2001].

By the time the PNLP was established, there was no operational program for IRS in Mali although the national strategies recommended its use in epidemic prone areas. In 2008 PMI began to support IRS scale up in two distrcts, Bla and Koulikoro, in conjunction with PNLP efforts at larviciding. These two districts had an estimated population 406,000 people in 87,200 households [PMI 2009 Report]. Lambda-cyhalothrin (ICON-CS®), a pyrethroid, was the insecticide choses for IRS. In 2011, Baraoueli became the third district supported for IRS by PMI protecting a combined population of 700,000 in the three districts (Figure 6.5) [PMI report 2014]. An almost 100% coverage have been achieved to so far (Table 6.2)

Figure 6.5: Districts targeted for IRS through PMI support in Mali. 1= Koulikoro, 2= Baraoueli, 3= Bla.

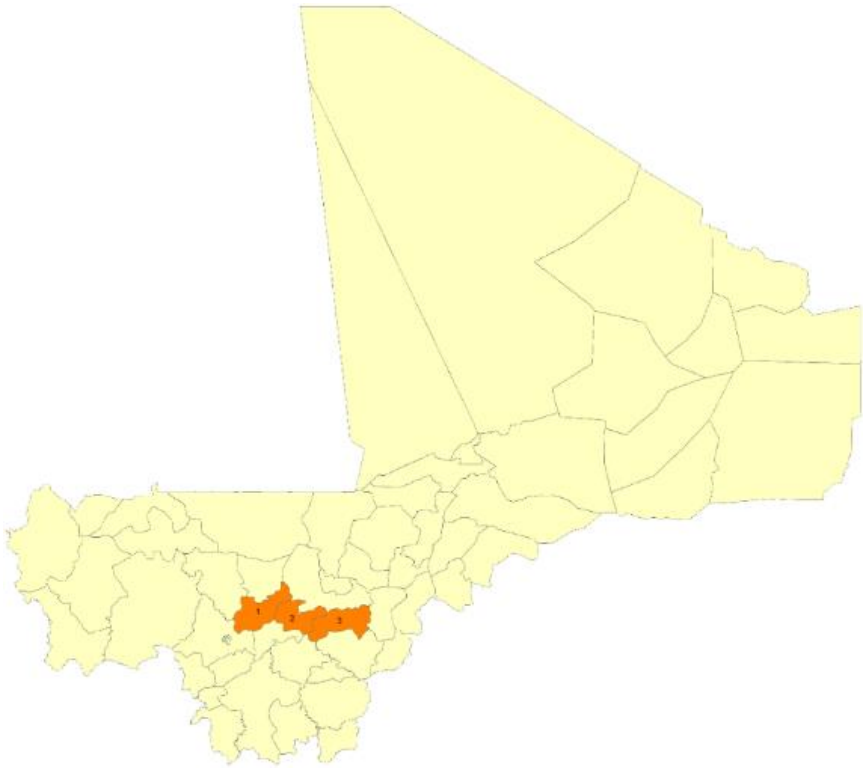


Table 6.2 The coverage of IRS in the three targeted districts of Mali from 2010-2014

District	Year	Eligible Structures	Structures sprayed	Population protected
Koulikoro	2011	52, 565	51,140	
	2012	53,404	51,405	191,271
	2013	65,711		234,735
	2014	62,491		223,012
Bla	2011	87, 222	85,617	
	2012	87,145	86,311	314,367
	2013	102,453		368,492
	2014	97,989		334,115
Baraouéli	2011	69, 211	66, 064	
	2012	69,668	68,579	256,508
	2013	72,329		251,404
	2014	73,226		279,441

7. Seasonal Malaria Chemoprevention – target districts and populations from 2014-2015

7.1. Background

Seasonal Malaria Chemoprevention (SMC) recognizes the potential to protect children from the acute seasonal risk of new infections in areas where vector proliferations are concentrated within a few months of every year [Meremikwu et al., 2012]. Combinations of drugs, with at least one partner drug having a long-half life, offer opportunities to reduce the clinical consequences of new infections within a short window of transmission [Greenwood et al., 2011; Wilson et al. 2011; Meremikwu et al., 2012]. Clinical burdens in acutely seasonal transmission areas are high as they are more adapted to synchronized infections leading to higher host parasite densities [Mckenzie et al., 2001] and because young children have poorly designed clinical immunity, due to widely spaced natural immunization [Caniero et al., 2010; Greenwood et al., 1991]. According to a recent Cochrane review of the efficacy of SMC, prophylaxis of children with SP+AQ under the age of five years in areas of marked seasonal malaria transmission resulted in 75% reduction in both overall and severe malaria episodes [Meremikwu et al., 2012].

In Mali, a randomized cohort study in Bandiagara district children in one arm were given a treatment dose of SP and the other received no treatment at the beginning of the transmission season [Coulibaly et al., 2002]. Although the study showed that age-specific incidence of clinical episodes was similar between the two groups, those who received intermittent preventive treatment (IPT) with SP had a delayed median time to first clinical episode while parasite densities during disease episodes were lower in the treatment group. A subsequent study showed that in Kambila district of Mali, IPT with SP reduced overall malaria incidence by almost 43% among children 6 months to 20 years [Dicko et al 2008].

In February 2012, the World Health Organization approved a recommendation for the use of sulphadoxine-pyrimethamine plus amodiaquine (SP-AQ) at monthly intervals for SMC for children aged 3-59 months, principally in the Sahelian region of Africa [WHO, 2013]. In September 2012, the Nouakchott Initiative was launched to coordinate the SMC response in eight countries that occupy the Sahel and sub-Sahel: Burkina Faso, Chad, The Gambia, Senegal, Mali, Mauritania, Niger and nine northern States in Nigeria [RBM, 2012]. In these countries, it has been estimated that 16.3 million children below the age of five years reside in areas of stable, *Plasmodium falciparum* transmission locations that would support an average annual incidence of 1 clinical attack per 10,000 children per year and 60% of annual rainfall is concentrated in three continuous months [Cairns et al., 2012].

Consequently, the MSF Mali and the PNLP began an SMC implementation pilot project in Koutiala health district in Sikasso region covering an area of 42 health treatment centres and 26 villages [http://www.msf.fr/sites/www.msf.fr/files/201307_smc_mali_-eng.pdf]. The first round started in August 2012 using door-to-door and fixed site distribution approaches. There were distributions every four weeks ending October 2012. The study showed huge reductions in pediatric uncomplicated malaria cases, hospitalizations and deaths compared to estimates a four weeks preceding the intervention. Average cost of intervention was estimated to be 4.5 Euros per child for four rounds.

The potential size of the target population likely to benefit from SMC is a useful advocacy tool to mobilize international resources and set priorities for new control tools. This requires finer resolution, higher precision data on the location of human population, the distribution and characteristics of malaria risk and resolved to health sector units of information that can be used to effectively plan and resource requirements.

In 2014, the INFORM project was commissioned by the Clinton Health Access Initiative (CHAI) to undertake analysis of the spatial targeting of seasonal malaria chemoprevention in eight countries of the sub-Sahel including Mali with funding support from the RBM and DFID [Noor et al 2014b]. Here we present a summary of this work specific to Mali to improve the precision of targeted SMC across health districts using higher resolution, more precise estimates of intrinsic transmission intensity potential adjusted to the location of human population and configured to decision-making units necessary in each country to plan and allocate resources.

7.2. Methods and outputs

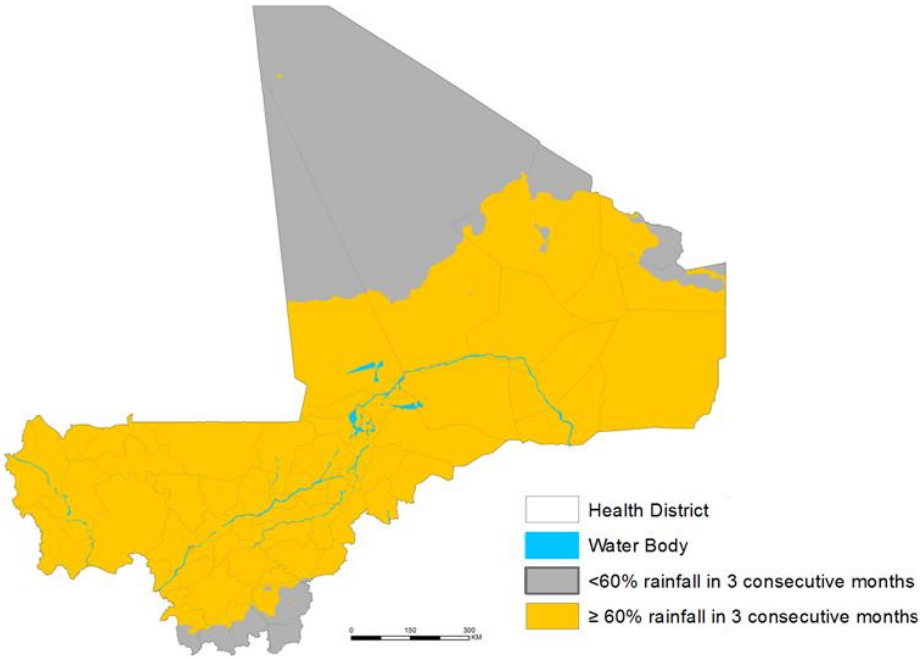
7.2.1. Overview of methods

We have used layers of modelled spatial information in a step-wise approach to identify the target childhood populations within health administrative units most likely to benefit from SMC during the malaria transmission seasons of 2014 and 2015.

The process began by creating an seasonality surface for the Sahel where areas where at least 60% of annual rainfall is concentrated in three continuous months were defined as acutely seasonal [Cairns et al., 2012]. To generate this surface, dekadal (10 day) Africa Rainfall Estimates version 2 (RFE 2.0) data from 2002-2009 at 10 × 10 km spatial resolution [NOAA, 2013][12]. These RFE gridded data were then resampled to 1 x 1 km spatial resolution. These data were then combined generate monthly RFE surfaces by year and an synoptic monthly average RFE was obtained from the 14 year data series. The total rainfall for each three overlapping blocks of months were computed and the percentage of rainfall of the annual average RFE occurring in each block was computed. Areas where 60% of annual rainfall occurred in at least one block of three continuous months were defined as acutely seasonal. This seasonality surface was used together with the 1 x 1 km spatial resolution population distribution map (Figure 2.5) to compute the proportion of population in the newly reconfigured health districts (Figure 2.6) to define the proportion of population in 2010 that lived in areas that were seasonal. Districts were then classified as seasonal if ≥80% of the population lived in areas where at least 60% of the annual rainfall occurred in three consecutive months (Figure 7.1).

[12] The dataset was developed as a collaborative programme between NOAA's Climate Prediction centre (CPC), USAID/Famine Early Systems Network (FEWS). The input data used for RFE2.0 rainfall estimates are obtained from 4 sources; 1) Daily Global Telecommunication Station (GTS) rain gauge data for up to 1000 stations which are then interpolated; 2) Advanced Microwave Sounding Unit (AMSU) microwave satellite precipitation estimates up to 4 times per day; 3) NOAA Special Sensor Microwave/ Imager (SSM/I) satellite rainfall estimates up to 4 times per day 4) GEOS Precipitation Index (GPI) cloud-top IR temperature precipitation estimates on a half-hour basis [NOAA CPC, 2001; Novella and Thiaw, 2012]

Figure 7.1: Map of health districts (n=60) in Mali showing areas (orange) where 60% or more of the annual total rainfall occurs in any three consecutive months. These areas are considered to have the seasonality threshold required for targeting with SMC. Areas shaded grey are those where less than 60% of the annual total rainfall occurs in any three consecutive months.



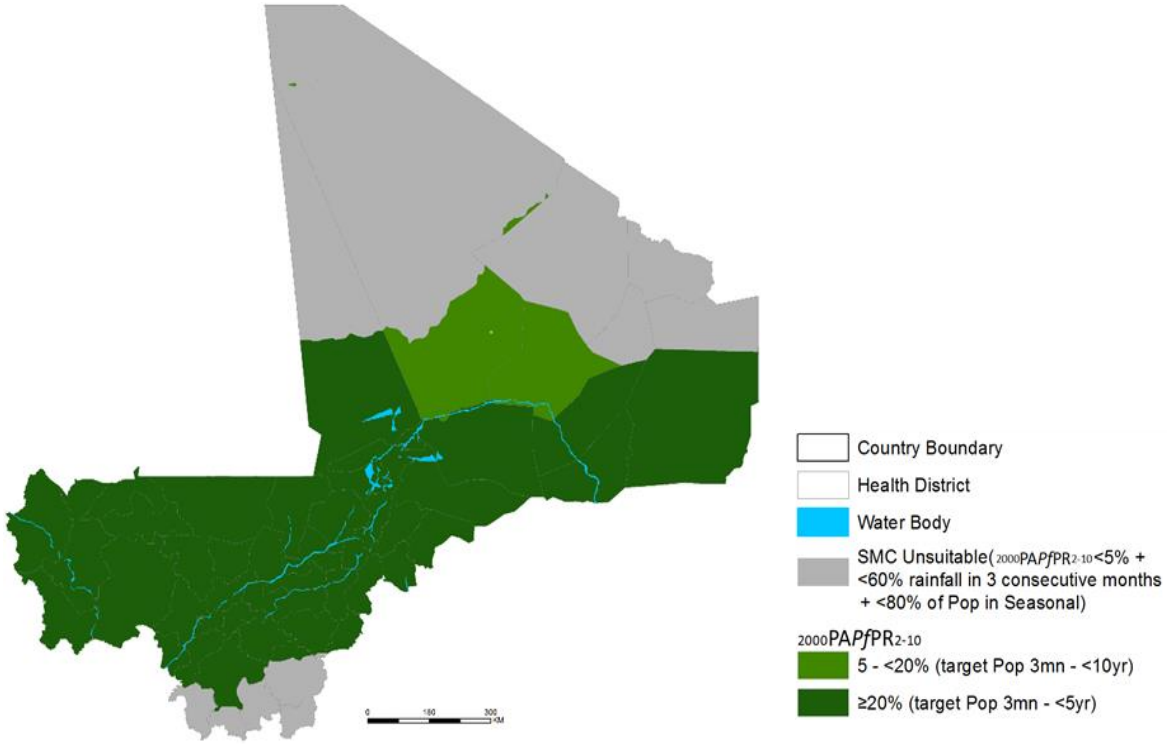
SMC has been targeted only where predicted infection risks are moderate-to-high; cross-sectional parasite rates in children aged 2-10 years (PfPR$_{2\text{-}10}$) greater than 8.8% and 17.3% corresponding to approximately 0.1 and 0.2 clinical attacks per child aged less than five years per year respectively [Cairns et al., 2012]. These criteria are, however, arbitrary with wide confidence margins based on limited clinical incidence data [Hay et al., 2010; Patil et al., 2009] and presume a level of endemicity prediction rarely possible based on the input data. What is evident is that areas of Africa that have historically supported transmission intensities characterised by PfPR$_{2\text{-}10}$ of less than 1% have comparatively very low disease burdens, clinical risks are equivalent across all age groups [Snow and Marsh, 2002] and very spatially focal [Cohen et al., 2010; Bousema et al., 2012]. As transmission intensity (PfPR$_{2\text{-}10}$) increases through its hypoendemic range [Metselaar and van Thiel, 1959], disease risks increase sharply and become more concentrated in young children [Snow and Marsh, 1995, 1998, 2002; Snow et al. 1997; Okiro et al., 2009].

Here we aim to predict areas that have an average predicted prevalence of PfPR$_{2\text{-}10}$ >= 5% across the Sahel, representing a close approximation to previous predictions of clinical incidence in young children of 0.1 clinical attacks per year. We have selected the year 2000, rather than a more contemporary year, as this is likely to represent the intensity of *P. falciparum* transmission before wide-scale investment in vector control including insecticide treated nets (ITN) and indoor residual house-spraying (IRS). The year 2000 also marks a prelude to a decade of drought in the sub-region [Hadley Centre, 2010], which while having posed a threat to other domains of health and survival, will have suppressed malaria transmission. For Mali, the population adjusted $_{2000}Pf$PR$_{2\text{-}10}$ ($_{2000}$PAPfPR$_{2\text{-}10}$) by health district (Figure 4.13) was used to reclassify district into those below or ≥5% $_{2000}$PAPfPR$_{2\text{-}10}$.

After the seasonality (Figure 7.1) and malaria risk thresholds were defined, the final step was implemented to use this information to identify health districts to be targeted for SMC in Mali.

Health districts identified as SMC targets were further classified into areas were $_{2000}$PA*Pf*PR$_{2\text{-}10}$ ≥5% to <20% to target children aged 3 months to 10 years; and $_{2000}$PA*Pf*PR$_{2\text{-}10}$ >20% to target children aged 3 months to 5 years (Figure 7.4). Estimates of the target population for 2014 and 2015 were extracted for each health district from the population raster surfaces in ArcGIS 10.1 (Table 7.1). The numbers of children age 3 to 59 months of age and 3 to 119 months of age in 2014 and 2015 were extracted per stable, endemic risk class suited for SMC per health administration unit using the *zonal statistics* function in ArcGIS 10.1.

Figure 7.4: Map of SMC health districts (n=52) in Mali. These districts are those where $_{2000}$PA*Pf*PR$_{2\text{-}10}$ is ≥5% and 80%* of the population live in areas where ≥60% or more of the annual total rainfall occurs in any three consecutive months). In addition, in SMC health districts where $_{2000}$PA*Pf*PR$_{2\text{-}10}$ is ≥5% - <20% children 3 months to <10 years of age are targeted for SMC while those her $_{2000}$PA*Pf*PR$_{2\text{-}10}$ is >20% only children 3 months to <5 years of age are targeted.



*In Mali although one health district (Tomboctou) on the margins of the Sahel had <80% of the population living in seasonal areas but had risk of >5% $_{2000}$PA*Pf*PR$_{2\text{-}10}$ it was nonetheless selected for SMC targeting as it was surrounded by districts that had met both the risk and seasonality criteria.

Table 7.1 is a list of 52 out 60 health district that met the seasonality, transmission and population density thresholds for SMC suitability. Only two districts (Bourem and Tombouctou) are had 5% to <20% PA*Pf*PR$_{2\text{-}10}$ in 2000 and would have required targeting of children 3 months to 10 years of age. For these reasons it is practical that across all 52 districts that are SMC suitable children 3 months to 5 years of age are targeted. Under this condition a total of 855,556 and 274,392 children in rural and urban areas respectively would be targeted for SMC in 2014. In 2015 these would have risen to 874,248 and 287,668 in rural and urban areas respectively.

Table 7.1: A summary of estimated children targeted for SMC in 2014 and 2015 by urban and rural in health district in Mali. In districts that have the seasonal profile but where $_{2000}$PA*Pf*PR$_{2\text{-}10}$ if 5%-<20% only children 3 months to 5 years are targeted. Children 3 months to 10 years are targeted in districts where $_{2000}$PA*Pf*PR$_{2\text{-}10}$ >= 20%.

			2014				2015			
Region	District	$_{2000}PAPfPR_{2-10}$	Rural 3 month to 5 years of age	Urban 3 month to 5 years of age	Rural 3 month to 10 years of age	Urban 3 month to 10 years of age	Rural 3 month to 5 years of age	Urban 3 month to 5 years of age	Rural 3 month to 10 years of age	Urban 3 month to 10 years of age
Bamako	1.Commune 1	40.19	619	21,999	1,145	40,695	650	23,092	1,204	42,768
Bamako	2.Commune 2	37.71	477	9,891	883	18,295	501	10,383	928	19,227
Bamako	3.Commune 3	35.43	293	12,205	541	22,575	307	12,812	569	23,725
Bamako	4.Commune 4	42.92	4,738	14,374	8,765	26,590	4,855	15,067	8,991	27,907
Bamako	5.Commune 5	37.95	762	22,054	1,409	40,794	799	23,150	1,479	42,871
Bamako	6.Commune 6	44.44	2,479	35,785	4,588	66,239	2,582	37,553	4,786	69,594
Gao	7.Ansongo	71.11	6,450	438	11,344	771	6,599	460	11,619	810
Gao	8.Bourem	16.73	1,396	80	2,651	152	1,423	84	2,705	160
Gao	9.Gao	28.51	3,059	1,871	5,677	3,473	3,113	1,950	5,783	3,623
Gao	10.Menaka	30.79	615	147	1,151	276	627	154	1,174	288
Kayes	11.Bafoulabe	69.72	22,169	1,539	40,672	2,823	22,620	1,614	41,548	2,965
Kayes	12.Diema	48.64	15,883	1,874	28,943	3,415	16,271	1,964	29,685	3,583
Kayes	13.Kayes	42.01	23,977	9,775	45,153	18,409	24,519	10,239	46,230	19,306
Kayes	14.Kenieba	56.36	19,730	1,922	36,493	3,556	20,127	2,016	37,273	3,734
Kayes	15.Kita	60.87	43,953	2,843	79,847	5,165	44,857	2,983	81,584	5,425
Kayes	16.Nioro	41.20	11,410	2,911	21,808	5,564	11,660	3,048	22,312	5,833
Kayes	17.Yelimane	46.81	11,340	321	21,097	597	11,646	336	21,693	626
Koulikoro	18.Banamba	66.10	12,821	4,190	24,278	7,933	13,111	4,391	24,857	8,324
Koulikoro	19.Dioila	81.04	34,793	2,192	65,003	4,095	35,520	2,299	66,441	4,301
Koulikoro	20.Fana	76.11	14,405	3,202	26,897	5,978	14,703	3,356	27,486	6,274
Koulikoro	21.Kangaba	48.41	10,753	1,044	19,512	1,894	10,980	1,095	19,948	1,989
Koulikoro	22.Kati	55.41	47,138	34,164	87,915	63,716	48,293	35,792	90,176	66,834
Koulikoro	23.Kolokani	61.59	16,911	4,845	31,640	9,065	17,278	5,076	32,366	9,509
Koulikoro	24.Koulikoro	64.14	15,626	3,427	29,352	6,438	15,978	3,591	30,051	6,755
Koulikoro	25.Nara	55.71	14,693	1,640	27,875	3,112	14,991	1,720	28,475	3,266
Koulikoro	26.Ouelessebougou	73.71	15,687	655	29,264	1,221	16,012	687	29,906	1,283
Mopti	27.Bandiagara	87.94	29,775	802	57,514	1,549	30,435	841	58,863	1,627
Mopti	28.Bankass	89.23	26,151	0	49,075	0	26,710	0	50,185	0
Mopti	29.Djenne	80.48	16,611	1,698	30,295	3,097	16,957	1,781	30,963	3,252
Mopti	30.Douentza	68.39	15,341	827	28,494	1,535	15,675	867	29,148	1,612
Mopti	31.Koro	80.02	27,405	1,564	50,986	2,909	27,978	1,640	52,116	3,055
Mopti	32.Mopti	67.73	17,278	7,071	32,105	13,139	17,716	7,398	32,958	13,762
Mopti	33.Tenenkou	76.28	12,310	1,187	23,382	2,254	12,587	1,244	23,937	2,366
Mopti	34.Youwarou	78.92	7,298	0	13,641	0	7,447	0	13,937	0
Segou	35.Baroueli	80.29	18,534	2,541	34,094	4,675	18,937	2,665	34,876	4,908
Segou	36.Bla	79.65	29,596	2,052	54,658	3,790	30,218	2,153	55,874	3,980
Segou	37.Macina	76.71	22,271	544	40,485	989	22,727	571	41,362	1,039
Segou	38.Markala	64.70	10,973	3,850	20,709	7,265	11,209	4,028	21,181	7,611
Segou	39.Niono	56.29	22,932	6,107	40,672	10,831	23,485	6,396	41,699	11,357
Segou	40.San	76.16	28,768	5,528	53,741	10,327	29,341	5,796	54,877	10,840
Segou	41.Segou	69.51	21,607	13,046	40,763	24,612	22,018	13,626	41,589	25,738
Segou	42.Tominian	85.66	23,429	0	44,505	0	23,909	0	45,472	0
Sikasso	43.Bougouni	83.47	50,933	8,727	93,907	16,091	51,980	9,155	95,951	16,899
Sikasso	44.Kignan	79.84	9,453	1,935	17,297	3,540	9,661	2,029	17,698	3,716
Sikasso	45.Koutiala	84.17	57,360	12,063	104,737	22,026	58,663	12,648	107,240	23,121
Sikasso	46.Selingue	56.43	6,266	1,917	11,526	3,526	6,404	2,009	11,793	3,700
Sikasso	47.Yorosso	85.70	23,735	4,114	43,460	7,533	24,251	4,314	44,457	7,909
Tombouctou	48.Dire	44.54	3,799	848	6,712	1,498	3,882	888	6,866	1,570
Tombouctou	49.Goundam	42.85	5,385	937	9,749	1,696	5,521	982	10,008	1,779
Tombouctou	50.Gourma-rharous	48.92	4,935	0	8,502	0	5,036	0	8,686	0
Tombouctou	51.Niafunke	66.24	9,536	1,063	17,458	1,945	9,733	1,114	17,839	2,042
Tombouctou	52.Tombouctou	14.13	1698	584	3059	1053	1748	611	3151	1101
Total			**855,556**	**274,392**	**1,585,428**	**508,718**	**874,248**	**287,668**	**1,621,995**	**533,965**

7.3. SMC implementation activities in Mali

Following the successful 2012 pilot study in Koutiala led by the MSF, the Minister of Health, through the PNLP and partners, extended SMC to additional five health districts (Banamba, Koutiala, San, Bankass and Diré) in 2013. Activities consisted of the administration of therapeutic doses of SP-AQ combination during the period of high malaria transmission. Medications were given once per month for four months to children 3 – 59 months. After administration of SP+AQ on day one and AQ on days two and three, the child was assumed to be protected for four weeks. The cycle of administration of additional was repeated every four weeks over four rounds. Of a total of 343,752 expected children, 359,288 (104.5%) received SP-AQ doses in Round 1 (Table 7.1). The higher than expected number of children may have been due to population coming in from outside the targeted districts particularly during the period of harvests. In Round 2, a total

of 366 858 children received SP-AQ doses. Round 3 and 4 focused mainly on Koutiala district. In all the rounds, children who were symptomatic were tested for malaria and those positive were not given AS-AQ but were treated with ACTs. In Round 1, of the 14,653 children who were tested, about 72% were positive for malaria (Table 7.3). Almost half the same number (7,086) were tested in Round 2 and 59.5% were posiive.

Table7.2 The SMC targeted and treated children 3-59 months in six health districts in Mali in 2013

		Target			Treated population			Coverage rate %		
ROUND 1	Health Districts	3 - 11 m	12 – 59 m	Total	3 - 11 m	12 – 59 m	Total	3 - 11 m	12 – 59 m	Total
	Banamba	7,715	36,269	44,084	7,368	36,726	44,094	95.5	101.0	100.0
	Koutiala	30,145	103,833	133,978	22,025	139,093	161,118	73.0	134.0	120.0
	San	13,869	65,382	79,250	10,748	53,027	63,775	87.4	90.3	89.8
	Bankass	10,531	50,400	60,931	10,706	51,104	61,810	101.7	99.7	101.4
	Diré	4,464	21,045	25,509	4,543	23,948	28,491	101.8	113.8	111.7
	Total	**48,478**	**190,260**	**343,752**	**55,390**	**303,898**	**359,288**	**114.3**	**159.7**	**104.5**
ROUND 2		7,715	36,269	44,084	6,860	36,726	43,586	89.0	100.1	98.9
		30,145	103,833	133,978	21,594	136,689	158,283	71.6	131.6	118.1
		13,869	65,382	79,250	13,559	61,114	74,673	97.8	93.5	94.2
		10,531	50,400	60,931	10,244	54,565	64,809	96.1	108.6	106.4
		4,464	21,044	25,508	4,463	21,044	25,507	99.0	125.7	121.7
	Total	**48,478**	**190,259**	**343,752**	**56,720**	**310,138**	**366,858**	**117.0**	**163.0**	**106.7**
ROUND 3	Banamba									
	Koutiala	30,145	103,833	133,978	21,735	139,019	160,754	72.1	133.9	120.0
	San									
	Bankass									
	Diré									
	Total	**30,145**	**103,833**	**133,978**	**21,735**	**139,019**	**160,754**	**72.1**	**133.9**	**120.0**
ROUND 4	Banamba									
	Koutiala	30,145	103,833	133,978	22,608	147,828	170,436	75.0	142.3	127.2
	San									
	Bankass									
	Diré									
	Total	**30,145**	**103,833**	**133,978**	**22,608**	**147,828**	**170,436**	**75.0**	**142.4**	**127.2**
TOTAL		**157,246**	**588,185**	**955,460**	**156,453**	**900,883**	**1,057,336**	**99.5**	**153.2**	**110.7**

Table7.3 The SMC targeted and treated children 3-59 months who were symptomatic and were treated with ACTs in six health districts in Mali in 2013

		Population not treated with AS+AQ					
	Health Districts	3 - 11 m	12 – 59 m	Total	RDT done	RDT positive tests	ACTs given
Round 1	Banamba	388	2,094	2,482	3,672	2,498	2,498
	Koutiala	412	1,823	2,235	?	?	?
	San	456	2,302	2,758	1,628	1,224	1,224
	Bankass	3,601	3,842	7,743	7,886	6,586	6,586
	Diré	148	356	504	1,467	192	192
	Total	**5,005**	**10,417**	**15,722**	**14,653**	**10,500**	**10,500**
Round 2	Banamba	260	984	1,244	1,886	1,221	1,221
	Koutiala	384	2,217	2,601	?	?	?
	San	417	1,431	1,848	369	236	236
	Bankass	701	2,022	2,723	3,609	2,578	2,578
	Diré	70	382	452	1,222	184	184
	Total	**1,832**	**7,036**	**8,868**	**7,086**	**4,219**	**4,104**
Round 3	Banamba						
	Koutiala	503	3,487	3,990			
	San						
	Bankass						
	Diré						
	Total						
Round 4	Banamba						

	Koutiala	630	4,738	5,368	
	San				
	Bankass				
	Diré				
	Total				
TOTAL					

7.3.1 Challenges in implementation of SMC activities in Mali

During the extended pilot scale up of SMC in Mali, the PNLP reported several benefits of the implementation activities including:

- The development of an operation action plan that can be adapted for other districts.
- The training of health workers on orientation and micro-planning at the health district level.
- The involvement of politicians, administrative authorities and opinion leaders.
- The adherence of populations to SMC and the high coverage rates.
- An SOP to manage SMC medication side effects.
- The systematic case management of all clinical episodes diagnosed on sites.

However, several challenges were experienced during these process including:

- Delay in making financial resources available at the beginning of the campaign.
- The micro-planning budget did not include all the items that were eventually needed in the field
- Absence of sensitization materials (posters) in the community health centers.
- Problems with data collection including missing observations of the two doses of AQ taken at home.
- Inadequate communication between field staff during SMC activities.
- Insufficienrt of support in the interpretation of data.
- The lack of dispersible tablets of SP/AQ medicine.

To address the operation challenges were reported (observed during the implementations of SMC activities in the six pilot districts, and the PNLP and partners made a number of recommendations targeted at different operational levels. At the central level it was recommended that: better training of trainers was undertaken; appropriate sensitization materials were designed and made available at all delivery structures; dispersible tablets were made available for ease of drug administration; and follow-up and the supervision of the staff during the campaign was strengthened. At the district level suggested improvements included: streghthening of interpersonal communication regarding the two doses of AQ taken at home; monitoring of correct completion of activities by distributor agents; reinforcing the follow-up and the supervision of the staff agents during the campaign. Finally, a request was made to partners to ensure timely availability of financial and material resources including additional critical support during field work that may have not been budgeted for during the micro-planning stage.

8. Conclusions and future recommendations

8.1 Defining the spatial extents of *P. falciparum* risk

Empirical data have been used to stratify the spatial extent of malaria transmission intensity across Mali for the years 2000, 2010 and 2013.

The analysis show a heterogeneous pattern of transmission of malaria in Mali in which the southern districts in the Sudanese and Guinean eco-climate zones experience a predominantly hyperendemic to holoendemic malaria where the PA*Pf*PR_{2-10} is >=50% in which about 66% of the population lived in 2013 (Figure 4.13). By 2013 about 32% of the population lived in mesoendemic areas of mesoendemic transmission (PA*Pf*PR_{2-10} is >10% to 50%). Hypoendemic transmission appears 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 a few districts bordering the southern regions.

Comparisons of population at risk (PAR) indicate 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 (Figure 4.12).

The 2010 and 2013 predictions coincide with period when large scale national household surveys were undertaken. However, the 2013 survey did not include the regions of Tombouctou, Gao and Kidal and estimates for the regions will rely on the strength of data from other regions or past surveys are likely to be less precise. These regions have large areas of aridity or semi-aridity which are sparsely populated and are of generally low malaria transmission. To improve the precision of the malaria risk models additional parasite rate data are required in the regions of Tombouctou, Gao and Kidal (Action Point 1).

Given Mali's political situation additional data layers are necessary to effectively plan a malaria control service. Notable among these are the estimated hundreds of thousands of internally displaced and refugees. In addition, the pastoralist Touareg community are hard to reach and although generally exposed to very low levels of malaria transmission are susceptible to epidemics whose consequences can be worsened by the frequent droughts, malnutrition and the recent insecurity in the north (Section 2.2 and 2.5). These special groups need better, more reliable mapping and enumeration for sub-national disease control planning and liaising with the different sectors in health and agriculture (Action Point 2).

There has been a tradition of urban malaria control in Mali which waned during the era of primary health care (Chapter 3). Since 1960, urbanization in Mali has almost doubled and is currently estimated that around 35% of the population reside in urban areas (Section 2.4). In the national malaria strategy there is no specific policy on urban malaria control nor is there an operational programmes for this population sub-group. Available data shows presence of malaria transmitting vectors and relatively high malaria transmission in urban areas in Mali (Section 4.3 and 5.4). Given the rapidly increasing urban population in Mali it is important that appropriate to develop a programme of work that examines urban malaria risks and opportunities for control (Action Point 3).

8.1 Defining the spatial extents of *P. falciparum* risk

Evidence from published studies show that *P. malariae* and to a lesser extent *P. vivax* are significant parasites in Mali. *P. vivax* seems to be increasingly important in northeastern regions and on norther border with Mauritania. However, little is known about the spatial intensity and distribution of these parasite across the country. The assembly of the secondary parasite species data in Mali and mapping of their distribution should be undertaken. National household surveys should include examinartion of these parasites in addition to *P. falciparum* (Action Point 4).

8.3 Mapping of vector control intervention coverage at health decision making units

Efforts have been made here to accurately define decision-making units and to apply stratifications of malaria transmission to these units (n = 60) (Section 2.7). It is hoped that the empirical stratifications of malaria and intervention coverage at these units will aid sub-national level planning of malaria control. Where these information is supplemented with the mapping of partners involved in malaria control at sub-national units, this will facilitate better coordination of malaria control activities in Mali.

We have attempted to map intervention coverage at these sub-national units using the data from the DHS of 2006, the A&P survey of 2010 and the DHS of 2012-2013. The maps show increasing coverage of ITNs over this period with majority of health districts estimated to have coverage of between 60% to 80%. However, the DHS 2012-13 did not include the three northern regions and therefore estimates for the health districts are not available. To allow for estimation of ITN coverage across all districts data on the numbers of nets distributed by district by month and year will be very helpful as a covariate. This will enable reliable estimation of ITN coverage in the regions missed during the recent national survey. This requires an assembly of ITN distribution data by health district available from the PNLP and partners (Action Point 5).

8.4 Health service mapping needs

Mapping of health facilities is not new in Mali and has been used for previous health programmes such as the Guinea worm eradication. The UNOCHA appears to have undertaken a systematic development of nationwide spatial database of health facilities (Section 8).

A geo-coded national level master health facility list, covering the multiple service providers across the country especially where health care is decentralized, is critical to designing health sector initiatives (including malaria control), providing a logistics and management platform for the adequate delivery of clinical commodities and the informed use of health information[13].

A list obtained from UNOCHA was used as the basis to develop a health facility database in Mali. Additional work was undertaken to removed duplicates, correct coordinates, geocode those that were not mapped using online databases and reclassify facilities into those that are public or private or those that provide only diagnostic services and not treatment. The final database contained 1325 public health facilities made up of 85 hospitals (hospitals, clinics and referral

[13] Recent work in Namibia has demonstrated the value of combining information of fever treatment behaviours, linked to population access to diagnostic and reporting centres and incomplete HMIS malaria data using MBG to define malaria incidence at high spatial resolutions [Alegana et al., 2012; 2013]. These modelled approaches to interpolating data in time and space require layers of GIS and HMIS linked data to provide higher resolution information for planning and monitoring malaria control.

health centres), 95 clinics and 1145 CSComs (Figure 2.10). In addition there hundreds of private clinics and other outlets that remain unverified. Further scrutiny, updating and verification of the health facility database by the Ministry of Health and partners is required (Action Point 6).

8.5 Seasonal malaria chemoprevention

Mali is one the countries where the early evidence on the efficacy of seasonal malaria prophylaxis of children emerged. A study in three localities in Kati showed that IPTc with AS+AQ targeting the transmission season showed that it provided substantial protection against *P. falciparum* malaria illness, infection, and anaemia in children between 3-59 months using an LLIN (Chapter 3). SMC was adopted in the new 2013-2017 NSP and all 60 districts in Mali are considered to be suitable for SMC. Mali has a phased plan to scale up SMC due to resource constraints and to date four districts have been selected for SMC with children 3-59 months as the target population.

However, our empirical analysis shows that 52/60 districts in Mali meet the suitability criteria for SMC. It also indicates that the appropriate target population sub-group is indeed the 3-59 months old children (Section 7.2). Under this condition a total of 855,556 and 274,392 children in rural and urban areas respectively would be targeted for SMC in 2014. In 2015 these would have risen to 874,248 and 287,668 in rural and urban areas respectively.

Further improvements on the SMC analysis may be possible if higher resolution rainfall data, such as the products from the AGROMET project, were compared with the seasonality surfaces developed from the RFE surfaces. In addition, future effective targeting of SMC is dependent on ability to predict the start and end of the transmission season. Future analysis should the explore use of higher resolution weather and climate platforms to improve the targeting of SMC and forecasting of transmission season patterns (Action Point 7).

Annex A

A.1. Parasite prevalence data assembly

The following sections provide a detailed description of how empirical parasite prevalence data were assembled, geo-positioned and pre-processed. This description should serve as a meta-data for the final database of contemporary parasite prevalence data in the Mali; and therefore a reference source to the final curated database.

A.1.1. Parasite prevalence data search strategy

Electronic data searches: Online electronic databases were used as one means for identifying peer-reviewed, published data on malaria infection prevalence. Due to its wide coverage of the biomedical literature, PubMed [http://www.ncbi.nlm.nih.gov/sites/entrez] was used as the basis for all the initial online searches of published sources. In addition, we used the library services of the Institute of Tropical Medicine, Antwerp [http://lib.itg.be/], the Armed Forces Pest Management Board – Literature Retrieval System [http://www.afpmb.org/publications.htm]; The World Health Organization Library Database [http://www.who.int/library]; the Institute de Recherché pour le Development on-line digital library service [http://www.ird.fr]; and African Journals Online (AJOL) [http://www.ajol.info]. In all digital electronic database searches for published work the free text keywords "*malaria*" and "*Mali* and "*malaria*" and "*French Soudan*" were used. We avoided using specialised Medical Subject Headings (MeSH) terms in digital archive searches to ensure as wide as possible search inclusion. The last complete digital library search was undertaken in June 2014.

Titles and abstracts from digital searches were used to identify possible parasite cross-sectional survey data undertaken since 1980 in a variety of forms: either as community surveys, school surveys, other parasite screening methods or intervention trials. We also investigated studies of the prevalence of conditions associated with malaria when presented as part of investigations of anaemia, haemoglobinopathies, blood transfusion or nutritional status to identify coincidental reporting of malaria prevalence. In addition, it was common practice during early antimalarial drug sensitivity protocols to screen community members or school attendees to recruit infected individuals into post-treatment follow-up surveys, often data from the survey sites present the numbers screened and positive. Surveys of febrile populations or those attending clinics were excluded.

Publications with titles or abstracts suggestive of possible parasite data were either downloaded from journal archives where these have been made Open Access (OA) or sourced from HINARI [http://www.who.int/hinari]. If publications were not available OA from HINARI we visited UK library archives at the London School of Hygiene and Tropical Medicine, the Liverpool School of Tropical Medicine, the Bodleian library at the University of Oxford and the library and archive the Wellcome Trust, UK and the Tropical Medicine Institute in Antwerp. References not found following these searches were requested using world catalogue searches through the Oxford libraries at a per-page cost. All publications from which data were extracted were cross-referenced using the bibliographies for additional sources that may have been missed or that may correspond to unpublished or 'grey' literature (i.e. not controlled by commercial publishers). In addition, tropical medicine and malaria meeting abstract books were identified from as many

sources as possible produced as part of national and international conferences and congresses. These were used to signal possible data that were followed up through correspondence with abstract authors.

Unpublished archived survey reports: We undertook manual searches of archives at the Tropical Medicine library in Antwerp and the World Health Organization (WHO) libraries in Geneva and Brazzaville at separate archive locations as Project, Country and Parasitology Department files. Data from the parasite surveys undertaken during the anemia and parasitaemia surveys were provided from the MEASURE DHS website. The Mali DHS 2012-13 prevalence was obtained from Dr Ibrahima Soce Fall of the WHO-AFRO. Malariologists who work in the Mali, particularly at the MRTC, were also contacted individually to provide unpublished data from survey work or disaggregated data published as summaries.

A.1.2 Data abstraction

The minimum required data fields for each record were: description of the study area (name, administrative divisions), the start and end dates of the survey (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, Rapid Diagnostic Tests (RDTs), Polymerase Chain Reaction (PCR) or combinations) and the lowest and highest age in the surveyed population. Given its ubiquity as a means for malaria diagnosis, the preferred parasite detection method was microscopy. No differentiation was made between light and fluorescent microscopy.

Data derived from randomized controlled intervention trials were only selected when described for baseline/ pre-intervention and subsequent follow-up cross-sectional surveys among control populations. When cohorts of individuals were surveyed repeatedly in time we endeavoured to include only the first survey and subsequent surveys if these were separated by at least five months from the initial survey to avoid a dependence between observations based on treatment of preceding infected individuals. If it was not possible to disaggregate repeat surveys these were finally excluded from the analysis. Where age was not specified in the report for each survey but stated that the entire village or primary school children were examined we assumed age ranges to be 0-99 years or 5-14 years respectively. Occasionally, reports presented the total numbers of people examined across a number of villages and only the percentage positive per village; here we assumed the denominator per village to be equivalent to the total examined divided by the total number of villages. Where additional information to provide unique time, village specific data was necessary we contacted authors to provide any missing information.

A.1.3. Data geo-coding

Data geo-coding, defining a decimal longitude and latitude for each survey location, was a particularly demanding task. According to their spatial representation, data were classified as individual villages, communities or schools or a collection of communities within a definable area, corresponding to an area within 5 km grid or approximately 0.05 decimal degrees at the equator. Where possible we aimed to retain disaggregated village, "point" level data rather than data across a "wide-area". More recent use of Global Positioning Systems (GPS) during survey work does enable a re-aggregation of household survey data with greater precision and useful in maintaining 5 km grid criteria while combining clusters of small sample sizes in space. To position each survey location where GPS coordinates were not available in space we used a variety of

digital resources, amongst which the most useful were Microsoft Encarta Encyclopedia (Microsoft, 2004) and Google Earth (Google, 2009). Other sources of digital place name archives routinely used included GEOnet Names Server of the National Geospatial-Intelligence Agency, USA [http://www.earth-info.nga.mil/gns/html/cntry_files.html]; Falling Rain Genomics' Global Gazetteer [http://www.fallingrain.com]; and Alexandria Digital Library prepared by University of California, USA [http://www.alexandria.ucsb.edu]. Old Belgian names for towns and villages were checked s they conformed to today's naming using the following blog space http://www.kosubaawate.blogspot.com/

Although standard nomenclatures and unique naming strategies are attempted in digital gazetteers [Hill, 2000], these are difficult to achieve at national levels where spellings change between authors, overtime and where the same names are replicated across different places in the country. As such, during the 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 geo-coding 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. 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. As routine we therefore rechecked all GPS data from all sources using place names and/or Google Earth to ensure coordinates were located on communities.

All coordinates were subject to a final check using second level administrative boundary Global Administrative Units Layers (GAUL) spatial database developed and revised in 2008 by Food and Agriculture Organization (FAO) of the United Nations [GAUL, 2008]. The Global lakes and Wetlands (GLWD) database developed by the World Wildlife Fund [Lehner and Doll, 2004] was used to ensure inland points were within defined land area. Here we aimed to identify survey coordinates that fell slightly on the lakes or in incorrect administrative units, every anomaly was re-checked and re-positioned using small shifts in combination with Google Earth.

A.1.4. Database fidelity checks, pre-processing and summaries

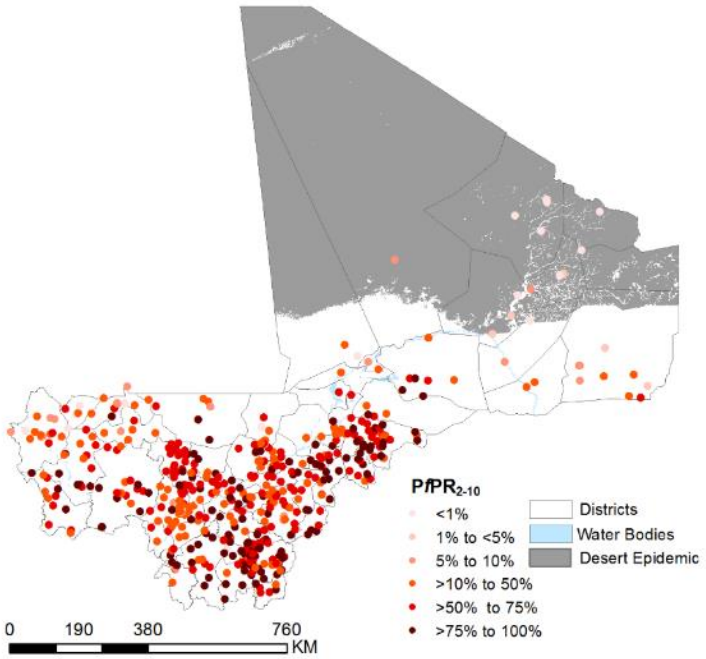
The entire database was first checked with a series of simple range-check constraint queries to identify potential errors that could have occurred during data entry. These queries assessed all data fields relevant to modelling for missing or inconsistent information. The final objective was to check for any duplicates introduced during the iterative data assembly process. Pairs of survey sites found within 1 km or within five months at the same location were identified. These may have been entered erroneously into the data assembly where multiple reviewed reports describing similar data. These were listed, checked and duplicates removed.

The search strategy identified 649 geocoded survey data points where malaria infection prevalence had been recorded between 1980 and 2013. Twenty four surveys had sampled less than 10 people and were excluded to preserve survey estimate precision [Gregory and Blackburn, 1991; Jovani and Tella, 2006]. Survey sources are presented in Table A.1.

There was a large diversity among studies in the age ranges of sampled populations. To make any meaningful comparisons in time and space, a single standardized age range is required. Correction to a standard age for *P. falciparum* is possible based on the observation and theory of infectious

diseases where partial immunity is acquired following repeated exposure from birth. We have retained the classical age range of 2-10 years as this best describes the exposure to infection among semi-immune hosts at any given location and conforms to classifications established in the 1950s [Metselaar and Van Thiel, 1959]. We have adapted catalytic conversion Muench models, first used in malaria by Pull and Grab (1974), into static equations in R-script that uses the lower and upper range of the sample and the overall prevalence to transform into a predicted estimate in children aged 2-10 years, *Pf*PR_{2-10} [Smith et al., 2007]. Only microscopy data were accepted across all surveys and their age-corrected distribution is shown in Figure A.1.

Figures A.1 (a) location of data 1980 – 2013 in Mali with sample size of 10 or more persons examined (n = 625) used to make predictions of risk in 2000, 2010 and 2013 (darker red higher *Pf*PR_{2-10})



Source	Number of surveys	Number of persons examined	Lower age (yrs)	Upper age (yrs)	Year(s)
Amagana D (1997). Reponse immunitaire anti-TRAP (Thrombospodin Related Adhesive Protein) et morbidite palustre dans une zone d'hyperendemie palustre du Mali (Afrique de l'Ouest). Thesis, Universte di Roma "La Sapienza", Italy	1	1085	0.0	9.0	1994
Barger B, Maiga H, Traore OB, Tekete M, Tembine I, Dara A, Traore ZI, Gantt S, Doumbo OK, Djimde AA (2009). Intermittent preventive treatment using artemisinin-based combination therapy reduces malaria morbidity among school-aged children in Mali. Tropical Medicine and International Health, 14: 784-791	2	392	6.0	13.0	2007-2008
Bouvier P, Rougemont A, Breslow N, Doumbo O, Delley V, Dicko A, Diakite M, Mauris A, Robert CF (1997). Seasonality and malaria in a west African village: does high parasite density predict fever incidence? American Journal of Epidemiology, 145: 850-857	1	998	1.0	12.0	1993
Ceesay SJ, Bojang KA, Nwakanma D, Conway DJ, Koita OA, Doumbia SO, Ndiaye D, Coulibaly M, Ndiaye JL, Sarr O, Gaye O, Konate L, Sy N, Faye B, Faye O, N, Jawara M, Dao A, Poudiougou B, Diawara S, Okebe J, Sangare L, Abubakar I, Sissako A, Diarra A, Keita M, Kandeh B, Long CA, Fairhurst RM, Duraisingh M, Perry R, Muskavitch MAT, Valim C, Volkman SK, Wirth DF, Krogstad DJ (2011). Sahel, savana, riverine and	1	1288	0.0	18.0	2008

urban malaria in West Africa: similar control policies with different outcomes. Acta Tropica, 121: 166-174					
Chabasse D, Roure C, Ag Rhaly A, Maiga D, Traore M, Tounkara A, Dumon H, Ranque P (1983). Evaluation de l'etat sanitaire des populations nomades et semi-nomades du Gourma-Mali - Approche epidemiologique. Medecine Tropicale, 40: 127-134	1	167	0.0	7.0	1982
Chabasse D, Roure C, Rhaly AAG, Maiga D, Traore M, Tounkara A, Dumon H, Ranque P (1983). Evaluation de L'etat sanitaire des populations nomades et semi-nomades du Gourma-Mali - Approche epidemiologique. II results globaux et conclusion. Medicine Tropicale, 43: 127-135	5	554	0.0	99.0	1981
Crompton PD, Traore B, Kayentao K, Doumbo S, Ongoiba A, Diakite SA, Krause MA, Doumtabe D, Kone Y, Weiss G, Huang CY, Doumbia S, Guindo A, Fairhurst RM, Miller LH, Pierce SK, Doumbo OK (2008). Sickle cell trait is associated with a delayed onset of malaria: implications for time-to-event analysis in clinical studies of malaria. Journal of Infectious Diseases, 198: 1265-1275	1	176	2.0	10.0	2006
Dembele H (1995). Paludisme et grossesse, saisonnalite et relations avec anemie et petits poids de naissance au Bougoula-Hameau (Sikasso Mali). Thesis, Ecole Nationale de Medecine et de Pharmacie du Mali (ENMP), Mali	1	200	0.0	44.0	1992
Diakite H (1982). Donnees parasitologiques sur le paludisme de la premiere region du Mali: Comparaison entre la saison seche et la saison pluvieuse. PhD thesis, University of Mali, Bamako	15	1165	2.0	9.0	1981
Dicko A (1996). Enquete Parasito Clinique/PEEM- WARDA, Niono-Mali. Bamako, Mali, Reunion inter-institutions Malienne. ENMP-INRSP-IER, unpublished WARDA report	10	3988	0.0	15.0	1995
Dicko A, Diallo AI, Tembine I, Dicko Y, Dara N, Sidibe Y, Santara G, Diawara H, Conaré T, Djimde A, Chandramohan D, Cousens S, Milligan PJ, Diallo DA, Doumbo OK, Greenwood B (2011). Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Mali: a randomised, double-blind placebo-controlled trial. PLoS Medicine, 8: e1000407; and upublished raw data provided by Diadier Diallo, LSHTM on 6th July 2011	3	1359	1.0	7.0	2009
Dicko A, Sagara I, Doumba O (2009). Malaria parasites prevalence in 26 areas (villages) of the district of Kolokani in the region of Koulikoro, Mali, unpublished report and personal communication 14th December 2009 by Issaka Sagara	28	5167	0.0	47.0	2004-2007
Dicko A, Sagara I, Sissoko MS, Guindo O, Diallo AI, Kone M, Toure OB, Sacko M, Doumbo OK (2008). Impact of intermittent preventive treatment with sulphadoxine-pyrimethamine targeting the transmission season on the incidence of clinical malaria in children in Mali. Malaria Journal, 7: e123	1	262	0.5	10.0	2002
Dicko AA (1995). Épidémiologie du paludisme dans la région de Mopti en vue de l'élaboration d'un programme régional de lutte. Thesis, Ecole Nationale de Médecine et de Pharmacie du Mali (ENMP), Bamako, Mali	21	29790	0.0	99.0	1993-1994
Djimde (2009). Unpublished data	2	795	3.0	16.0	2006-2007
Dolo A, Camara F, Poudiougo B, Toure A, Kouriba B, Bagayogo M, Sangare D, Diallo M, Bosman A, Modiano D, Toure YT, Doumbo O (2003). Epidemiology of malaria in a village of Sudanese savannah area in Mali (Bancoumana). 2. Entomo-parasitological and clinical study. Bulletin de la Société de Pathologie Exotique, 96: 308-312	1	1259	0.5	9.0	1993
Dolo A, Modiano D, Maiga B, Daou M, Dolo G, Guindo H, Ba M, Maiga H, Coulibaly D, Perlman H, Blomberg MT, Toure YT, Coluzzi M, Doumbo O (2005). Difference in susceptibility to malaria between two sympatric ethnic groups in Mali. American Journal of Tropical Medicine and Hygiene, 72: 243-248; and help provided by Ogabara DOumbo and Ousmane Toure at MRTC	5	3106	0.0	99.0	1998-2001
Doumbia S (2012). Malariometric parameters evolution during teh co-infection Schistomsa Heamatobium and Plasmodium falciaprum in Mali. American Journal of Tropical Medicine and Hygiene, 87 Supplement 5, abstract 132, Proceedings of 61st Annual Conference, Atlanta, Georgia, USA November 11-15 2012.	2	632	11.0	14.0	2005-2006
Doumbo O and Sagara I (2005). Personal communication of assembled MARA to Bob Snow on behalf of MRTC, Bamako on 21st November 2009 (contact isagara@icermali.org and okd@icermali.org)	40	25854	0.0	45.0	1985-2005
Doumbo O (1992). Épidemiologie du paludisme au Mali: étude de la chloroquine résistance, essai de stratégie de contrôle basée sur l'utilisation de rideaux imprégnés de permethrine associée au	7	1700	0.0	99.0	1988

traitement systématique des accès fébriles. Doctoral thesis. Université Montpellier II, France					
Doumbo O (1992). Epidemiologie du paludisme dans la Region de Mopti en vue de l'elaboration d'un programme regional de lutte. Thesis Ecole Nationale de Medecine et de Pharmacie du Mali (ENMP)	3	665	6.0	14.0	1989
Doumbo O, Koita O, Traore SF, Sangare D, Coulibaly A, Robert V, Soula G, Quilici M, Toure YT (1991a). Les aspects parasitologiques de l'épidemiologie du paludisme dans le Sahara Malien. Médecine d'Afrique Noire, 38: 103-109	2	399	0.0	15.0	1989
Doumbo O, Traore SF, Sow Y, Dembele M, Soula G, Coulibaly A, Dolo A, Sangare O, Koita O, Pichard E, Toure YT (1991b). Impact of curtains and blankets impregnated with permethrin on the malarial indicators and the number of malarial attacks per child in a village in an area hyperendemic for malaria on the Malian savannah (preliminary results of the first year study). Bulletin de la Société de Pathologie Exotique, 84: 761-774	6	2131	0.0	44.0	1988-1990
Fondjo E (1996). Étude du comportement du complexe An. gambiae et de la transmission du paludisme dans deux faciès écologiques au Mali et au Cameroun. Thesis, Institut Superieur de Formation et de Recherche Applique. Université de Bamako, Bamako, Mali	2	450	0.0	15.0	1994-1995
Goriup S (1990). Rapprt d'une visite au Mali. WHO-AFRO archives collected on 060213	5	6973	0.0	99.0	1980-1986
Guiguemdé TR, Gbary AR, Ouedraogo JB, Gayibor A, Lamizana L, Maiga AS, Boureima HS, Comlanvi CE, Faye O, Niang SD (1991). Point actuel sur le chimioresistance du paludisme des sujets autochtones dans les etats de l'OCCGE (Afrique de l'ouest). Annales de la Societe Belge de Medecine Tropicale, 71: 199-207	1	29	0.0	12.0	1990
Israelsson (2009). Unpublished data	1	328	1.0	60.0	2005
Koita OA, Sangare L, Sango HA, Dao S, Keita N, Maiga M, Mounkoro M, Fane Z, Maiga AS, Traore K, Diallo A, Krogstad (2012). Effect of seasonality and ecological factors on the prevalence of the four malaria parasite species in Northern Mali. Journal of Tropical Medicine, doi:10.1155/2012/367160	18	1194	0.0	9.0	2004-2005
Maiga AS and Brinkmann A (1987). Risk in a national malaria control programme in Mali: underdosage of antimalarials. Tropical Medicine and Parasitology, 38: 333-334	1	259	7.0	14.0	1986
Maiga MA, Sanogo N, Kone N (1992). Paludisme dans les villages colons a kolongotomo office du niger, enquetes demographique, epidemiologique et socio-economique. Medecine d'Afrique Noire, 39: 474 - 479	1	172	15.0	19.0	1987
Maiga MHD, Diallo H, Yi M (1989). Paludisme en zone irriguée: enquête épidemiologique dans les villages colons de Kolongotomo (Office du Niger). Médecine d'Afrique Noire, 36: 206-209	1	344	8.0	14.0	1989
N	303	5509	0.0	4.9	2012-2013
Ouedraogo J (1987). Enquête sur la chimiosensibilité du paludisme et formation d'une équipe nationale aux tests de chimiosensibilité au Mali (Bamako). OCCGE, Centre Muraz	3	1012	1.0	9.0	1987
Rhee M, Sissoko M, Perry S, McFarland W, Parsonnet J, Doumbo O (2005). Use of insecticide-treated nets (ITNs) following a malaria education intervention in Piron, Mali: a control trial with systematic allocation of households. Malaria Journal, 4: e35	1	122	1.0	9.0	2000
Rouhani s, Roschnik N and Clarke S (2013). Unpublished work from school surveys in 2010 in Mali. Also: Clarke SE, Roschnik N, Rouhani S, Diarra S, Bamadio M, Sacko M, Traore D, Ly AB, Gaye O, Sembene M, Fall FB (2012). Malaria in school children under a new policy of universal coverage of nets: Recent data from Mali and Senegal. American Journal of Tropical Medicine and Hygiene, 87 Supplement 5, abstract 1466, Proceedings of 61st Annual Conference, Atlanta, Georgia, USA November 11-15 2012	35	1744	5.0	17.0	2010
Sagara I, Dicko A, Ellis RD, Fay MP, Diawara SI, Assadou MH, Sissoko MS, Kone M, Diallo AI, Saye R, Guindo MA, Kante O, Niambele MB, Miura K, Mullen GE, Pierce M, Martin LB, Dolo A, Diallo DA, Doumbo OK, Miller LH, Saul A (2009). A randomized controlled phase 2 trial of the blood stage AMA1-C1/Alhydrogel malaria vaccine in children in Mali. Vaccine, 27: 3090-3098	1	300	2.0	3.0	2006
Sangare D (1996). Etude de la Transmission du paludisme a Doneguebougou (Arrondissement de Kati). Thesis, Institut Supérieur de Formation et de Recherche Appliquée (ISFRA), Bamako	1	358	0.0	9.0	1994
Tall M (1995). Epidemiologie du paludisme et phenomene de chloroquinoresistance a Doneguebougou (Kati, Mali). Thesis, Ecole de Formation Paramedicale d'Alger, Algeria	1	315	0.0	9.0	1995

Toure YT, Traore SF, Sankare O, Sow MY, Coulibaly A, Esposito F, Petrarca V (1996). Perennial transmission of malaria by the Anopheles gambiae complex in a north Sudan Savanna area of Mali. Medical and Veterinary Entomology, 10: 197-199	1	108	2.0	9.0	1988
Traoré K, Mariko S, Doumbia B and Berthé S (2010). Enquête sur la prévalence de l'Anémie et de la Parasitémie palustre chez les enfants (EAandP) au Mali 2010. Ministère de la Santé Programme National de Lutte contre le Paludisme (PNLP) INFO-STAT Bamako, Mali	79	1718	0.5	4.9	2010
Traore S (1996). Epidémiologie du Paludisme en zone de savane sud-soudanienne au Mali: le village de Pimperna dans la région de Sikasso de Juin 1992 a Septembre 1993. Thesis, Ecole Nationale de Médecine et de Pharmacie (ENMP) Bamako, Mali	2	485	0.0	15.0	1992-1993
Traore Y (1988). Caractéristiques entomologiques et parasitologiques de l'épidemiologie du paludisme au Banambani. Institut Supérieur de Formation et de Recherche Appliquée (ISFRA) Bamako, Mali	1	97	0.0	14.0	1986
UNDP (2007). The Millenium Villages Project: Annual Report for Tiby, Mali. New York, United Nations Development Program	4	387	0.0	49.0	2006
Vafa M, Israelsson E, Maiga B, Dolo A, Doumbo OK, Troye-Blomberg M (2009). Relationship between immunoglobulin isotype response to Plasmodium falciparum blood stage antigens and parasitological indexes as well as splenomegaly in sympatric ethnic groups living in Mali. Acta Tropica, 109: 12-16;	4	691	0.6	65.0	2005
Total	**625**	**105727**	**0.0**	**99.0**	**1980-2013**

A.2. Model development

A.2.1. Selection of covariates

In statistical modelling, a set of independent covariates of the main outcome measure is often used to improve the model fit and increase the precision of predicted estimates. The inclusion of these covariates increase model complexity and, if not carefully selected, risk over-fitting (using up too many degrees of freedom), which occurs when more terms or covariates than is necessary are used in the model fitting process [Babyak, 2004; Murtaugh, 2009]. Over-fitting can lead to poor quality predictions because coefficients fitted to these covariates add random variations to subsequent predictions and make replication of findings difficult [Babyak, 2004]. Where too many covariates are used, the model tends to produce highly fluctuating regression coefficients increasing the chances of large covariate coefficients and an overly optimistic fit, especially with small sample sizes of empirical. This problem can be particularly pronounced when data assembled are from observational studies based on different study designs, sampling considerations and sample sizes which are then combined to describe a random process [Craig et al., 2007].

The choice of covariates should be underpinned by the principle of parsimony (few strong and easily interpretable covariates) and plausibility (a clearly understood mechanism by which the covariate influences the outcome). In disease mapping there must a pre-determined aetiological explanation of the relationship of the disease and the covariate under consideration. The important determinants of uncontrolled malaria transmission are climate (rainfall and temperature) and ecological (potential breeding sites and urbanisation) [Molineaux, 1988; Snow and Gilles, 2002]. These factors affect the development and survival of the *P. falciparum* parasite and the malaria-transmitting *Anopheles* vector thereby reducing the risks of infection.

We tested four covariates against the empirical age-corrected parasite survey data: 1) *Temperature Suitability Index* (TSI) as a continuous variable ranging from 0 to 1 (Figure 2.2c); 2)

Synoptic mean monthly precipitation raster surfaces at 1 × 1 km resolution, downloaded from the WorldClim website [http://www.worldclim.org/] (Figure 2.2a); 3) Fourier processed mean annual enhanced vegetation index (EVI), derived from the MODerate-resolution Imaging Spectroradiometer (MODIS) sensor imagery and available at approximately 1×1 km spatial resolution [Figure 2.2b; Scharlemann et al., 2008]; and 6) Urbanisation developed from information from the Global Rural Urban Mapping Project (GRUMP) [Balk et al., 2006] and the Afripop project [Linard et al., 2012]. Urban areas were defined as locations with a density of more than 1000 persons per km^2 with the rest of the GRUMP urban extent defined as peri-urban and in the final test models both were combined.

To begin the covariate selection process the values of the assembled covariates were extracted to each *Pf*$PR_{2\text{-}10}$ survey location using ArcGIS 10 *Spatial Analyst* (ESRI Inc. NY, USA) tool. A correlation test was then undertaken to examine variable that were highly correlated (>0.85). Where two covariates had correlation >0.85, the aim was to select the one with the highest Bayesian Inference Criteria (BIC) for inclusion in the bootstrap and total set analysis using the results of a bivariate regression analysis. Using total-set analysis, the *bestglm* algorithm selected the covariates resulting best-fit model and displayed these together with their coefficients, 95% CI and P-values.

The relationship of *Pf*$PR_{2\text{-}10}$ with TSI, EVI, precipitation and urbanisation were all tested against the *Pf*$PR_{2\text{-}10}$ data 1980-2013. TSI provided the best fit model: coefficient 0.563 (95% CI: 0.434, 0.693, P<0.001). All covariates were selected in the best-fit model.

A.2.2. Pf$PR_{2\text{-}10}$ Model specification

A Bayesian hierarchical spatial-temporal model was implemented through SPDE approach using R-INLA library [R-INLA, 2013] to produce continuous maps of *Pf*$PR_{2\text{-}10}$ at 1 × 1 km spatial resolution for year 2000, 2010 and 2013. The continuous indexed GF with covariance function was represented as a discretely indexed random process, that is, as a Gaussian Markov Random Field (GMRF) [Rue and Held, 2005; Lindgren et al., 2011; Cameletti et al., 2012]. This is where an explicit link between Gaussian Field (GF) and GMRF formulated as a basis function is provided through (SPDE) approach [Lindgren et al., 2011; Bolin and Lindgren, 2011; Simpson et al., 2012a; 2012b]. The solution for SPDE can be expressed as

$$(k^2-\Delta)^{\alpha/2}(\tau x(u)=W(u)\,,\quad u\in\mathbb{R}^d\,,\quad \alpha=\nu+d/2\,,\quad \sigma^2-\Gamma(\nu)(\Gamma(\alpha)(4\pi)^{d/2}k^{2\nu}\tau^2)^{-1}$$
$$k>0\,,\ \nu>0\,, \qquad \text{(Equation A.2.1)}$$

This SPDE is a Gaussian random field with Matérn covariance function where W, is the spatial Gaussian white noise process, Δ is the Laplacian, α controls the smoothness of the realizations and τ controls the variance. The link between Matérn smoothness ν and variance σ^2 is $\alpha=\nu+d/2$ and $\sigma^2=\Gamma(\nu)(\Gamma(\alpha)(4\pi)^{d/2}k^{2\nu}\tau^2)^{-1}$, where d is the spatial dimension [Lindgren and Rue, 2013]. An approximation of this SPDE can be solved using a finite element method (FEM), which is a numerical technique for solving partial differential equations [Lindgren et al., 2011]. In this case, the spatio-temporal covariance function and dense covariance matrix of the GF are replaced by a neighbourhood structure and a sparse precision matrix respectively and together define a GMRF. A GMRF can be described as a spatial process that models spatial dependence of data observed at a spatial unit like grid or geographical region and it can be expressed as

$u = (u_1 \ldots\ldots, u_n)'$ with $u \sim (\mu, Q^{-1})$. This is an n-dimensional GMRF with mean μ and a symmetrical positive definite precision matrix Q computed as the inverse of the covariance matrix [Cameletti et al., 2012]. Thus the density of u is given by

$$\pi(\mathrm{u}) = (2\pi)^{-n/2} |Q|^{1/2} \exp(-\frac{1}{2}(\mathrm{u}-\mu)' \mathrm{Q}(\mathrm{u}-\mu)) \qquad \text{(Equation A.2.2)}$$

The sparse precision matrix Q offers computational advantage when making inference with GMRF. This is because the linear algebra operations can be performed using numerical methods for the sparse matrices which results in a considerable computational gain and this is further enhanced by using INLA algorithm for Bayesian inference [Rue and Held, 2005; Rue et al., 2009; Cameletti et al., 2012]. The infinite-dimensional Gaussian Random Field (GRF) is replaced with a finite-dimensional basis function representation

$$x(u) = \sum_{i=1}^{n} \psi_i(u) w_i \quad , \qquad \text{(Equation A.2.3)}$$

where w_i represents the Gaussian distribution weights and Ψ_i are piece-wise linear basis functions defined on a triangulation of the domain with n nodes which are defined as mesh in the code [Lindgren et al., 2011]. The basic functions are deterministic and are defined by each node in the triangulation while the stochastic property of the process is determined by the weights. The model used in this paper assumed non-stationary GRFs because environmental phenomenas which are known to influence *Pf*$PR_{2\text{-}10}$ are non-stationary in nature and therefore the distribution of *Pf*$PR_{2\text{-}10}$ is non-stationary [Daly et al., 1994]. The non-stationarity assumption l was made possible by the flexible nature of SPDE models which allows modification of the SPDE rather than the covariance function to obtain the GRFs with other dependence structures other than the stationary Matérn covariance. The stationary isotropic Matérn covariance function, between locations u and v in $\square^{d}$ is expressed as

$$C(u,v) = \frac{\sigma^2}{2^{v-1}\Gamma(v)} (k\|v-u\|)^{v} K_v(k\|v-u\|) \ , \qquad \text{(Equation A.2.4)}$$

Where K_V is the modified Bessel function of the second kind, $\|\cdot\|$ denotes the Euclidean distance and order $v > 0$. $k > 0$ is a scaling parameter and σ^2 is the marginal variance. For the stationary model, k and v are constant in space. The parameter k is linked to the range p by the empirically derived relationship $p = \sqrt{8}/k$. k , here can be described as the range parameter presiding over the spatial dependence structure of the GRF [Lindgren et al 2011]. For the non-stationary, τ and k space-dependent covariance parameters are introduced as functions of the spatial location u , $u \in D$, where D is the spatial domain. Therefore the modified SPDE becomes

$$(k(u)^2 - D)(t(u)x(u)) = W(u) \ , \ u \in \square^{2} \ , \qquad \text{(Equation A.2.5)}$$

where x is a non-stationary GRF because τ and k vary by location and as the consequence the variance and correlation range vary by location. The non-stationary described above is defined on

the mesh because it controls the local distance metric in the manifold. $\log\tau(u)$ and $\log k(u)$ can be defined as the sum of the basis function, where the basis functions $\left\{\mathrm{B}_i^{(\cdot)}(\cdot)\right\}$ are smooth over the domain of interest.

$$\log(k^2(u)) = \sum b_i^{(k^2)}\mathrm{B}_i^{(k^2)}(u) \quad \text{and} \quad \log(\tau(\mathrm{u})) = \sum \beta_i^{(\tau)}\mathrm{B}_i^{(\tau)}(\mathrm{u}), \qquad \text{(Equation A.2.6)}$$

Using this SPDE approach, the overall hierarchical space-time binomial and zero-inflated binomial models of the prevalence to malaria parasite were used denoted by

$$y(s,t) = z(s,t)\beta + \xi(s,t) + \varepsilon(s,t), \qquad \text{(Equation A.2.7)}$$

This model is characterised by a GF *y(**s**, t)* built from covariate information *z(**s**,t)*, measurement error *ε(**s**, t)*, and a second order autoregressive dynamic model for the latent process *ξ(**s**, t)* with spatially correlated innovations *ω(**s**, t)*. The *Pf*PR$_{2\text{-}10}$ survey data were modelled as realizations of this spatial process (random field) changing in time. These realizations were used to make inference about the process and predict it at desired locations and at a specified time. This is where $y(s_i,t)$ was the realization of a spatial-temporal process representing the *Pf*PR$_{2\text{-}10}$ at the community location s_i , where $i = 1...n$, and year t_j where $j = 1...m$, $z(s_i,t_j) = (z_1(s_i,t_j)\ldots z_p(s_t,t_j))$ represents fixed effect from the covariates for cluster s_i at time t_j , $\beta = (\beta_1\ldots,\beta_p)'$ is the coefficient vector, $\varepsilon(s_i,t) \sim N(0,\sigma_\varepsilon^2)$ is the measurement error defined by the Gaussian white noise process, and $y(s_i,t_j)$ is the predicted posterior mean prevalence of the plasmodium parasite in cluster i at time j . In the model formulation the large scale component that depends on the covariates is defined as $Z(s_i,t_j)\beta$ while the measurement error variance or the nugget effect is σ_e^2 . The realization of state process or the unobserved level of *Pf*PR$_{2\text{-}10}$ in this case is defined by $\xi(s_i,t_j)$ as a spatial-temporal GRF that changes in time as a second-order autoregressive function.

The prior for the SPDE model by default are Gaussian. In the latest version of SPDE function, the default priors are chosen heuristically to match the spatial scale of the MESH domain. The user can override the defaults by supplying a "hyper" parameter [Lindgren, 2013]. This is normally suitable when the dataset lacks enough information for the likelihood to fully identify the parameters for the prior distribution. In this paper the SPDE default priors were sufficient for the model.

A.2.3. Constructing a suitable MESH

A finite element representation is used to outline the GRF as a linear combination of basic functions defined on a triangulation of the domain, say D . This is achieved by subdividing D into non-intersecting triangles meeting in at most common edge or corner, thus a *mesh*. The GRF in the triangulation is given by Equation (A.2.3), where n is the total number of vertices, $\{\psi,(s)\}$ are the basis functions and $\{\omega_l\}$ are normally distributed weights [Lindgren et al., 2011; Cameletti et al., 2012].

The mesh function (*inla.mesh.create.helper*) in INLA is used to create a Constrained Refined Delaunay Triangulation (CRDT). The overall effect of the triangulation construction is that, if desired, one can have smaller triangles, and hence higher accuracy of the field representation. However, this will have an effect on the computation of the model. There is therefore a need to balance the number of triangles and the computation time required. If the data points (cluster coordinates) are used to construct the mesh, a cut-off value (specified in the function represents the maximum distance in which data points are represented by a single vertex. If the boundary of the area domain is used to construct the mesh, (i.e. using the function points.domain=border), then the mesh is constructed to cover the border of the domain using restrictions provided in other arguments. But if both data points and area domain (boundary) are used the restrictions are combined. In this model, the mesh was constructed using the boundary of the area domain. This method produces a mesh with regular size of triangles. A cut-off value was specified to avoid building many small triangles around *Pf*$PR_{2\text{-}10}$ input locations. A reasonable offset value was used to specify the size of the inner and outer extensions around the data locations. The maximum edge value was used to specify the maximum allowed triangle edge lengths in the inner domain and in the outer extension. The inner maximum edge value was made small enough to allow the triangulation to support representing functions with small enough features, and typically smaller than the spatial correlation range of the model. Therefore this value was adjusted to fit the range of the area domain in the model.

A matrix was then constructed to link the *Pf*$PR_{2\text{-}10}$ input locations to the triangles on the mesh defined by $\eta^* = A(x + 1\beta_0)$ and in the INLA code in the following *inla.spde.make. A* function. This makes each row in the matrix to have three non-zero elements since every data point is inside a triangle and the corresponding columns are expected to have non-zero elements. In order to obtain a square matrix for the model, the response was linked to the index of the random field, where the length of the index vector was the same as the length of the projection matrix. In order to estimate the intercept, the stack function introduces a vector of ones in the matrix and this is removed in the formula by putting [-1] [Lindgren, 2013].

A.2.4. Model predictions

Final continuous 1 x 1 km model predictions of *Pf*$PR_{2\text{-}10}$ maps are shown in Figures A.2. a for 2000; A.2. b for 2010 and A.2. c for 2013 respectively.

A series of model uncertainty and validation statistics were generated to assess model performance. For each prediction year, the standard deviations of *Pf*$PR_{2\text{-}10}$ were first computed for each 1 × 1 km grid location. The probability of belonging to an endemicity class was also computed from the posterior marginal distributions at similar spatial resolutions. Conventional model accuracy was estimated by computing the linear correlation, the mean prediction error (MPE) and mean absolute prediction error (MAPE) of the observations and predictions of a 10% hold-out dataset[14].

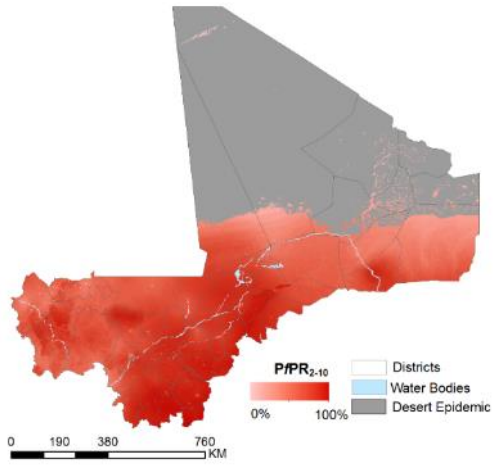
[14] The hold-out set was selected using a spatially and temporally declustered algorithm [Isaacs and Svritsava, 1989] which defined Thiessen polygons around each survey location. Each data point had a probability of selection proportional to the area of its Thiessen polygon so that data located in densely surveyed regions had a lower probability of selection than those in sparsely surveyed regions setting a high threshold for model performance. Sampling and testing hold out sets was done for each regional and time-segmented tile. The Bayesian SPDE using INLA was then implemented in full using the remaining 90% of data and predictions were made to the 10% hold-out within each regional tile.

The MPE, MAPE and the correlation coefficient of the observed and predicted *Pf*PR$_{2-10}$ for the space time *Pf*PR$_{2-10}$ model was -1.4%, 8.3 % and 0.93 respectively indicating very good model accuracy.

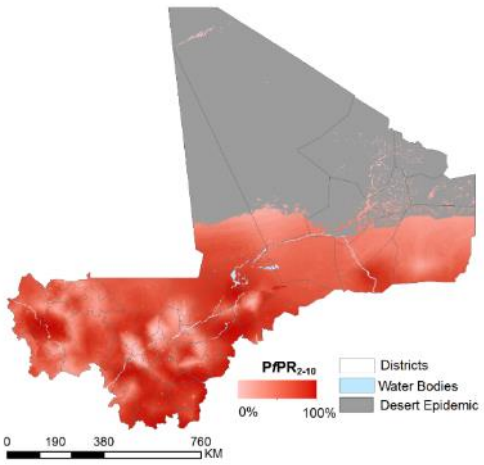
The standard deviation is a measure of the variability or dispersion of an expected value of a variable from its mean. High/low standard deviations indicate that data points are far/close to the mean. Of particular importance is the distance of the standard deviation (SD) from the mean, because the absolute value of the standard deviation could be both because of uncertainty but also a function of generally high base (mean) values of the measure under consideration. In this study, the distance (number) of the standard deviations of the mean *Pf*PR$_{2-10}$ were computed for the years 2000 (Figure A.3a); 2010 (A.3b) and 2013 (A.3.c). All predictions were with 2 standard deviations of the posterior mean and overall was slightly highest in 2013 predictions.

Figure A.2 Continuous 1 x 1 predicted mean *Pf*PR$_{2-10}$ for the year a) 1939; b) 2007

a)



b)



c)

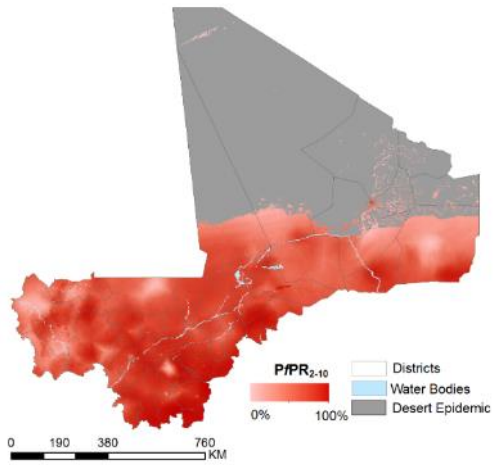
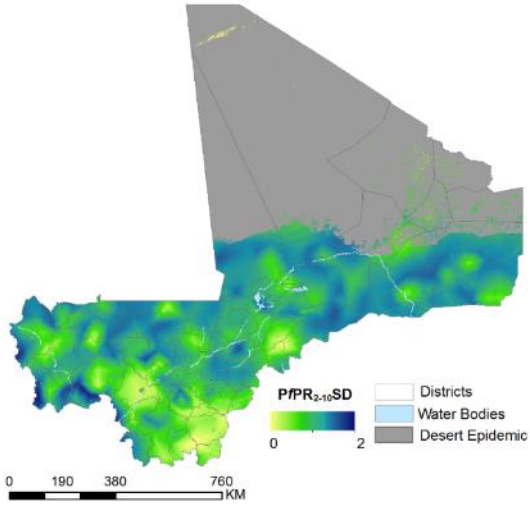
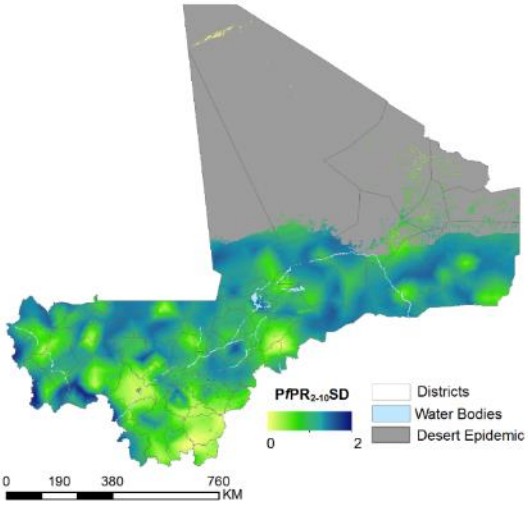


Figure A.3 Continuous 1 x 1 predicted mean *Pf*PR$_{2-10}$ for the year a) 1939; b) 2007; grey mask represents no malaria risk due to low ambient temperatures

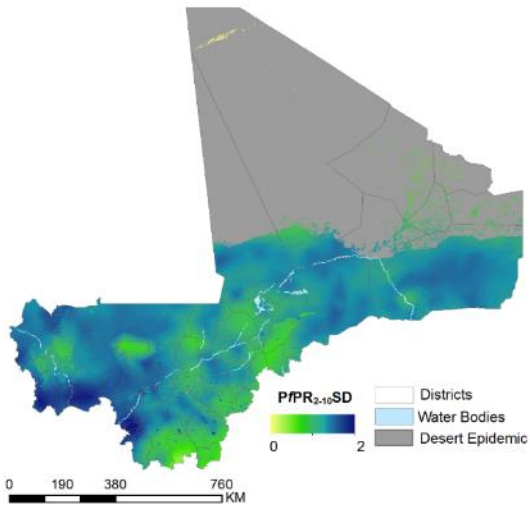
a)



b)



c)



Annex B Small area Estimation using INLA

B.1. Methods

The main Gaol of Small Area Estimation (SAE) is to provide model based estimates of target variables which can be used for model selection, classification, ranking and policy making in the respective administrative units and for predicting the target variables in the areas with no data [Pfefferman, 2002; Gomez-Rubio, 2009]

In this report a SAE Bayesian inference for ITN distribution was carried out in R-INLA which implements the Integrated Nested Laplace approximation for the latent Gaussian models [Rue et al, 2009; Martino and Rue, 2009]. In Bayesian inference models all unknown quantities and parameters of interest p_i (proportions of persons who slept under ITN in the i^{th} health district) were considered to be random variables, where inference was based on the posterior distribution of p_i given the observed data [Gomez-Rubio, 2009]. The approximated values of p_i were obtained by using the approximate method of Integrated Nested Laplace Approximation which was implemented in R-INLA [Martino and Rue, 2009]. The aggregated cluster data were used with the cluster as a random effect. Data for the national surveys of 2006, 2010 and 2012-13 were modelled separately.

The objective of this analysis was to develop point estimates of proportions for persons who slept under ITN in the i^{th} health district (p_i) . Thus p_i can be written as

$$p_i = \sum_j y_{ij} / N_i \qquad \text{(Equation B1)}$$

where N_i is the examined number of persons in health district i, and y_{ij} represents an individual sleeping under ITN.

The estimator for p_i in (1) as proposed by Royall (1970) is estimated by:

$$\hat{p}_i = \left(\sum_{j \in S} y_{ij} + \sum_{j \in S'} \hat{y}_{ij} \right) \Big/ N_i \qquad \text{(Equation B2)}$$

where the sum over $j \in S$ of y_{ij} is the sum of the persons sleeping under ITN from the i^{th} health district , and the sum over $j \in S'$ of $\hat{y}_{ij}$ is the sum of the estimated persons sleeping under ITN for the non-sampled individuals in the i^{th} health district.

The values for $\hat{y}_{ij}$ can be obtained from the model which describes the probability, μ_{ij}, that the j^{th} person within the i^{th} health district uses ITN. The model is given as

$$y_{ij} / \mu_{ij} \sim i.i.d.\ \text{Bernoulli}(\mu_{ij}),\ \text{logit}(\mu_{ij}) = \overline{X}_{ij}\beta + \delta_i \qquad \text{(Equation B3)}$$

So that $$\mu_{ij} = \left[1 + \exp\left\{-\left(\overline{X}_{ij}\beta + \delta_i\right)\right\}\right]^{-1} \qquad \text{(Equation B4)}$$

where β is the vector of the coefficients of the covariates X_{ij}, δ_i is the random effects associated with the i^{th} health district and is $\delta_i \sim i.i.d.\,\text{Normal}(0,\tau^2)$ where $\tau^2 \sim \text{Inverse Gamma}\,(a,b)$ The inverse gamma distribution parameters a and b are both set to zero or a value near to zero [Farrell, 2010].

Taking into consideration data distribution the hierarchical Bayes estimates for the model (3) can be developed. Let Y and Δ be vectors of data y_{ij} and δ_i respectively, then the data are distributed as the product of binomial:

$$f\left(Y/\mathrm{B},\Delta\right) \propto \prod_{ij} \mu_{ij}^{y_{ij}} \left(1-\mu_{ij}\right)^{1-y_{ij}} \qquad \text{(Equation B5)}$$

Using flat priors in the fixed effects parameters, we have

$$f\left(\beta,\delta/\tau^2\right) \propto \tau^{-n} \exp\left(-\sum_i \delta_i^2/2\tau^2\right) \qquad \text{(Equation B6)}$$

where n is the number of health districts. The distribution associated with τ^2 is given by:

$$f\left(\tau^2\right) = \frac{b^a \exp\left(-b/\tau^2\right)}{\tau^{2(a-1)}\Gamma\left(a\right)} \qquad \text{(Equation B7)}$$

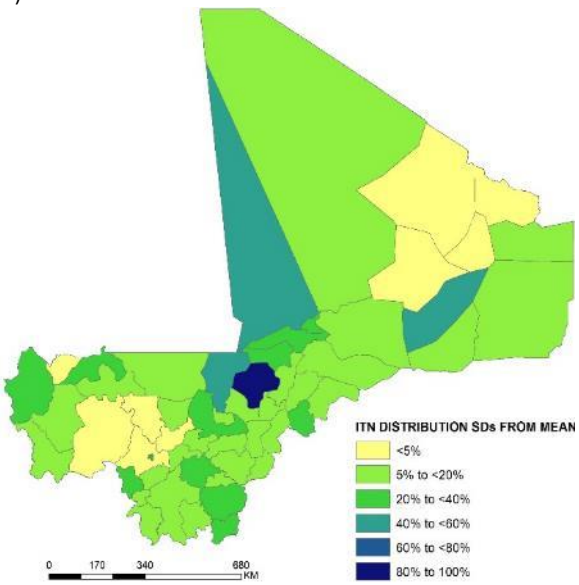
Thus, distributions (5), (6) and (7) can be used to specify that

$$f\left(Y,\mathrm{B},\Delta,\tau^2\right) \propto \prod_{ij} \mu_{ij}^{y_{ij}} \left(1-\mu_{ij}\right)^{1-y_{ij}} \tau^{-n} \exp\left(-\sum_{ij} \delta_i^2/2\tau^2\right) \frac{b^a \exp\left(-b/\tau^2\right)}{\tau^{2(a-1)}\Gamma\left(a\right)} \qquad \text{(Equation B8)}$$

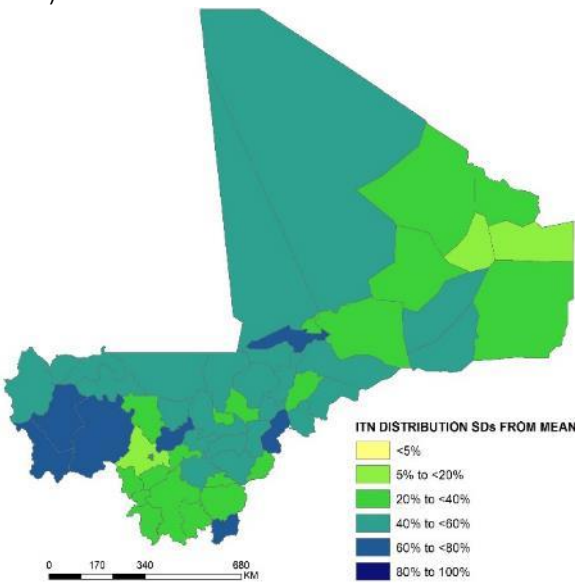
The Generalized linear mixed model (8) for ITN distribution was then implemented through an adapted stochastic partial differential equations (SPDE) approach with integrated nested Laplace approximation methods for inference to obtain the ITN estimates $\hat{p}_i$ [Martino and Rue, 2009, Farrell, 2010].

Figure B.1. The standard deviation around the estimated mean ITN coverage among all ages using small-areas estimation methods by health districts using data from the: a) DHS 2006; b) Anemia and parasitaemia survey of 2010; and c) DHS 2012-13. The DHS 2012-13 did not include the three northern regions of Tomboctou, Gao and Kidal due to security reasons (grey) due to security reasons and therefore no ITN coverage estimates are available for 2013.

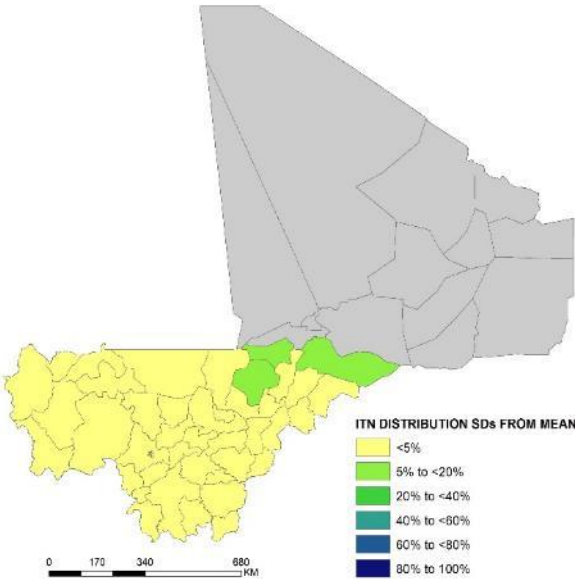
a)



b)



c)



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