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Exploring spatial variations in malaria burden among under five in Burkina Faso: indications for effective prevention

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To my Wife, Fati

To my children, Leïla, Ismaël and Habib

To our families

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List of abbreviations

ACT	Artemisinin-based Combination Therapy
CHWs	Community-based Health Workers
DHS	Demographic and Health Surveys
HMIS	Health Management Information Systems
HRP2	Histidine-Rich Protein 2
IRS	Indoor Residual Spraying
ITNs	Insecticide-Treated Nets
IPTp	Intermittent Preventive Treatment in pregnancy
LLINs	Long Lasting Insecticide-Treated Nets
MICS	Multiple Indicator Cluster Survey
NDVI	Normalized Difference Vegetation Index
NMCP	National Malaria Control Program
PCR	Polymerase Chain Reaction
RBM	Roll Back Malaria
RDT	Rapid Diagnostic Test
SMC	Seasonal malaria chemoprevention
WHO	World Health Organization

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Summary

Despite current efforts, malaria remains a major public health problem in Burkina Faso. Malaria parasitemia prevalence is regarded as a suitable indicator of the public health burden of malaria. Understanding the spatial distribution of malaria parasite prevalence is useful in order to locate the infectious reservoirs that further transmission as well as to assess the relationship between antimalarial interventions and malaria morbidity. However, prevalence data is often incomplete in remote rural areas due to the lack of microscopy, the reference technique for malaria diagnosis.

The main objective of this thesis was to explore the determinants of malaria burden among children under five years old in Burkina Faso through the analysis of: i) spatial heterogeneity of Plasmodium malaria prevalence distribution, ii) spatial heterogeneity of Paracheck® rapid diagnostic test (RDT) performance, and iii) geographic disparities in coverage of malaria vector control interventions. Community based survey data, health management information systems data, climatic and environmental data were combined first and then submitted to spatial statistical analyses.

Although considerable progress has been achieved in mosquito net coverage in Burkina Faso between 2003 and 2014, our data depict for the first time the existence of high heterogeneity in malaria prevalence at the community level. Additionally, our results suggest that paracheck® RDT use without microscopy for malaria screening could bias the estimation of malaria burden. Collectively, these findings indicate that management of community based

malaria determinants could represent the preferred approach to reduce malaria transmission in Burkina Faso.

Résumé

Au Burkina Faso, malgré les efforts déployés, le paludisme demeure un problème de santé publique majeur. La prévalence parasitaire de *Plasmodium* est considérée comme un indicateur utile de ce fardeau. La connaissance de la distribution spatiale de cette prévalence permet d'une part, de localiser le réservoir infectieux qui perpétue la transmission du paludisme et d'autre part, d'évaluer la relation entre les interventions antipaludiques et la morbidité palustre. Malheureusement, les données nécessaires pour estimer cette prévalence sont souvent incomplètes, à cause entre autre de l'absence d'accès à la microscopie, la technique de référence diagnostique de la pathologie, dans les zones reculées.

L'objectif principal de cette thèse était d'explorer les déterminants du fardeau du paludisme chez les enfants de moins de 5 ans au Burkina Faso à travers l'analyse i) de l'hétérogénéité spatiale de la distribution de la prévalence parasitaire de *Plasmodium*, ii) de l'hétérogénéité spatiale de la performance diagnostique du test de dépistage rapide (TDR) du paludisme Paracheck® et iii) des disparités géographiques dans la couverture des interventions de lutte antivectorielle. Des méthodes d'analyse statistique spatiale ont été appliquées à la combinaison de données d'enquêtes communautaires, de données de routine collectées par les districts de santé, de données climatiques et environnementales.

En dépit des progrès réalisés dans la couverture des moustiquaires au Burkina Faso entre 2003 et 2014, nos données montrent pour la première fois, l'existence d'une forte hétérogénéité de l'infection parasitaire du paludisme

à l'échelle communautaire. Aussi, nos résultats suggèrent que l'utilisation du TDR Paracheck® sans microscopie pour le dépistage de la parasitémie palustre pourrait biaiser l'estimation du fardeau du paludisme. En conclusion, nos résultats indiquent que la prise en charge des déterminants communautaires de l'infection palustre serait la piste à privilégier pour réduire la transmission du paludisme au Burkina Faso.

1. INTRODUCTION

1.1.Study Context

Malaria is a vector-borne parasitic disease caused by a *Plasmodium* hematozoon, which infects and destroys red blood cells. It is transmitted to humans through the bite of an infected female mosquito, of the genus *Anopheles*, during a blood meal. Five plasmodial species (*Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale*, *Plasmodium vivax,* and *Plasmodium knowlesi*) are responsible for malaria, of which *P. falciparum* is the most powerful in terms of number of clinical cases and severity of the disease.

Several regions in Africa, Asia, and Latin America are affected by malaria. In 2015, the number of clinical cases was estimated at 212 million, including 429,000 deaths [1]. More than 90% of clinical cases occur in sub-Saharan Africa [1] where *P. falciparum* is predominant. Asia and Latin America are mostly affected by *Plasmodium vivax* [1].

The World Health Organization (WHO) estimated a 41% reduction in the global malaria incidence rate between 2000 and 2015 [1], with a 21% reduction from 2010 to 2015. Over half of the 91 countries affected by malaria were on track to meeting the WHO target of reducing the malaria incidence and the associated mortality by at least 40% in 2015 [1]. However, decreased vigilance in eradication measures has been seen, for example, by Venezuela's rapid re-emergence of malaria in 2014 [2].

In sub-Sarahan Africa, the environmental variability adds to the burden of reducing malaria, as it exists even within small geographical spaces [3]. This

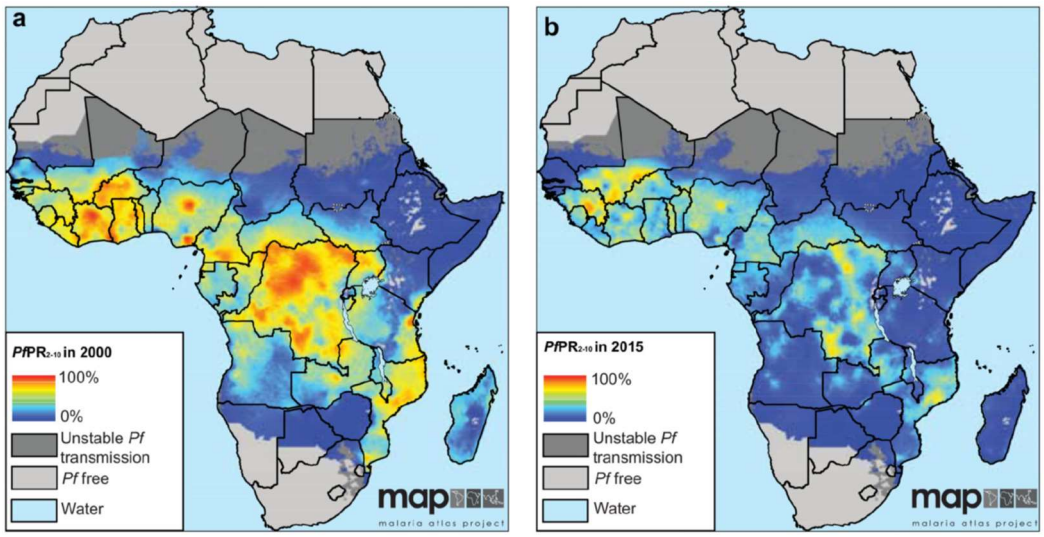
finding is confirmed by maps estimating the prevalence of *Plasmodium falciparum* infections among children in 2000 and 2015 (Figure 1). Currently, the prevalence is still very high (above 25%) in Burkina Faso and six other countries (Cameroon, Equatorial Guinea, Guinea, Mali, Sierra Leone and Togo) [1].

The parasite prevalence of *Plasmodium* is considered a useful indicator of the malaria burden, and an approximate measure of transmission [4, 5]. Knowledge of the spatial distribution of prevalence provides, on the one hand, useful information about malaria transmission and associated factors, and, on the other hand, the possibility to evaluate the relationship between anti-malarial interventions and malaria morbidity [6, 7]. Regular estimation of prevalence is necessary for the epidemiological surveillance of malaria [6]. It helps guide malaria control interventions to the most affected areas and populations [6].

In Burkina Faso, the National Malaria Control Program (NMCP) recommends focusing research activities on burden assessment, understanding the epidemiological profile of malaria, exploring the determinants of mosquito net use, and studying the impact of seasonal malaria chemoprevention (SMC) [8]. Unfortunately, the data required to estimate the malaria burden are often scattered or incomplete. Moreover, they are often not done in a sufficiently small location to allow for the study of local variability in the transmission of malaria.

In order to explore the distribution of this burden (measured here by parasite prevalence), we have built a single database, combining data from Demographic and Health Surveys (DHS), from the national Health

Management Information Systems, as well as from other climatic and environmental co-variables, measured by remote sensing. Robust estimation methods were used to predict parasite prevalence in areas where information was unavailable.



Source: https://www.nature.com/articles/nature15535

Figure 1: Estimate of the prevalence of P. falciparum infection among children aged 2-10 (PfPR2-10) in 2000 (a) and 2015 (b), predicted with a 5 × 5 km resolution [9]

1.2.History of Malaria

Malaria is a very old parasitosis. Reports of fatal fevers due to malaria date back to 6000 or even 5500 BC. The parasite responsible for malaria was discovered by Charles Laveran in 1880, while the mosquito that transmits the disease was first suspected by Ross in 1897, and confirmed by Grassi in 1898 [10]. The different plasmodial species that infect humans were discovered by Golgi (*Plasmodium malariae* in 1886), by Celli (*Plasmodium falciparum*), by Machiafava (*Plasmodium vivax*), and by Stephens (*Plasmodium ovale* in 1922 [10] and *Plasmodium knowlesi*, which mainly infects monkeys, but was recently isolated in human malarial infections in Southeast Asia) [11-13].

The first known treatment against malaria was reported from Peru to Europe by a Jesuit missionary named Don Fancisco Lopez in 1630 [10]. However, it was in 1820 that Pellerier and Caventou isolated quinine, an active alkaloid for the treatment of malaria [10]. The first synthetic antimalarial drug (chloroquine) was discovered in Germany in 1934 [10]. In 1960, chloroquine resistant strains of *P. falciparum* developed due to excessive use and probably inadequate doses [14].

The history of the fight against malaria has been marked by major WHO campaigns (in 1955) aimed at eradicating mosquitos using Dichlorodiphenyltrichloroethane (DDT) [14]. The emergence of insecticide resistant vectors, the financial cost of insecticides, and the uncertainty of vector ecology were all reasons that led the WHO to put an end to the global malaria eradication program in 1972 [15]. Since then, the most recent development in the fight against malaria was the launching of the “Roll Back

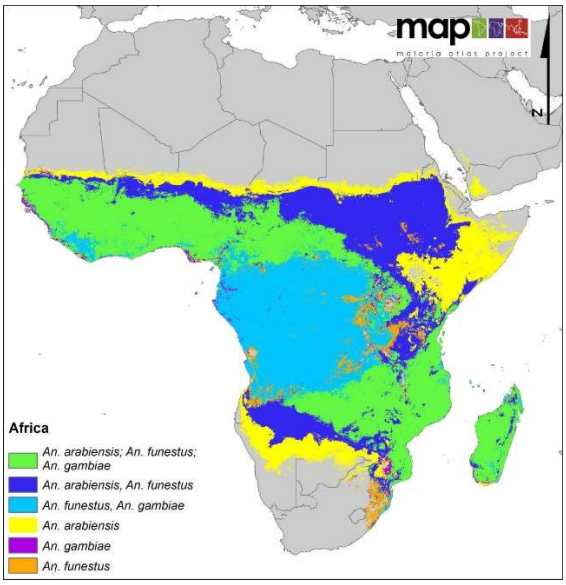
Malaria" initiative by the WHO, UNICEF, UNDP and the World Bank. This initiative mobilized major partners in the fight against malaria to, "halve the mortality due to malaria by 2010, and again in 2015." In 2000, the RBM initiative was approved by African states in a statement at a special summit in Abuja, Nigeria. The main strategies for this objective were:

- improving access to treatment for malaria,
- promoting the use of Insecticide-Treated Nets (ITNs),
- prevention and control of malaria in pregnant women (ITNs, IPTp),
- detection and control of malaria epidemics.

1.3.Epidemiology of Malaria

1.3.1. Malaria Vectors

More than 450 species of *Anopheles* mosquitos have been identified [16]. Only 40 of these species are significant vectors of malaria [16, 17]. *Anopheles gambiae s.l.*, *Anopheles funestus* and *Anopheles arabiensis* are the main vectors of malarial transmission [16]. In Africa, in most countries, malaria transmission involves several *Anopheles* species (Figure 2).



Source: https://parasitesandvectors.biomedcentral.com/articles/10.1186/1756-3305-5-69

Figure 2: Distribution of the three main vectors of malaria transmission in Africa

1.3.2. Malaria Parasites and the Evolutionary Cycle

Malaria is caused by a blood protozoan of the genus *Plasmodium*, which belongs to the phylum Apicomplexa (Sporozoa), the class Haemosporidea and the order Haemosporida. Five species are known to infect humans: *P. falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi*. Among these species, *P. falciparum* is responsible for the majority of malaria related deaths. It is also the predominant infectious species in most parts of Africa.

Throughout their evolutionary cycle (Figure 3), *Plasmodium* change their morphology, antigenicity, and size. They go through two reproduction cycles. The asexual cycle, or schizogony, takes place in humans (intermediate host); the sexual cycle, sporogony, takes place in the female *Anopheles* (definitive host and vector) [18].

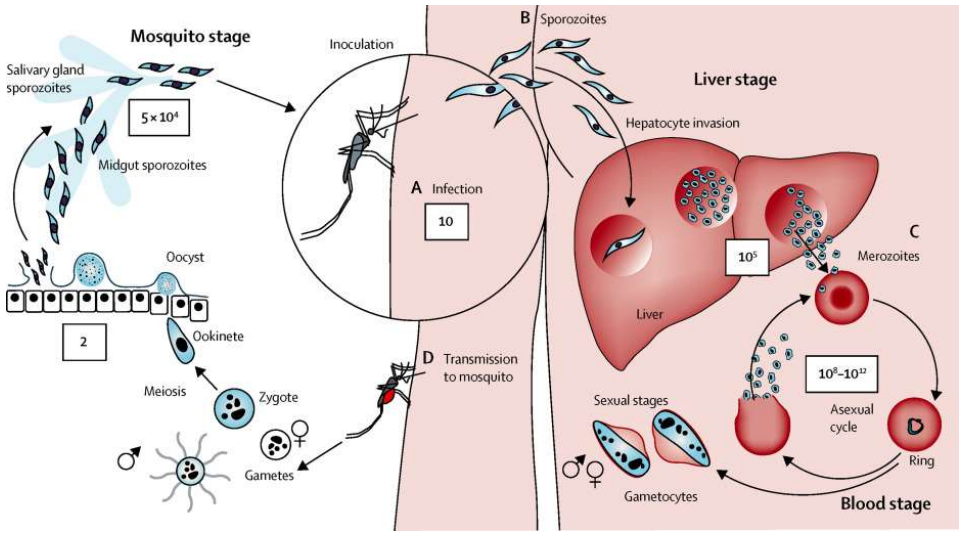
The parasitic cycle in humans is biphasic: an exo-erythrocytic or hepatic phase during which the parasites enter hepatocytes, and an endo-erythrocytic phase during which the plasmodia invade red blood cells.

The exo-erythrocytic cycle (A), begins with the injection of the sporozoite (infective form of the parasite) through a bite of the human host by an infected mosquito. These sporozoites pass through the blood stream to reach the liver within 24 hours. Some sporozoites are able to enter the liver cells (B). For about a week, they grow and multiply to give a multinucleated cell mass called a schizont, or a blue body. This intrahepatic phase is asymptomatic. At maturity, the schizonts rupture and release into the bloodstream the thousands of merozoites that will infect other red blood cells (C). However, in the case of *Plasmodium vivax* and *Plasmodium ovale*, some sporozoites, also called

hypnozoites may remain quiescent for a variable amount of time (a few months to several years) in hepatocytes. These hypnozoites may lead to future malaria relapses.

Throughout this endo-erythrocytic phase, merozoites that penetrated red blood cells undergo asexual multiplication and become trophozoites, and then endo-erythocytic schizontes. The lysis of the schizontes releases new trophozoites, which will infect other red blood cells. The duration of this cycle varies between 48 and 72 hours, depending on the plasmodial species. In the absence of immunity, the erythrocyte cycle will lead to clinical symptoms. Some trophozoites differentiate into a sexual form, or gametocytes (gamogonic erythrocyte cycle), which are ingested by the *Anopheles* mosquito during a blood meal (D), perpetuating transmission.

The sexual cycle, or sporogony, takes place in female Anopheles. During a blood meal from a malaria infected being, the mosquito ingests male and female gametocytes (D). In the mosquito's stomach, male and female gametocytes conjugate to form a zygote, which successively transforms into an ookinete, an oocyst, and finally into a sporocyst. Once ripe, the oocyst dislocates and releases sporozoites that migrate into the salivary glands of the mosquito. From this point on, the mosquito becomes infective and can perpetuate transmission. Each stage of the parasite cycle is a potential target for malaria control measures.



Source: http://www.thelancet.com/action/showFullTextImages?pii=S0140-6736%2813%2960024-0

Figure 3: Lifecycle of *Plasmodium falciparum* (boxed numbers represent the estimated number of parasites for each stage)

1.3.3. Immunity Against Malaria Infection

Malaria immunity can be natural; that is, it can be inherent to the genetic makeup of the host, independent of any prior contact with the parasite. It can also be an acquired immunity after a first infectious contact with the parasite.

Innate resistance to malaria is considered a refractory state of the host to the parasite due to its genetic constitution [19]. This resistance may be specific to the plasmodial species and its evolutionary stages, including the mechanisms involving membranous and intracellular erythrocytic factors. In fact, individuals with red blood cells lacking the Duffy blood group antigen are resistant to *P. vivax* infection [20]. These antigens are associated with determinants that constitute specific receptors for the adhesion and subsequent penetration of *P. vivax* [20]. In addition, certain hemoglobinopathies (particularly with AS and AC hemoglobin, as well as β-thalassemia) confer a partial resistance in heterozygous individuals, with HbS hemoglobin playing an obvious role against severe forms of malaria [21]. Modiano et *al*. showed that HbC hemoglobin is associated with one of the clinical manifestations of malaria [22], whereas hemoglobin F (HbF) in neonates inhibits the growth of *P. falciparum* within red blood cells [23]. Certain human leukocyte antigens have been associated with protection against cerebral malaria and severe anemia [21]. Glucose-6-phosphate dehydrogenase (G6PD) deficiency provides protection against infection with the malaria parasite [24], although there is no consensus in the literature.

Acquired anti-malarial immunity has several aspects and is a result of the combined action of cellular and humoral factors, dependent on the

physiological state of the host. At first, subjects living in endemic areas develop an asymptomatic carrier state, known as “premonition,” which is maintained by repeated exposure to infectious mosquito bites. This type of immunity is precarious because it can fade after leaving the endemic area. Nonetheless, passive transmission of protective antibodies from a mother to her child, through transplacental passage or breastfeeding, confers immunity against malaria to young infants. [25-27].

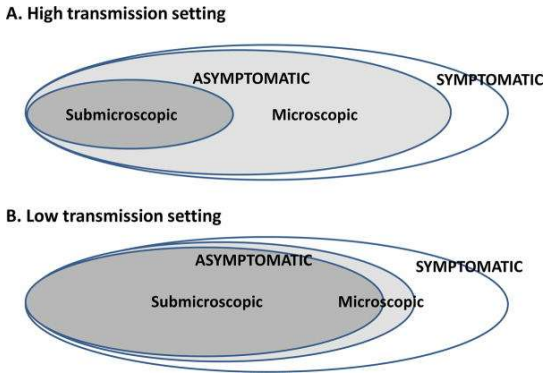
1.4.Prevalence of Malaria Parasitemia

1.4.1. Definitions

Malaria infection refers to the presence of malaria parasites (*Plasmodium*) in a subject with or without clinical symptoms. It can manifest in many ways, going from asymptomatic malaria (absence of clinical manifestations) to severe malaria that can lead to death. Between these two extremes, infected children can present with a wide variety of non-specific symptoms such as fever, malaise, vomiting and headache.

Prevalence of the *Plasmodium* parasite or **prevalence of malaria parasitemia** refers to the proportion of people in a population in whom a *Plasmodium* infection was detected at a particular time, using a diagnostic test (usually by microscopic examination or a rapid diagnostic test). This is the prevalence that is estimated through DHS among children 6 to 59 months.

The majority of infections studied in the population (malaria parasitemia) in endemic areas are asymptomatic [5, 28-30]. From a diagnostic standpoint, the asymptomatic group is composed of microscopic and submicroscopic parasitemias (Figure 4), which are distributed differently according to the transmission context. [31]. Only the microscopic group has a high potential for infection from humans to mosquitos (vectors of malaria) [31, 32].

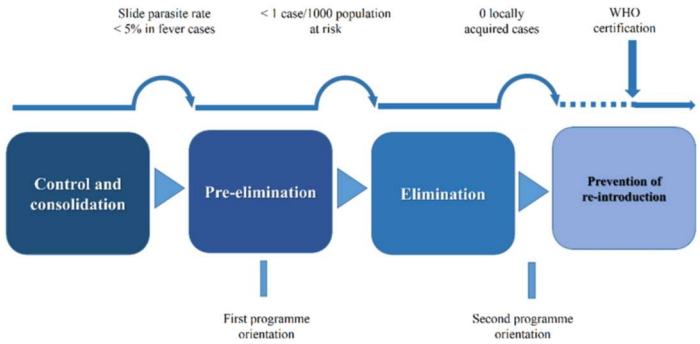


Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4049069/

Figure 4: Divisions in the asymptomatic malaria group, according to transmission setting

1.4.2. Malaria Parasitemia and Malaria Control

The prevalence of the parasite *Plasmodium* is a reflection of the level of malaria transmission. As such, slide positivity rate (SPR) is used by the WHO to classify the status of malaria transmission (Figure 5). This rate is the annual proportion of microscopically examined slides found to be positive among all the slides examined for fever cases. Countries with a SPR > 5 per 1000 inhabitants at risk are classified into the "malaria control phase". In these areas (which includes Burkina Faso), malaria control programs should focus on decreasing mortality and the number of cases [6].



Source: Malaria elimination: a field manual for low and moderate endemic countries. Geneva, World Health Organization (WHO, 2007)

Figure 5: Steps of a program for the elimination of Malaria

1.4.3. The Impact of Malaria Parasitemia on Health

An individual infected by *Plasmodium* can remain asymptomatic or can progress to simple or even severe malaria (Figure 6).

Although there are no strict diagnostic criteria for defining an asymptomatic infection, the absence of fever or any other clinical symptom for at least one week, and the presence of a positive blood smear or PCR test, are used to define a malaria infection as asymptomatic [33, 34]. Infections below the detectability threshold are also considered as asymptomatic. Despite the absence of acute symptoms, studies suggest that a chronic asymptomatic infection may have long term consequences for morbidity, particularly related to anemia [35-40], malnutrition [41], growth restriction and a decline in cognitive function [42].

Asymptomatic carriage can progress to simple malaria (Figure 6), generally occurring in non-immunized individuals. Symptoms appear six to ten days after inoculation, during the asexual stage of the erythrocytic schizogony [18]. Clinical manifestations are characterized by fever with a variety of non-specific symptoms such as headache, arthralgia, myalgia, malaise or sweating [18, 43]. Hemolytic anemia occurs following the destruction of erythrocytes by the parasite [35]. Globally, it is estimated that 90% of cases of simple malaria are due to *P. falciparum* [1].

Finally, a malaria infection can lead to severe malaria, with symptoms such as respiratory distress, severe anemia, prostration, convulsions or coma [44]. Other complications such as acidosis, hemoglobinuria, pulmonary edema, or

hypoglycemia may occur, further worsening the prognosis [44]. The sequelae following severe malaria, particularly cerebral malaria, are highly variable and may include neurological and developmental disorders [45-47] as well as the possibility of blindness, epilepsy, or cerebral palsy [48].

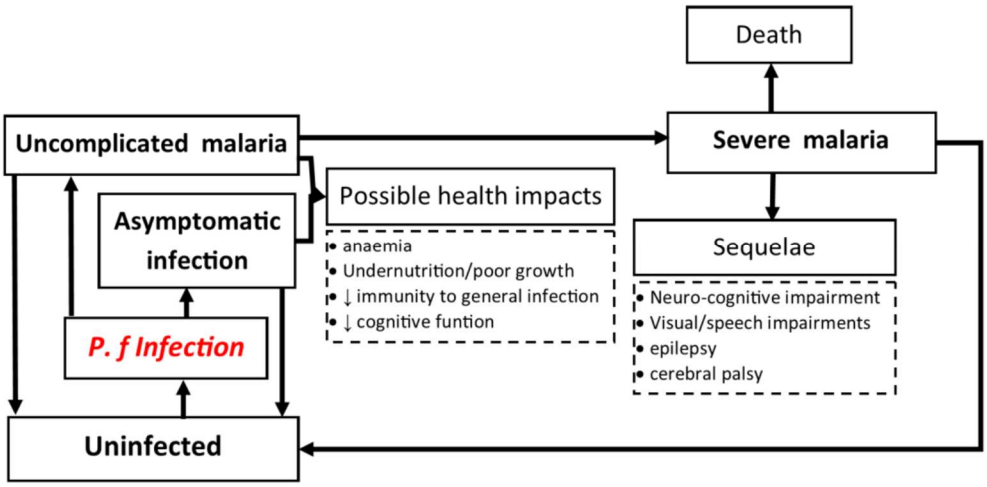


Figure 6: Representation of pathological states of malaria infection from *P. falciparum* Adapted from Snow et al. [49]

1.4.4. Determinants of Plasmodium Infection

The prevalence of malaria parasites among children under 5 years of age depends, according to multiple population studies, on individual, household and community factors.

At the individual level, the prevalence of malaria parasites increases with age [50-54] and does not vary with gender [51]. Children whose mothers have at least a high school education are less likely to present with a malaria infection [50, 51]. However, the effect of the use of mosquito nets by children on the probability of being infected with *Plamodium* is unclear. Some studies suggest a protective effect [50, 55, 56]. In contrast, many studies have found no association [57, 58], probably because the protective effect of net use varies with the level of malaria transmission [55].

At the household-level, children from households with lower socioeconomic status are more likely to have a positive parasitemia [50, 51, 53, 54, 57, 59, 60]. This link can be explained by the fact that households with a higher socioeconomic status have better access to quality materials for the prevention and treatment of malaria. In fact, certain characteristics of habitat materials (construction materials used for walls, the roof and the floor) [61, 62] have been associated with the risk of being infected by *Plasmodium*. In addition, the greater the number of inhabitants in a household, the greater the probability of a malaria infection among children [63]. In contrast, the protective effect of indoor residual spraying (IRS) has not been clearly established by Demographic Health Surveys. Multiple studies have addressed this question and have found no association between IRS and the probability

of malaria infection in children [54, 64]. However, some studies have shown that IRS decreases the risk of malaria infection [55, 57, 65].

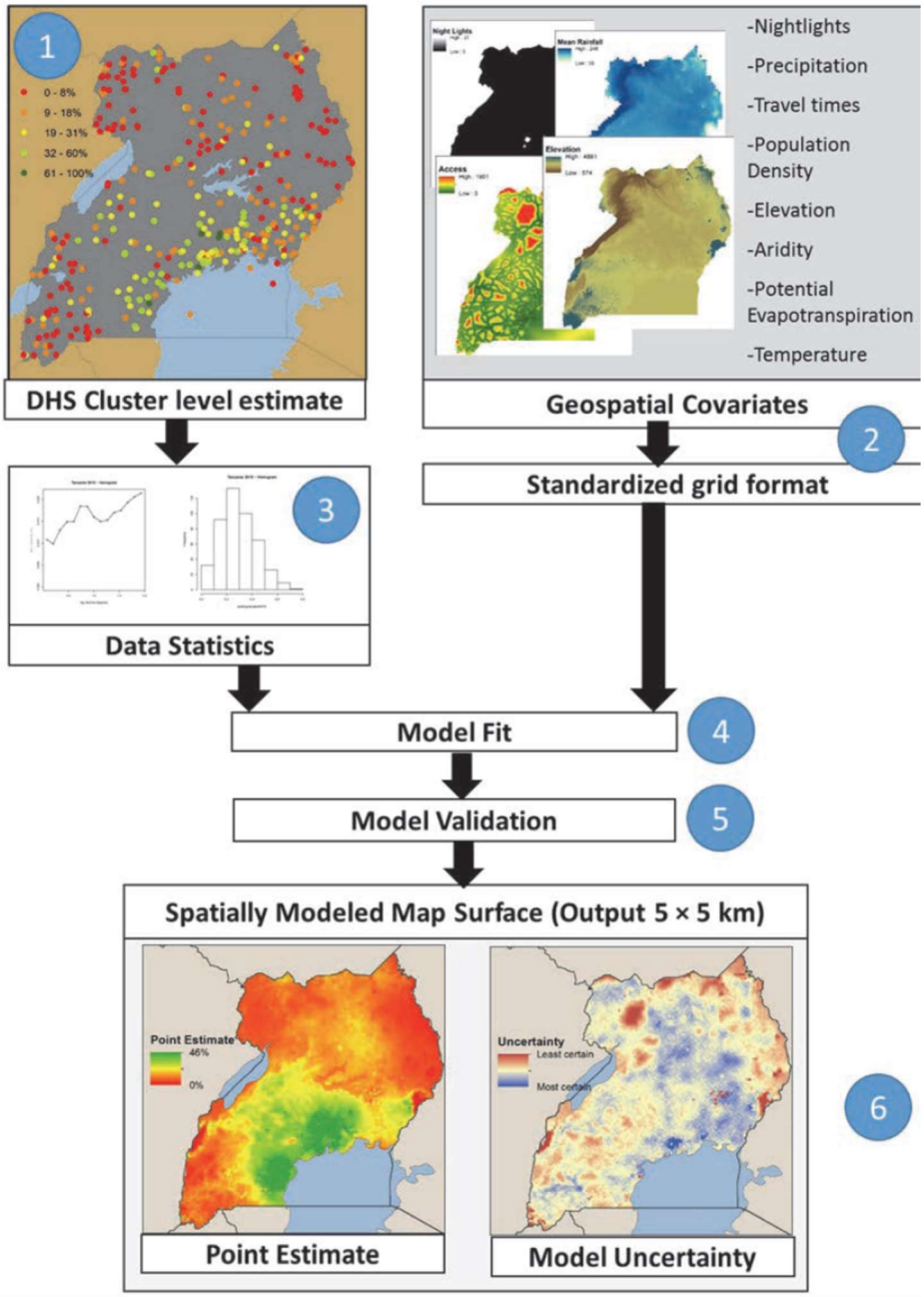
At the community level, the prevalence of malaria parasites is determined by climatic conditions, such as rainfall patterns [66, 67], temperature [68, 69] and humidity, which all influence the survival of mosquitos, and, as a result, the transmission of malaria. Multiple studies have shown that the epidemiology of malaria depends on local meteorological conditions [67, 70-72]. Children living in rural communities [50, 53, 54] and those with limited access to the healthcare system are more frequently infected with the malaria parasite [73].

1.4.5. Mapping Parasite Prevalence

Mapping the prevalence of the malaria parasites is useful for locating infectious reservoirs of malaria and for evaluating the impact of malaria control interventions. To be efficient, malaria control in countries with a heterogeneous transmission should target the most affected areas [74, 75].

In malaria endemic countries, there is no geographic data that is sufficiently precise to provide a continuous map of parasite prevalence. Geostatistical models have recently been applied to malaria parasite prevalence surveys to produce malaria risk distribution maps, and to estimate the number of infected children [54, 55, 76-78]. These are georeferenced data (or geostatistical data) that are collected in an irregular fashion and at a fixed number of sites. This type of data allows for prediction of a value for the variable of interest, with a certain degree of uncertainty, through spatial interpolation, at any point in the field of study [79, 80].

Recently, a six-step model, using data from DHS, has been proposed (Figure 7). The rate of parasitemia (proportion of infected individuals) in the selected areas is the starting point for this model. The prediction of the rate in unsampled locations accounts for potential environmental covariables and for the spatial correlation of the distribution of malaria infection cases [81].



Source: https://dhsprogram.com/pubs/pdf/SAR14/SAR14.pdf

Figure 7: Procedure for the creation of a continuous surface map using DHS indicators

1.5. Active Screening for Malaria Parasitemia

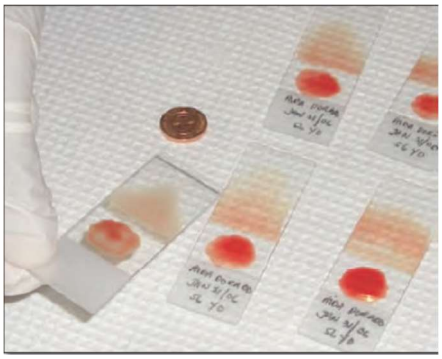
DHS surveys are used to evaluate the burden of malaria and the impact of anti-malaria interventions in sub-Saharan Africa. Parasite prevalence is the main indicator of this assessment. The results of this screening may be influenced by the tests used (Rapid Diagnostic Tests, microscopy, or molecular diagnosis), and also by the age of the subject and the level of transmission [82-84]. In addition to microscopy, which is considered the standard reference, RDTs are increasingly used for this type of screening. Molecular diagnosis (such as the amplification by polymerase chain reaction, PCR) is generally used in research contexts, and for surveillance in zones where malaria is being eliminated.

1.5.1. Diagnosis of Malaria by Microscopy

Microscopy is often considered the standard method for the detection of malaria parasites. In addition to detection, it can quantify and detect different *Plasmodium* species [85]. For this screening, two types of smears are used (Figure 8): the thick smear and a blood film (thin smear).

The thick smear is very sensitive because it has a detection threshold of 5 to 10 parasites per microliter, which corresponds to a parasite density of 0.0001% of infected red blood cells [86]. It is a technique that concentrates red blood cells. The blood film is very specific as it allows for the diagnosis of the species since the cells are spread out in a single layer.

Microscopy provides diagnostic certainty. It is capable of detecting approximately 75% of malaria infections in high-transmission areas [87]. However, it requires highly qualified microscopists, quality equipment, and ample time for reading samples.



Source: http://apps.who.int/iris/bitstream/10665/164472/1/9789242547825_fre.pdf

Figure 8: Picture of a thick smear and a blood film

1.5.2. Rapid Diagnostic Tests for Malaria

RDTs have become the most common method of screening for malaria infection. They are antigenic tests capable of detecting different plasmodial antigens (Table 1). For the screening of *P. falciparum* in regions of sub-Saharan Africa, the WHO recommends targeting histidine-rich protein 2 (HRP2) or *P. falciparum* lactate dehydrogenase (pLDH-Pf) [88].

HRP2 is produced solely by *P. falciparum*, while aldolase is produced by all four species (Table 1). Aldolase can therefore be used to identify each of the four species. pLDH is also common to all four species. It can be detected with the help of antigenic epitopes that bind to antibodies that are found in all four species or are specific to a given species (Table 1). Recently, a new RDT method for the diagnosis of *P. knowlesi* has been developed [89].

RDTs have the advantage of being easy to use and do not require a high level of technical ability to use. However, a RDT may remain positive for several weeks, even in the absence of a parasite, since the presence of antigens, and not the actual parasites, are measured [90]. This can lead to false positive results and an overestimation of the prevalence. On the other hand, deletions and mutations within the PfHPR-2 gene, and the prozone effect, could lead to false negatives [91, 92].

Finally, the sensitivity of RDTs may deteriorate at extreme temperatures and at high humidity levels during on-site use [93]. Given these limitations, many research studies recommend using RDTs only in comparison to microscopy in malaria surveys [83, 84, 94, 95].

Table 1: Antigenic targets of malaria Rapid Diagnostic Tests

		P. falciparum	*P. vivax*	*P. malariae*	*P. ovale*	*P. knowlesi*
HRP2		X				
Aldolase		X	X	X	X	X
pLDH	pLDH-pan	X	X	X	X	X
	pLDH-Pf	X				
	pLDH-Pvom		X	X	X	
	pLDH-Pv		X			

HRP2 – Histidine-Rich Protéine 2, pLDH – *Plasmodium* lactate dehydrogenase, Pf – *P. falciparum*, pan – all of the *Plasmodium* species, Pvom – *P. vivax, ovale* and *malariae*, Pv – *P. vivax*.

Source : adaptée de http://www.who.int/malaria/publications/atoz/9789241501125/fr/

1.5.3. Screening and Molecular Testing by PCR

Molecular biology (including PCR) is certainly the most sensitive technique, particularly for mixed infections and low-density parasite infections (1 to 5 parasites per microliter of blood) [96]. It cannot be used for emergency diagnoses. It is a costly test that requires a special equipment and skill. The test allows for the differentiation of strains and is essentially reserved for the study of mutations and genes involved in mutation. New gene amplification techniques, known as, "Loop Mediated Iso-Thermal Amplification," (LAMP), have been introduced for the detection of *Plasmodium* [90]. These techniques are claimed to have a similar sensitivity to PCR and could be used for field screening [90].

1.6.Prevention of Malaria Infection

In malaria-endemic areas, malaria prevention strategies, particularly among children, aim to i) prevent contact between humans and mosquito vectors of malaria by using LLINs (Long Lasting Insecticidal Nets), ii) reduce the vector population by Indoor Residual Spraying (IRS) of insecticides, iii) reduce malaria infection by Seasonal Malaria Chemoprevention (SMC), iv) develop an anti-malaria vaccine, and v) monitor anti-malarial drug resistance.

1.6.1. Use of LLINs

The current goal of malaria-endemic countries is to ensure universal coverage of LLINs (at least one mosquito net per two people for the entire population) and that at least 80% of mosquito nets are effectively used by the population. This level of coverage is assumed to reduce the transmission of malaria [97].

The protective effect of insecticide-treated nets has been established in various randomized trials [98, 99]. It was calculated that mosquito nets contribute to approximately 70% of the decline in malaria prevalence [3]. In children under 5 years old, the use of LLINs has reduced malaria associated mortality by 55% [100, 101]. However, the impact of LLINs on malaria reduction varies according to transmission intensity [102].

Recent mass LLIN distribution campaigns, the distribution of mosquito nets during prenatal consultations, and vaccination campaigns have increased the population's ownership and use of mosquito nets [1, 103]. Nonetheless,

discrepancies between net ownership (number of households with at least one ITN) and household ownership of a sufficient number of nets (number of households with at least one ITN per two people) have been reported [104-106]. Similar differences were found between population access to mosquito nets and their actual use [104-106]. As a result, it is necessary to regularly evaluate the use of LLINs by populations [107]. At the same time, effective communication strategies need to be established so that each individual at risk of malaria infection sleeps under a LLIN [107].

Unfortunately, recent studies have reported barriers to mosquito net use. In Burkina Faso, factors associated with the non-use of LLINs included misconception of the usefulness of the nets, the inconvenience of having a bulky net hanging above the bed [108] and household size [109]. In addition, the season, the discomfort, and preferences for net shape, size or colour, have often been cited as determinants of LLIN non-utilization [102, 110].

1.6.2. Seasonal Malaria Chemoprevention

In areas of high seasonal malaria transmission, the WHO has recommended malaria chemoprevention (SMC) during the high transmission season. This consists of giving children ages 3 to 59 months a complete treatment for malaria at one month intervals, with a maximum of four cycles [111]. However, SMC does not provide complete protection against malaria, and requires the establishment of a drug distribution network [112]. Some studies have reported the risk of the emergence of resistance to drugs such as sulfadoxine-pyrimethamine and amodiquine, which are currently used for SMC [112]. Starting in 2016, health authorities in Burkina Faso suggested the implementation of SMC in all health districts [8].

1.6.3. Vaccines and Malaria Prevention

Transmission of malaria remains high in many regions, despite efforts of prevention. A low-cost vaccine that provides effective prevention is an important component that should be a part of malaria control strategies [113]. According to results from a mathematical model, the addition of the RTS,S/AS01 vaccine to the routine childhood immunization program, would prevent 200 to 700 deaths per 100,000 due to malaria in endemic areas [114]. Currently, the RTS, S / AS01 vaccine, from GlaxoSmithKline (GSK), is the most advanced candidate among anti-malarial vaccines.

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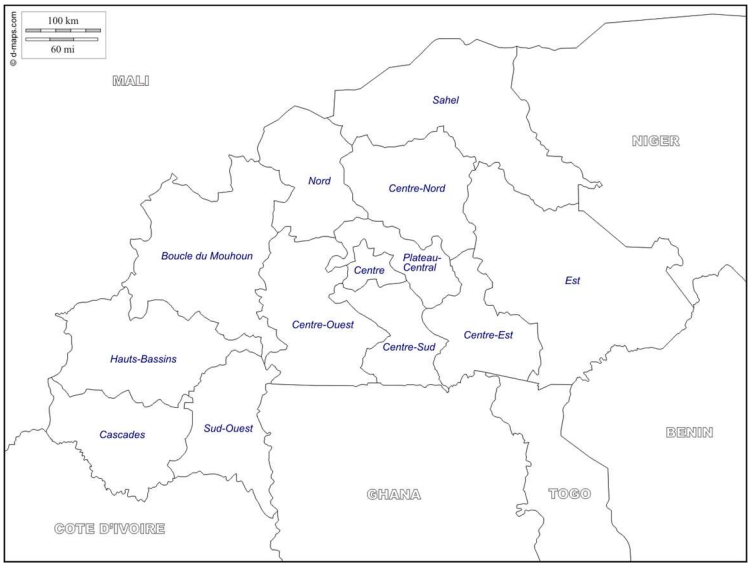
2. MALARIA AMONG CHILDREN IN BURKINA FASO

2.1.Context of Burkina Faso

2.1.1. Geography and Climate

Burkina Faso is a vast and flat landlocked country with a landmass of 274,900 square kilometers located in West Africa. It shares common borders with six other nations: Mali to the north and west, Niger to the northeast, Togo, Ghana and Cote d'Ivoire to the south and Benin to the southeast. The bordering regions with Niger and Mali have been affected by many tribal conflicts following the Touareg's rebellion. The country's average altitude is 400 meters. The hydrographic network includes three main rivers: Mouhoun, Nazinon and Nakambe. Administratively, the country is divided into 45 provinces organized within 13 regions (Figure 9).

In Burkina Faso three climatic profiles are present from tropical to sudano sahelian climate. Precipitation has seasonal patterns with a rainy season from July to October, and a dry season from November to June. A transitional season, between November and February, separates the dry and rainy seasons. [1]. Average rainfall increases from the northern part of the country (average 350 mm) towards the southwestern part of the country (average above 1.000 mm).



Source : http://d-maps.com/m/africa/burkina/burkina18.gif

Figure 9 : Map of Burkina Faso highlighting the 13 administrative regions.

2.1.2. Demography and Economy

The country has a population of 18 million inhabitants, 77% of which live in rural areas [2]. Children under 5 years old represent more than 17% of the population.[2]. Demographic growth is about 3.1% [2] whereas infant mortality is 83 deaths for 1000 live births. Life expectancy at birth is 57 years, and the crude mortality rate is 12‰ [3].

The Burkina Faso's economy is often ranked among the world weakest. Despite recent developments in the mining sector, it remains an agricultural economy, dependent on climatic fluctuations. According to the United Nations Development Program's (UNDP) ranking, the country ranked 185th out of 188 countries according to the Human Development Index (HDI) in

2015 [4]. This condition of poverty affects several determinants of malaria, including access to health services, education, housing quality, and socio-economic inequalities. The country is engaged in socio-economic reforms favorable to development. With the purpose of achieving the Sustainable Development Goals (SDGs), several strategic plans are being implemented, including those related to the fight against malaria.

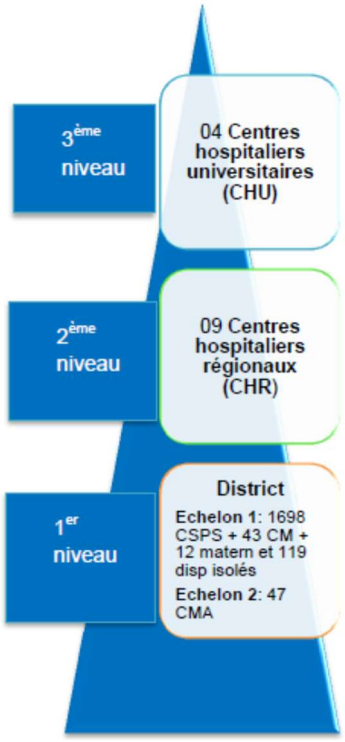
2.1.3. Burkina Faso's Healthcare System

The healthcare system of Burkina Faso has two organizational structures: the administrative organization and the organization of care.

The administrative organization structure is pyramidal with three levels [5]. The central level is responsible for the country's health policy design. The intermediate level includes 13 health regions that are in charge of supervising the health district's activities. The peripheral level is composed of operational units termed "health districts" where healthcare services are delivered, including those related to malaria control. Between 2010 and 2015, the number of health districts increased from 63 to 70.

Health care provision is organized within different sectors including the public, the private, and the traditional sectors with the more recent addition of the community based system. The public sector, the main provider of care, has three complementary levels ranging from the peripheral to the central level (Figure 10). At the base of this system, there are peripheral health centers and medical centers with surgical antenna (Centre Médical avec

Antenne chirurgicale - CMA). These are hierarchically attached to the 9 Regional Hospital Centers (Centres Hospitaliers Régionaux - CHR) representing the referral centers for the CMAs. At the top of the pyramid there were four (04) university teaching hospitals (Centres Hospitaliers Universitaires) in 2015.



Source : http://cns.bf/IMG/pdf/tableau_de_bord_2015_ms_vf.pdf

Figure 10 : Health care service organization in Burkina Faso.

In addition to this organization, community-based health workers (CHWs) and non-governmental organizations (NGOs) carry out community-based

healthcare activities. These activities consist of social engagement, health promotion, patient follow-up, family planning promotion, and treatment of malaria and diarrhea, etc. This community-based health care, now favored by Burkina Faso, ensures continuity and accessibility of health services to the population.

Finally, so-called "traditional" medicine is playing an increasingly important role in Burkina Faso's health system. Traditional healers are trained to recognize the symptoms of malaria severity in order to refer these cases to health facilities.

2.2.Epidemiological Profile of Malaria

In 2015, Burkina Faso’s healthcare centers reported 3,688,077 cases of malaria in children under 5 years old, which represented 45% of all malaria cases. In this age group, malaria remains the first reason for health care visits (53%), hospital admission (60%) and cause of death (39%) [5].

On average, a Burkinabe child has 1.3 to 2.4 uncomplicated malaria episodes per year [6-8] and all this, despite recent efforts that aim to improve the access to insecticide treated nets and effective artemisinin-based combination therapy [8]. During peak transmission period in 2013, malaria prevalence was 58% in Nouna (area of continuous transmission) and 42% in Sapone (area of seasonal transmission) among children between 6 months to 4 years old [9].

Malaria transmission is holo-endemic in Burkina Faso with significant seasonal upsurge. Almost 60% of malaria cases in the health centers are recorded between July and November [10]. This window of time is also used for the progressive implementation of seasonal malaria chemoprevention (SPC) in children.

Malaria transmission in the country is categorized into three groups that correspond to the climatic zones (Figure 11). The northern part of the country, which is located in the Sahelian region, has short seasonal transmission (two to three months). The central Sudano-Sahelian region has long seasonal transmission (four to six months). Finally, the South-West Sudano-Sahelian region experiences permanent transmission with peak transmission occurring during the rainy season. Recent socio-demographic, climatic and ecological changes in Burkina Faso may have changed this sub-division that has been present since 2003.

P. falciparum malaria represents 90% of malaria cases in the country [11] and is responsible for significant mortality [10]. *P. malariae* (3-8%) and *P. ovale* (0.5-2%) cause 10% of malaria cases [11]. Unlike *P. falciparum* infection, which is widespread throughout the country, *P. malariae* and *P. ovale* peak individually at the end of the rainy season in October [12].

Malaria is transmitted by female mosquitoes belonging to the *Anopheles gambiae s.l.* mainly *Anopheles gambiae s.s, An. Coluzzi* and *An. Arabiaensis* [11, 13]. In terms of numbers, *An. Funestus* is the second largest group of vectors following *An. Gambiae s.l.* and they are particularly important at the end of the rainy season [10].

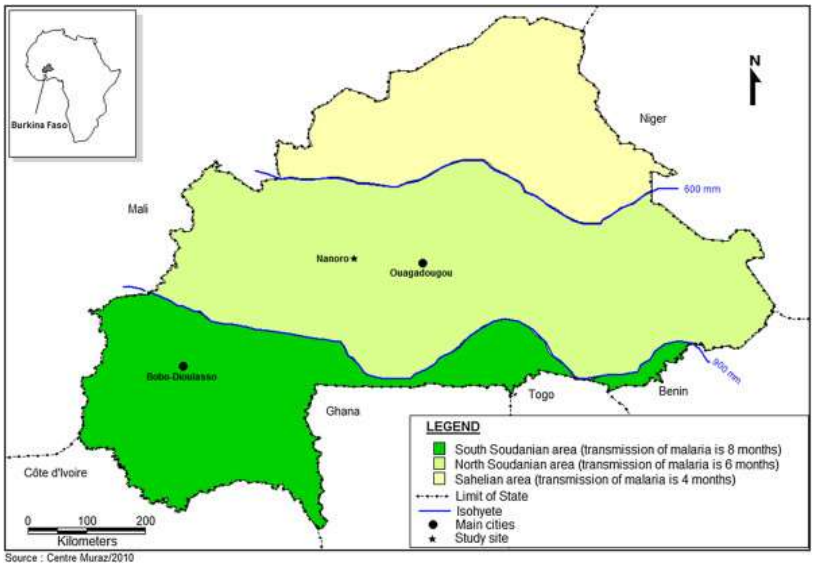


Figure 11 : Malaria Transmission Zones, Burkina Faso.

2.3.Problem of Malaria Control

Malaria control activities are coordinated by the National Malaria Control Program (NMCP) created in 1991 [10]. These activities are usually based on WHO recommendations.

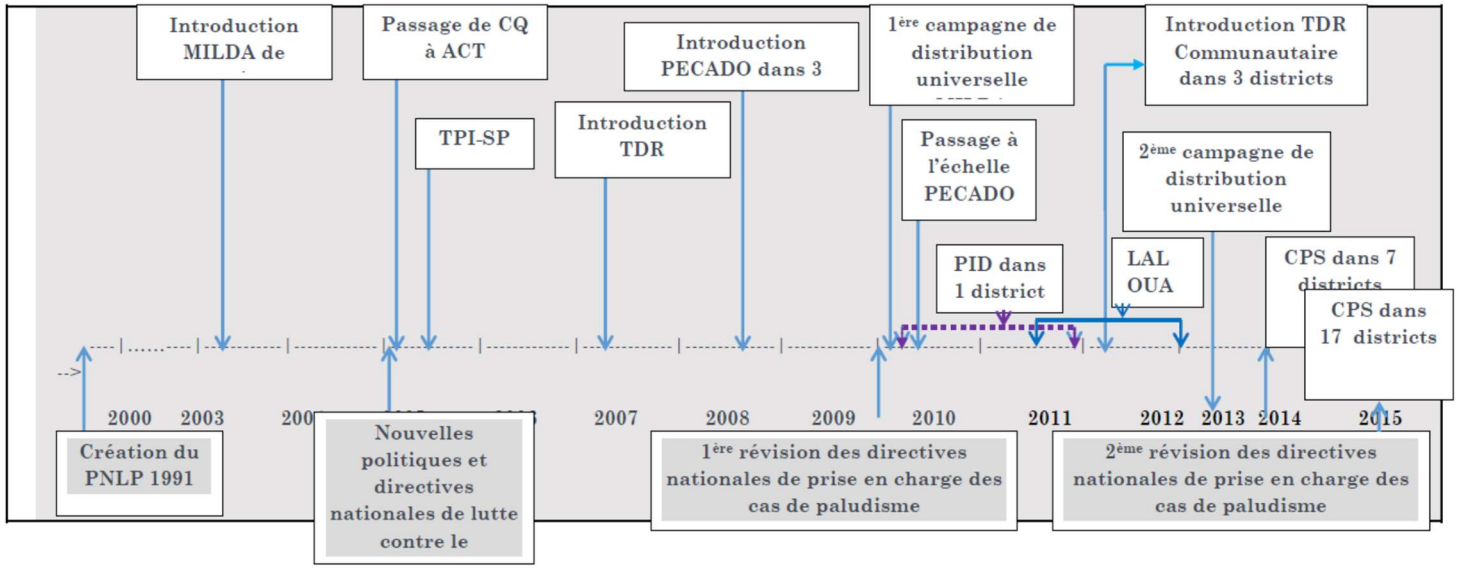
Among key milestones in the fight against malaria, we can cite the chloroquine replacement in 2005 as first line treatment by Artemisinin-based Combination Therapy (ACT) (Figure 12). Universal mosquito net distribution campaigns in 2010, 2013 and 2016 have also significantly contributed to the prevention of malaria. Mosquito nets are provided to the population during

antenatal visits and vaccination campaigns, although the contribution of these networks is currently limited. However, free distribution campaigns may prove to be ineffective in the long run due to lack of funding and the average 3 year lifespan of nets [14].

Indoor residual spraying (IRS) is also used for malaria vector control. This strategy is still marginal in Burkina Faso. It could be suitable for targeted interventions [11] although its funding could be a limiting factor in the Burkinabe context.

The parasitological diagnosis of malaria suspected cases is performed by microscopy or RDT. At the community level, CHWs are in charge of testing fever cases using RDT. However, RDT usage at the community level is still low[15]. Only a small proportion of malaria cases, called "*the ears of hippopotamus*" [16] are diagnosed on a biological basis. An accurate estimation of malaria burden is not possible using the routine surveillance system because of under notification of cases, but the information is useful for guiding malaria control interventions.

The prevalence of parasitemia in the population is under documented. To strengthen control measures in Burkina Faso, it is necessary to understand the spatial and temporal dynamics of the transmission reservoir [17, 18].



Source Rapport PLNP

ACT : Combinaison thérapeutique à base d'artémisinine, CPS : Chimio prévention du paludisme saisonnier, CQ : Chloroquine, LAL : Lutte anti larvaire, MILDA : Moustiquaires imprégnées d'insecticide à longue durée d'action, PECADO : Prise en charge à domicile, PID : Pulvérisation intra domiciliaire, PNLP : Programme national de lutte contre le paludisme, TDR : Test de diagnostic rapide, TPI-SP : Traitement préventif intermittent - Sulfadoxine-pyriméthamine.

Figure 12 : Principal steps of malaria control in Burkina Faso (source: NPMC 2016)

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3. RESEARCH OBJECTIVES

3.1.Study Rational

Malaria remains a major public health problem in Burkina Faso, even though the country has firmly committed itself in the last decade to the fight against malaria by deploying significant human and financial resources in vector control and case management.

The parasitological prevalence of malaria infection among Burkinabe infants is greater than 50% according to recent demographic and health surveys. This parasite carriage represents an infectious reservoir maintaining the high transmission level of malaria and has important health consequences.

A better understanding of the spatial variation of this infectious reservoir as well as the geographic inequalities in the access to resources available in the fight against malaria could contribute to the improvement of malaria control programs (Figure 13). At a time of policymaking decentralization in Burkina Faso, it is necessary to utilize available data to target the most affected areas and to evaluate the impact of control interventions.

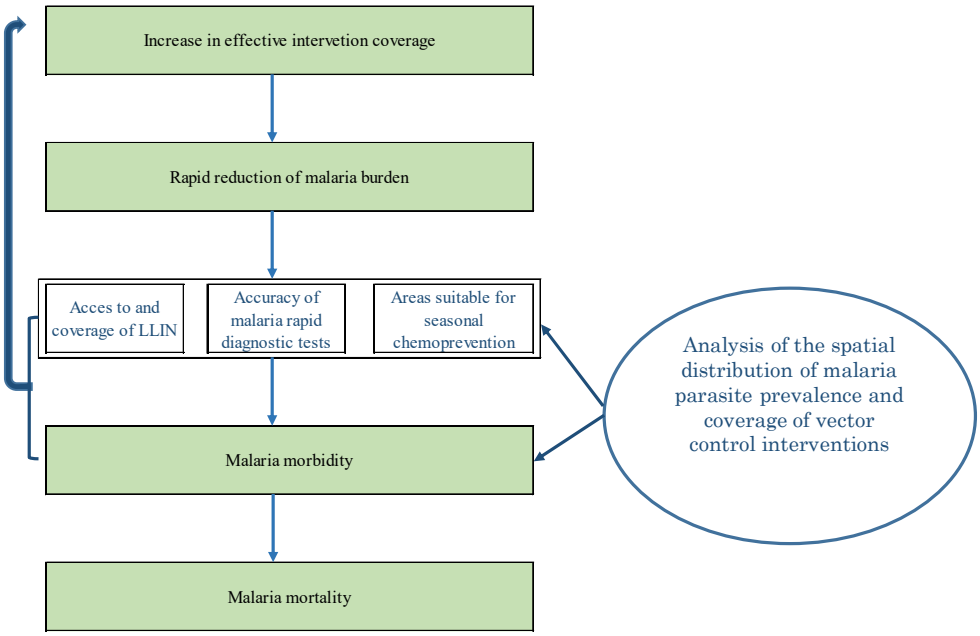

Figure 13 : Relational model upon which the thesis is based.

3.2.General Objective

The overall objective of this thesis is to contribute to the improvement of malaria prevention in children under 5 years old in Burkina Faso through a better understanding of the spatial distribution of *P. falciparum* malaria carriage prevalence and the geographic inequalities in access of the population to anti-malarial interventions.

3.3. Specific Objectives

- Describe the spatial distribution of malaria infection among children under 5 years old in Burkina Faso.
- Identify socio-demographic and environmental factors that determine this spatial distribution.
- Analyze the geographic variation of Paracheck® RDT performance and its implication for the estimation of malaria burden.
- Analyze the geographical disparities in the access and the use of long-lasting insecticide-treated nets (LLINs) to prevent the population's exposure to malaria vectors.

4. METHODS

4.1. Study Design

This thesis is based on a secondary analysis of cross-sectional demographic and health surveys conducted in Burkina Faso between 2003 and 2014 (Figure 14), in which malaria indicators were collected. The analysis also includes environmental data from remote sensing as well as routine data from the national Health Management Information Systems (HMIS).

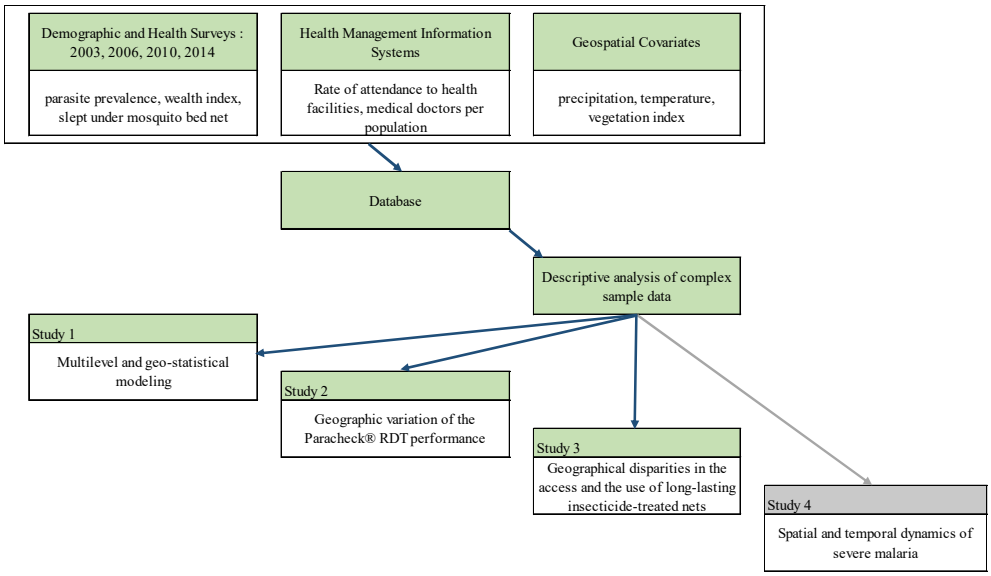

Figure 144 : Data sources

4.2.Study Sites

The study sites included in this thesis are the clusters selected by the DHS. A cluster represents a grouping of households generated for the needs of the general census of Burkina Faso's population. It roughly corresponds to a village (or a group of villages) in a rural area and a district in an urban area. In other words, a cluster refers to a "community" a group of respondents living in the same geographic environment. During DHS surveys, the longitude and latitude coordinates of the clusters were collected by Global Positioning System (GPS). Unfortunately, this information is underutilized in DHS studies. The clusters were selected to provide indicators that are representative of the 13 regions of Burkina Faso.

4.3. Target Population

This thesis focuses on children ages 6 to 59 months who were residents of the surveyed households. Together with pregnant women, they represent the population that is most vulnerable to malaria and to its transmission.

4.4.Sampling

Data included in the sample were collected during the DHS conducted in Burkina Faso in 2003, 2010, 2014 and the Multiple Indicator Cluster Survey (MICS) in 2006. The surveys were conducted by the National Institute of Statistics and Demography (Institut National de la Statistique et de la Démographie - INSD) and ICF Macro International.

Sample size calculations have been published [1-4]. Briefly, the samples were selected using a two-stage stratified clustering method. Stratification was done at the level of the region and the place of residence (urban or rural). The samples were drawn independently within each stratum with a probability proportional to the number of households. The primary sampling unit (PSU) for the 2003 DHS and the 2006 MICS was the cluster or enumeration area (EA), as defined by the 1996 census. For the 2010 DHS and 2014 the PSU was defined by the 2006 census.

Environmental variables likely to influence the transmission of malaria such as altitude, precipitation, temperature, and vegetation index were used as control variables. Similarly, control variables regarding the supply of care such as access to health centers and availability of health care staff have been incorporated. These variables were generated from routine data obtained from health facility monthly reports compiled in the national Health Management Information System (HMIS). The different data sources were merged using either the location (longitude, latitude) or the geographical area.

4.5. Data Collection

The data were collected using a household questionnaire and an individual questionnaire. These are standard questionnaires (adapted to the needs of Burkina Faso) developed by the DHS program, in collaboration with the Roll Back Malaria (RBM) Partnership. During the surveys, demographic, socio-economic and malaria indicators were collected. The location of the clusters was geocoded via Global Positioning System (GPS) receptors. These sites were moved randomly up to 2 km (urban) and 5 km (rural) according to the standard DHS protocol to protect the anonymity of respondents [5].

4.6.Statistical Analysis

Statistical analyses were conducted taking into account the complex survey design of the DHS (including strata, cluster effects and weights). To do this, the descriptive analyses were carried out by using the commands for complex survey data in Stata (svyset) [6] and in R (Survey package) [7]. Different statistical methods were used based on the distribution of the data in each study and the assumptions of the study.

In the study on malaria parasite prevalence mapping, a two-level logistic model was used to identify individual and community level factors associated with the risk of malaria infection. Subsequently, we used a predictive model commonly called model-based geostatistics (MBG) [8] to predict the prevalence of malaria in unsampled locations and to produce a continuous

map of malaria prevalence in Burkina Faso. This analysis was performed through a Bayesian approach using the R-INLA library of the R software [9]. This approach also helped to design maps of the uncertainties inherent to the estimation of the prevalence.

In the Paracheck® rapid diagnostic test study, the performance of the test for *P. falciparum* detection was assessed in comparison to microscopy. Several performance parameters were calculated including sensitivity, specificity and Youden (J) index. The analyses were stratified by place of residence and geographic region.

In the study regarding the coverage of anti-malarial interventions, geographical disparities in possession and use of nets were mapped and analyzed by socio-demographic groups. Four main indicators were considered: net possession, access to sufficient numbers of nets, use of nets, and gaps between possession and use.

4.7.Ethical Considerations

The data included in this thesis are from public domain material and were obtained on request from DHS. In accordance with the recommendations received during our request, the articles based on this thesis have been published on the DHS website (https://dhsprogram.com/). DHS protocols were approved by the national ethics committee of Burkina Faso and the ICF Macro-International Ethics Committee. The survey questionnaires were administered after obtaining informed and voluntary consent. For anemia and malaria screening in children, consent was sought from parents or a legal representative.

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5. RESULTS

5.1. Determinants and Spatial Distribution of Malaria Parasite Carriage

Samadoulougou *et al. Parasites & Vectors* 2014, **7**:350
http://www.parasitesandvectors.com/content/7/1/350

Parasites & Vectors

RESEARCH Open Access

Multilevel and geo-statistical modeling of malaria risk in children of Burkina Faso

Sekou Samadoulougou[1*], Mathieu Maheu-Giroux[2], Fati Kirakoya-Samadoulougou[1], Mathilde De Keukeleire[1,3], Marcia C Castro[2] and Annie Robert[1]

Abstract

Background: Previous research on determinants of malaria in Burkina Faso has largely focused on individual risk factors. Malaria risk, however, is also shaped by community, health system, and climatic/environmental characteristics. The aims of this study were: i) to identify such individual, household, community, and climatic/environmental risk factors for malaria in children under five years of age, and ii) to produce a parasitaemia risk map of Burkina Faso.

Methods: The 2010 Demographic and Health Survey (DHS) was the first in Burkina Faso that tested children for malaria parasitaemia. Multilevel and geo-statistical models were used to explore determinants of malaria using this nationally representative database.

Results: Parasitaemia was collected from 6,102 children, of which 66.0% (95% confidence interval (CI): 64.0-68.0%) were positive for *Plasmodium spp.* Older children (>23 months) were more likely to be parasitaemic than younger ones, while children from wealthier households and whose mother had higher education were at a lower risk. At the community level, living in a district with a rate of attendance to health facilities lower than 2 visits per year was significantly associated with greater odds of being infected. Malaria prevalence was also associated with higher normalized difference vegetation index, lower average monthly rainfall, and lower population densities. Predicted malaria parasitaemia was spatially variable with locations falling within an 11%-92% prevalence range. The number of parasitaemic children was nonetheless concentrated in areas of high population density, albeit malaria risk was notably higher in the sparsely populated rural areas.

Conclusion: Malaria prevalence in Burkina Faso is considerably higher than in neighbouring countries. Our spatially-explicit population-based estimates of malaria risk and infected number of children could be used by local decision-makers to identify priority areas where control efforts should be enhanced.

Keywords: Burkina Faso, *Plasmodium falciparum*, Geo-statistics, Random effect models, Bayesian variable selection, Malaria burden, Integrated Nested Laplace Approximation

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Résumé

Introduction: La recherche sur les déterminants du paludisme au Burkina Faso a permis d'identifier de nombreux facteurs liés aux caractéristiques individuelles. Cependant, le rôle des facteurs contextuels caractérisant l'ensemble des personnes d'un même ménage ou d'une même communauté, qui utilisent le même système de santé et qui vivent dans les mêmes conditions climatiques et environnementales a largement été ignoré. Les objectifs de cette étude chez les enfants âgés de moins de cinq ans étaient donc i) d'identifier les déterminants de la parasitémie palustre qui sont d'ordre individuels, ceux qui sont liés au ménage, ceux qui sont d'ordre communautaire, et ceux qui sont d'ordre climatique/environnemental et ii) de cartographier la prévalence de parasitémie palustre pour l'ensemble du Burkina Faso.

Méthodes: La quatrième Enquête Démographique et de Santé (DHS) réalisée en 2010 était la première enquête dans laquelle les enfants ont été testés pour les infections à *Plasmodium sp*. au Burkina Faso. A partir de cette enquête représentative au niveau national, des modèles multiniveaux et géostatistiques ont été utilisés pour explorer les déterminants du paludisme.

Résultats: Un total de 6,102 enfants ont été testés pour le paludisme et 66.0% (intervalle de confiance à 95%: 64.0-68.0%) d'entre eux étaient infectés par *Plasmodium spp*. Les plus âgés (>23 mois) avaient une parasitémie plus élevée. Les enfants des ménages ayant un statut socio-économique plus élevé et ceux dont la mère avait une scolarisation plus longue avaient une parasitémie plus faible. Au niveau communautaire, les enfants résidant dans les régions administratives où le taux de fréquentation des centres de santé n'atteignait pas deux visites par an étaient significativement plus à risque d'être parasités. Le risque de paludisme était également plus élevé quand l'indice de végétation normalisé était plus élevé, quand la moyenne des précipitations mensuelles était plus basse et quand la densité de population était plus faible. Les prédictions de la prévalence du paludisme variaient selon les localités, allant de 11% à 92%. Le nombre d'enfants ayant la parasitémie palustre est concentré dans les zones à haute densité de population alors que le risque parasitémique est plus élevé dans les zones rurales peu peuplées.

Conclusion: La prévalence du paludisme au Burkina Faso est considérablement plus élevée que celle des pays voisins, mais il existe une forte variabilité à l'intérieur du pays. Nos estimations du risque de parasitémie palustre et du nombre d'enfants infectés devraient permettre aux décideurs locaux d'identifier les zones d'intervention prioritaires pour le renforcement de la prévention et du contrôle de la maladie.

Background

In 2010, there were an estimated 216 million cases of malaria and an estimated 660,000 malaria deaths worldwide [1], with children under five years being the most affected. There are, however, major regional variations in the burden of malaria, with highest prevalences observed in sub-Saharan countries like Burkina Faso [1]. The costs of malaria to individuals, families, and communities are considerable in this landlocked country. In fact, malaria represents the leading cause of medical consultation in Burkina Faso. Among children under five years of age, malaria accounted for 61.4% of medical consultations, 77.7% of hospitalizations, and was responsible for almost 80% of deaths in 2011 [2]. These figures provide an incomplete estimate of the total malaria burden in this country because many Burkinabé lack proper access to health care services and are therefore not accounted for in the statistics presented above.

According to the 2013 World Malaria Report, the entire population of Burkina Faso is at high risk of malaria [3]. Coverage of insecticide-treated nets (ITNs) has been estimated at 57% of households in Burkina Faso and less than half of children aged less than five years are sleeping under an ITN [4]. Although an artemisinin-based combination therapy (ACT) policy has been adopted by Burkina Faso as first-line treatment against malaria in 2005 [5], these treatments are not yet free of charge for children. In the country, district-specific statistics suggest that there are considerable variations in malaria prevalence because of different ecological conditions, variations in health system performance, and socioeconomic differentials or intervention coverage. Efficient interventions and preventive efforts could be improved by furthering our understanding of geographic prevalence patterns and the factors underlying them. Previous studies conducted in Burkina Faso have described potential determinants of malaria at the individual level but contextual factors have been suggested to play an important role [6,7]. Yet, few studies have addressed the impact of such factors that could operate at a broader scale and play a role in the performance of preventive programs. For example, environmental factors such as rainfall, altitude and temperature, that affect *Anopheles sp.* bionomics, are associated with malaria transmission in endemic countries [8-11].

Although Burkina Faso is considered as one of the most highly malaria-endemic countries in Africa [1], geographic

variability in disease prevalence within this country is poorly understood. Bayesian geo-statistical models have been successfully used to map malaria risk in a number of countries [12-16] and could be useful to target interventions in regions most at need. Previously published prevalence data for Burkina Faso are of limited value because they were extrapolated from convenience samples or from non-random sentinel populations. Demographic and Health Surveys (DHSs) provide nationally- and regionally-representative data on socio-demographic characteristics and on the burden of malaria prevalence and its determinants [4]. From April 2010 to January 2011, Burkina Faso performed its fourth DHS, and it included for the first time a malaria parasitaemia test among children under five years of age. This DHS offers a unique opportunity to determine geographic patterns of malaria and to explore determinants of prevalence among children. The goals of this study were thus: i) to examine individual, household, community characteristics and climatic/environmental factors associated with malaria infection, and ii) to produce a high-resolution map of parasitaemia risk in Burkina Faso in order to improve control efforts.

Methods

Study area

Burkina Faso is a landlocked country of 274,200 km^2 located in West Africa: it shares borders with Ivory Coast, Ghana, Togo and Benin in the South, Mali in the North and Niger in the North-West. The total population is estimated at 17 million. Most of central Burkina Faso is on a savanna plateau while the south is green and the north is arid.

Burkina Faso has a tropical climate with two seasons: the country receives between 600 and 900 millimeters of rainfall during the rainy season and a hot dry wind from the Sahara blows during the dry season. The rainy season lasts approximately four months, July to October, and is shorter in the north of the country. Three climatic zones can be defined: the Sahel, the Sudan-Sahel, and the Sudan-Guinea. The Sahel in the north typically receives less than 600 millimeters [17] of rainfall per year and has high temperatures that can reach up to 47°C. The Sudan-Sahel region is a transitional zone with regards to rainfall and temperature. Further to the south, the Sudan-Guinea zone receives more than 900 millimeters [17] of rain each year and has cooler average temperatures. This is why the duration of the high malaria transmission season, which is the rainy season, varies slightly from the northern to the southern part of the country. The main malaria vectors are *An. gambiae* s.s., *An. arabiensis*, and to a lesser extent, *An. funestus* [18]. The predominant malaria parasite is *Plasmodium falciparum*, which accounts for more than 95% of infections in children under five years of age [19].

Demographic and health survey data

Children under five years of age were sampled from a total of 572 clusters in the 2010 Burkina Faso DHS. Clusters were defined as "Zones de dénombrement": the smallest administrative unit with an average population of 1,000 and of 1,200 in rural and in urban areas, respectively. Our study sample included all 6,102 children. The DHS is a national household-based survey conducted by the National Center for Statistics and Demography (NCSD) and Macro International in order to assess disease and risk factors among the population. The survey had a stratified two-stage design. A total of 574 clusters were selected at the first stage with a proportional-to-population-size-probability sample. At the second-stage, a complete listing of all households was carried out and households were randomly selected for inclusion in the survey with equal probability. Data were collected between April 2010 and January 2011.

Blood samples were drawn and interviews were conducted in the selected households (50% of households were selected for malaria testing). All children aged between 6 and 60 months living in these households were eligible for malaria testing. Parents or guardians provided consent for their children's participation (non-consent was 1%). The parasite prevalence survey was based on microscopic examinations of stained blood films. Two blood slides, each composed of thick and thin films, were taken from each participant. Blood slides were read by two technicians at a reference laboratory in Ouagadougou (i.e., the *Centre National de Recherche sur le Paludisme*) and classified qualitatively as either negative or positive infection. The presence of *Plasmodium sp.* parasites in blood films was the primary outcome of this study. Detailed information on the survey's design and laboratory procedures can be found in the Burkina Faso 2010 DHS report [4].

Potential determinants of malaria risk

Individual-level variables included: age (categorized as six-12 months, 13–23 months, 24–35 months, 36–47 months and 48–59 months), gender and a binary variable indicating if children slept under a bed net the night before the survey. At the household level, we considered: mother's education; household size reporting the number of children aged under five years living in the household; the wealth index, based on ownership of household assets, used as a proxy for socio-economic status (SES) [20]. The wealth index was divided into quintiles, corresponding to the poorest to the richest.

At the community level, we considered a number of district-specific variables such as: rate of attendance to health facilities, the population per medical doctor ratio, and the population per health worker ratio. This information was extracted from the Ministry of Health Statistical Yearbook of 2010 [2] which is an annual compilation of

reports and information gathered from all the 63 health districts in the country's healthcare system in 2010. These indicators were geographically linked to the DHS data by matching the centroid of the DHS cluster to a map of health districts.

Environmental conditions can impact on malaria transmission and we examined the effect of a number of climatic and environmental variables: distance from rivers and water bodies, distance from major roads, normalized-difference vegetation index (NDVI, a proxy for moisture), altitude, minimum temperature, maximum temperature, mean diurnal range in temperature, rainfall before the survey date, average monthly rainfall, precipitation seasonality, vegetation cover, and population density (i.e., a proxy for the rural–urban gradient). These climatic and environmental variables were assembled from a variety of sources summarized in Table 1. The geographic coordinates of the DHS clusters' centroid were used to link the climatic/environmental variables to the parasitaemia survey (for raster-based data, we assigned to each cluster the characteristics of the pixel that corresponded to its geographic location). All geospatial data manipulations were performed using the geographic information system (GIS) software QGIS version 2.0 [21].

Statistical analyses

Multilevel analysis

Descriptive statistics were used to examine the characteristics of the sample and, unless stated otherwise, sampling weights were not used in the statistical analyses. Given the hierarchical structure of the data, logistic random effect models were used in univariate and multivariate analyses to identify factors associated with malaria infection. Potential non-linear relationships between covariates and the malaria parasitaemia outcome were accounted for by either categorizing the covariate or including polynomial terms. The appropriate functional form was chosen by visually inspecting outcome-covariate scatter plots and through consideration of the Deviance Information Criterion (DIC) [22]. Specifically, a two-level model was specified with a binary response Y_{ij}, indicating if child i living in community j was found to be parasitaemic. The logistic regression model had the following form:

$$Y_{ij} \sim \text{Bernoulli}\left(\pi_{ij}\right)$$

$$\text{logit}\left(\pi_{ij}\right) = \beta_0 + \beta X_{ij} + \omega_j + \varepsilon_i$$

This generalized linear model has a fixed part ($\beta_0 + \beta X_{ij}$) estimating the conditional vector of coefficients $\beta = (\beta_1, \ldots, \beta_k)^T$ for the matrix of explanatory covariates (X_{ij}), a random intercept attributable to communities (ω_j), and a random error for child i that doesn't depend on community (ε_i). Note that preliminary analyses suggested that the inclusion of a household-level random effect was not required as its variance was extremely small. Statistical analyses were performed in a Bayesian framework and the marginal posterior distributions of the parameters were

Table 1 Overview of data sources for the climatic and environmental variables

Variables	Time period (Resolution)	Spatial resolution	Source
Minimum temperature*	Average of 1950-2000	~1 km	Global Climate Data http://www.worldclim.org
Average temperature			
Maximum temperature*			
Mean diurnal range in temperature			
Average monthly rainfall			
Precipitation seasonality			
Altitude	2000		
NDVI†	2001-2010 (5 days)	250 m	US Geological Survey http://earlywarning.usgs.gov/
Rainfall before the survey	2010 (10 days)	~8 km	
MODIS VCF§	2010	~250 m	Global Land Cover Facility http://glcf.umd.edu/data/vcf/
Distance to roads††	1998	Vector	DIVA-GIS http://www.diva-gis.org/
Distance to water bodies††	1998	Vector	*Food and Agriculture Organization* http://www.fao.org/geonetwork/srv/en/main.home
Population density	2010	~5 km	Gridded Population of the World (v3) http://sedac.ciesin.columbia.edu/data/collection/gpw-v3

Unless stated otherwise, the variables described above were linked to the Demographic and Health Survey (DHS) records by assigning them the information corresponding to the geographic location of the DHS clusters' centroid.
*Averages computed for minimum temperatures of the coldest month and maximum temperatures of the warmest month.
†NDVI: Normalized-Difference Vegetation Index.
§VCF: Vegetation Continuous Field.
††Distance to roads and water bodies were obtained by calculating the Euclidian distance from the DHS cluster' centroid to the closest road and water body.

estimated using Integrated Nested Laplace Approximations (INLA) [23].

In order to build parsimonious and well identifiable models, Bayesian variable selection was performed [22,24,25]. Specifically, we used a Gibbs variable selection algorithm [26] that used spike and slab priors on the model's coefficients [27] (see Additional file 1: Text S1 for details). Results are presented for the univariate analyses and for the reduced multivariate model that includes only the covariates from the Bayesian variable selection.

Bayesian geo-statistical model

The models described above do not consider the spatial relationships among community locations. The standard way of incorporating geographical dependence in the model is by introducing spatially correlated random effects at every sampled location, generally assuming that the spatial correlation decreases as distances between location increases. Predictions for un-sampled locations are also improved by explicitly modeling spatial dependence. Two models were fitted: model A that included individuals, household, community, and climatic/environmental variables, and model B that included the climatic and environmental variables. Producing a risk map of malaria requires that we have complete spatial information over the whole geographic area of Burkina Faso (at both sampled and unsampled locations) for all covariates included in the geo-statistical model. Because such information was unavailable in unsampled locations for SES, bednet usage, mother's education, etc., only model B could be used for prediction. These geo-statistical models have the following general form:

$$Y_{ij} \sim \text{Bernoulli}(\pi_{ij})$$

$$\text{logit}(\pi_{ij}) = \beta_0 + \beta X_{ij} + \omega_j + \varepsilon_i$$

where $\omega_j \sim N(0,\Sigma)$ with element $\Sigma_{kl} = \frac{\sigma^2(\kappa dkl)^\nu K\nu(\kappa dkl)}{2^{\nu-1}\Gamma(\nu)}$

Here, β_0, βX_{ij}, and ε_i are the same as described before but ω_j is now the spatial random effect for community j. Σ_{kl} represents the Matérn covariance between location k and l. It was assumed that this random effect has a multivariate normal distribution with mean zero. The covariance is a function of the variance of the spatial process (σ^2), a scaling parameter (κ), the Euclidean distance between location k and l (d_{kl}), a smoothness parameter (ν) fixed to one in this particular application, and K_ν and $\Gamma(\nu)$ are the modified Bessel function of second kind order and the Gamma function, respectively. Further, the range of the spatial process is defined to be $\sqrt{8\nu}/\kappa$, which is approximately the distance to which the covariance function becomes negligible (i.e., <0.1).

The relationships between climatic and environmental variables with malaria parasitaemia were visually examined to determine the appropriate functional form. Further, the Deviance Information Criterion (DIC) was used to choose among linear, categorical or polynomial form for each of the variables. Because of potential biologically determined lag between climatic variables and malaria transmission, the DIC was used to choose the appropriate lag time among a number of plausible lags ranging from 30 to 70 days for rainfall and 7 to 21 days for NDVI. Based on these preliminary analyses, the rainfall estimates were lagged by 60 days and NDVI by 7 days. The Gibbs variable selection algorithm described in the preceding section was used to select a parsimonious set of climatic/environmental variables for inclusion (called model B in the Results section). These variables could be correlated with individual, household, or community characteristics and we wanted to give precedence to the covariates for which complete spatial coverage was available. Bayesian variable selection was therefore carried out in two stages. First, we considered only the set of 13 climatic/environmental variables for inclusion (Stage 1). Second, based on the reduced set of covariates from stage 1, we performed variable selection on an additional set of 9 individual-, household-, and community-level covariates while adjusting for the climatic/environmental variables selected during the first stage (Stage 2).

The out-of-sample predictive ability of our model was assessed by fitting the model to a random sample of 80% of the locations (432 clusters) and predicting the remaining 20% (108 clusters). We calculated the posterior predictive distributions of the test locations and computed the proportion of the observed parasitaemia prevalence falling into different coverage distributions (e.g. 10% to 100%). The mean predictive error and the squared root of the mean square error (RMSE) between the observed and predicted cluster prevalence were also calculated as an index of accuracy. The Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) was used as an additional tool to assess model performance [28].

The computational burden of the geo-statistical models was overcome by fitting the model using INLA [23], which provides fast and accurate calculations of posterior marginal distributions [29]. Model parameters were estimated using the INLA library in R [30] and vague priors were used for all hyperparameters and parameters (see Additional file 1: Text S1 for details). Malaria risk and the estimated number of infected children for the entire country of Burkina Faso were mapped at a resolution of 2.5 km (44,206 unique locations) for the month of August 2010. This arbitrarily chosen reference period corresponds to the rainy season, which last from July to October in most of Burkina Faso.

Ethical approval

Informed consent was provided by all survey participants (or their guardian) before questionnaire administration and malaria testing. Further, all survey protocols have been approved by the Internal Review Board of ICF International in Calverton (USA) and by the "Comité National d'Éthique" in Burkina Faso.

Results

Sample characteristics

The total number of households selected for the survey was 4,029 in 572 communities, and microscopy data were available for 6,102 children. A total of 34 communities, totaling 361 children, were missing geographical coordinates and had to be dropped from our analyses. The mean age of children was 32.3 months (range: 6–59 months). Overall, 83.6% of the children lived in rural areas, 50.8% were boys, and most mothers had no education (84.4%). The average household size was 7.8 persons. Most of the data (62.3%) were collected between July and October 2010 but all data from Central Region (5.9%) were taken between May-June 2010. The ratio of population per medical doctor was higher than 20,000 for all communities, and only 13.5% of children had more than two contacts with health facilities in 2010. The weighted prevalence of malaria in Burkina Faso was estimated at 66.0% (95% CI: 63.1-66.7) ranging for 27.7% in the Central Region to 77.7% in the Sud Ouest Region (Additional file 2: Figure S1).

Multilevel analysis

Results of the multilevel logistic analyses are presented in Table 2. The unadjusted odds ratio (OR) multilevel analyses indicated that all predictors (except sex and population density) were significantly associated with malaria infection. Regarding individual-level variables, children who didn't sleep under a bed net the night before the survey and children above 23 months of age had higher malaria prevalence. At the household level, having a mother with no schooling significantly increased the odds of being infected with malaria. On the other hand, living in areas with a high population density (i.e., urban), in a household with less than 5 individuals, and having a greater wealth index were associated with lower odds of malaria parasitaemia. Moreover, living in a community with a health facility rate of attendance greater than two visits per year, a population/doctor ratio between 20,000 and 50,000, and a population/health worker ratio below 3,000 were associated with lower odds of malaria infection among children.

After performing Bayesian variable selection on these covariates (Table 2), the multivariate results showed that individual/household-level variables that significantly reduced the odds of having malaria were: age of the child, mother's education, and household wealth index. Different community-level covariates reduced the odds of individual parasitaemia: higher attendance rate to health facilities, NDVI, rainfall in previous 60 days before the survey, maximum temperature, and population density.

Geo-statistical analysis

The variables selected for inclusion in the final geo-statistical model are presented in Table 3. The posterior model probability of the 'best' climatic/environmental model was 3.2% - rather weak at the first stage but increasing to 40.9% when performing Bayesian variable selection on the individual and community covariates and after adjusting for the climatic/environmental variables at the second stage of the multilevel modeling.

Results from final model A (Table 3) demonstrated that age, mother's education, wealth, rate of attendance to health facilities, NDVI, rainfall before the survey, average monthly rainfall, and maximum temperature were independently associated with malaria after accounting for spatial dependence. The geo-statistical models also indicated that malaria risk can be highly variable over relatively short distances, with spatial variances of 0.48-0.63 and an estimated spatial range of roughly 9 km. Models A and B both had an AUC of 0.78, suggesting an acceptable/good predictive performance. Model B was used to predict malaria risk in children under five years at 44,206 unique locations. The malaria risk map produced for Burkina Faso is presented in Figure 1 and the maps of the posterior predictive distribution of the 2.5^{th} and 97.5^{th} percentiles are presented as supplementary online material (Additional file 3: Figure S2). Prevalence was very high (>60%) over vast areas of the country with a median predicted malaria prevalence of 77% (range of 11% to 92%). Areas of low risk were concentrated in major urban centers such as the capital Ouagadougou. The north of the country and the horizontal band between the cities of Bobo-Dioulasso and Ouagadougou were areas with the highest malaria risk.

Further, using 108 clusters as test locations (20%), the climatic/environmental (model B) geo-statistical model's predictions had a mean error of 0.005 and a RMSE of 0.19. This out-of-sample validation shows that predictions were fairly accurate, with 77% of tested locations falling within the 95% credible intervals (CrI) of the posterior predictive distribution. The proportions of test locations falling into specific CrI coverage of the predictive posterior distributions are presented in Figure 2.

Taking population density into account, the mean predicted malaria prevalence estimated from the geo-statistical model (model B) was 65%, a figure almost identical to that estimated from the DHS data alone. The map of the estimated number of infected children under 5 years showed that malaria burden was concentrated in major cities and in the districts around Ouagadougou (Figure 3).

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Table 2 Factors associated with malaria infection in univariate and multivariate random effect logistic regression analyses for children under five years of age in Burkina Faso (2010)

Covariates	Univariate multilevel OR* (95% CrI†)	Multivariate multilevel OR* (95% CrI†)
Individual level factors		
Age (6–12 months)	Reference	Reference
13-23 months	1.13 (0.91-1.40)	1.11 (0.90-1.37)
24-35 months	**1.46 (1.18-1.92)**	**1.41 (1.14-1.74)**
36-47 months	**1.71 (1.38-2.13)**	**1.70 (1.37-2.10)**
48-59 months	**1.92 (1.54-2.40)**	**1.81 (1.45-2.25)**
Female Gender	1.12 (0.99-1.27)	NI
Not sleeping under a bed net	**1.23 (1.08-1.41)**	NI
Household level factors		
Mother's Education Level[§] (No schooling)	Reference	Reference
Primary	**0.54 (0.45-0.66)**	**0.73 (0.59-0.89)**
Secondary or higher	**0.30 (0.22-0.40)**	**0.60 (0.44-0.82)**
Household size (<5 persons)	Reference	
5-7 persons	1.18 (0.99-1.40)	NI
>7 persons	**1.50 (1.26-1.78)**	NI
Household wealth index (Richest)	Reference	Reference
Richer	**3.05 (2.46-3.79)**	**1.84 (1.45-2.33)**
Middle	**4.41 (3.50-5.54)**	**2.35 (1.82-3.05)**
Poorer	**4.42 (3.49-5.59)**	**2.23 (1.70-2.90)**
Poorest	**5.68 (4.46-7.25)**	**3.02 (2.29-3.99)**
Community level factors		
Rate of attendance to health facilities (>2)	Reference	Reference
1-2 visits per year	**2.49 (1.81-3.40)**	**1.38 (1.05-1.82)**
<1 visits per year	**6.13 (4.07-9.21)**	**2.49 (1.77-3.51)**
Population per medical doctor (20,000-50,000)	Reference	
50,001–100,000	**2.32 (1.65-3.26)**	NI
>100 000	**2.76 (1.94-3.91)**	NI
Population per heath worker (>3,000)	**1.84 (1.46-2.33)**	NI
Climatic/Environmental factors		
Distance to river (<1 km)	Reference	
1 - 5 km	0.99 (0.52-1.87)	NI
≥5 km	**2.00 (1.10-3.62)**	NI
Distance to road: truncated at 16 km	**1.32 (1.22-1.43)**	NI
Distance to road: squared term	**0.99 (0.98-0.99)**	NI
NDVI (<0.3)	Reference	Reference
0.3 - 0.5	**1.82 (1.40-2.37)**	**1.34 (1.07-1.68)**
≥0.5	**2.77 (2.06-3.73)**	**1.71 (1.29-2.26)**
Average monthly rainfall (<50 mm)	Reference	
50 -100 mm	**0.49 (0.31-0.79)**	NI
≥100 mm	**0.32 (0.19-0.56)**	NI
Rainfall 60 days prior to survey (<100 mm)	**4.06 (2.54-6.47)**	**1.69 (1.14-2.53)**
Altitude (<300 m)	**1.82 (1.43-2.30)**	

Table 2 Factors associated with malaria infection in univariate and multivariate random effect logistic regression analyses for children under five years of age in Burkina Faso (2010) *(Continued)*

Maximum temperature (<38.5°C)	Reference	Reference
38.5 - 39.5°C	**0.72 (0.55-0.94)**	0.89 (0.70-1.12)
≥39.5°C	1.09 (0.78-1.51)	0.89 (0.67-1.19)
Population density: 100/km^2, truncated at 500/km^2	0.89 (0.57-1.37)	1.35 (0.88-2.06)
Population density: squared term	0.94 (0.87-1.02)	**0.91 (0.84-0.99)**

Statistically significant results are in bold.
*OR: Odds Ratio using the category between brackets as reference.
†CrI: Credible Interval.
§210 observations were missing mother's education information and these were removed from the models that included this variable.
NI: Not Included.

Thus, although malaria risk was higher in rural areas, malaria burden was concentrated in high population density districts.

Discussion

In the present study, we identified determinants of malaria using the first nationally representative survey of malaria parasitaemia in Burkina Faso. Model-based infection risk maps for 2010 were produced and the number of infected children was estimated. Mapping malaria risk is now considered an important tool for sub-national targeting of intervention for malaria control [31]. We found that the burden of malaria among children continues to be extremely high, with two-thirds of children infected with *Plasmodium* parasites in Burkina Faso. Prevalence of malaria was higher than the one reported from other sub-Saharan African countries where comparable nationally representative data are available (Table 4). Although differences between the timing of data collection with respect to seasons of peak malaria transmission somewhat hampers our ability to compare these surveys, Benin and Ivory Coast had prevalence 2–4 times lower than the one recorded in Burkina Faso despite sharing national boundaries with Burkina Faso. Because of relatively similar climatic and/or environmental conditions, we attribute these country differences to factors like season of data collection, intervention coverage of malaria interventions and/or performance of health systems. For example, community rate of attendance at health facilities was shown to be an important determinant of malaria transmission in Burkina Faso. Interventions aimed at strengthening delivery of and access to health services could impact malaria transmission as coverage of core interventions such as insecticide-treated net, intermittent-preventive therapy, and provision of artemisinin-based combination therapies (ACT) are currently far below targets in Burkina Faso [32].

Interestingly, rainfall was negatively associated with parasitaemia. This runs in opposition to a number of studies that reported that increased precipitation is associated with malaria transmission in Burkina Faso [19,33,34]. The survey used in this paper was, however, primarily conducted during the rainy season and malaria transmission often peaks at the beginning and at the end of this season. This association is believed to result from the negative impact of high precipitations on *Anopheles sp.* larval populations [35]. Our findings suggest that malaria is strongly associated with mother's education. This finding was also observed in the 2010 Zambia National Malaria Indicator Survey [36]. We hypothesize that maternal education is positively associated with preventive care, which in turn is negatively associated with malaria risk in children under five. Indeed, Engle *et al.* [37] found that higher maternal education improves the mother's ability to process information, acquire skills, and model behavior for their children.

With recent advances in geo-statistical modeling, spatially-explicit studies analyzing the relationship between disease status and ecological factors have given new insights into the epidemiology of malaria [10,15,38]. The accurate geographical identification and enumeration of individuals at risk is an important component of control efforts, facilitating better resource allocation, health management, and targeting interventions to maximize risk reduction.

The malaria risk map presented in this article shows a somewhat different pattern of malaria risk than the newly produced global *P. falciparum* map from the Malaria Atlas Project which estimated prevalence in children aged 2 to 10 years [39]. Notably, we estimated a higher prevalence of malaria in most areas of the country. Another map produced at a regional scale for West and Central Africa also estimated much lower prevalence (<20%) [40] than that predicted by our model. This regional map was based on surveys conducted in less than 375 locations over all of West Africa, however, these discrepancies may also be explained by additional factors. These two maps were based on historical data, comprising multiple surveys from different seasons with non-standardized data collection protocols and overlapping age groups. Importantly, we chose to predict malaria prevalence for the month of August, which corresponds

Table 3 Parameter estimates from the geo-statistical models of malaria prevalence in children under five years of age in Burkina Faso (2010)

Variables	Model A	Model B
	OR* (95% CrI†)	OR* (95% CrI†)
Individual level factor		
Age (6–12 months)	Reference	
13-23 months	1.10 (0.89-1.36)	
24-35 months	**1.41 (1.14-1.74)**	
36-47 months	**1.70 (1.37-2.10)**	
48-59 months	**1.79 (1.44-2.22)**	
Household level factors		
Mother's Education Level[§] (No schooling)	Reference	
Primary	**0.75 (0.62-0.92)**	
Secondary or higher	**0.58 (0.42-0.78)**	
Household wealth index (Richest)	Referent	
Richer	**1.77 (1.40-2.24)**	
Middle	**2.24 (1.73-2.90)**	
Poorer	**2.10 (1.61-2.73)**	
Poorest	**2.76 (2.09-3.64)**	
Rate of attendance to health facilities (>2)	Reference	
1-2 visits per year	**1.36 (1.01-1.83)**	
< 1 visit per year	**2.21 (1.56-3.13)**	
Climatic/Environmental factors		
NDVI (<0.3)	Reference	Reference
0.3 - 0.5	**1.23 (1.00-1.53)**	**1.28 (1.03-1.60)**
≥0.5	**1.66 (1.27-2.17)**	**1.87 (1.42-2.46)**
Average monthly rainfall (<50 mm)	Reference	Reference
50 - 100 mm	0.69 (0.45-1.05)	**0.55 (0.36-0.84)**
≥100 mm	**0.44 (0.26-0.76)**	**0.33 (0.19-0.58)**
Rainfall 60 days prior to survey (<100 mm)	**1.75 (1.18-2.58)**	**1.97 (1.33-2.91)**
Maximum temperature (<38.5°C)	Reference	Reference
38.5 - 39.5°C	**0.74 (0.56-0.98)**	**0.73 (0.54-0.97)**
≥39.5°C	**0.66 (0.47-0.93)**	0.73 (0.51-1.01)
Population density: 100/km^2, truncated at 500/km^2	1.25 (0.82-1.90)	1.10 (0.72-1.71)
Population density: squared term	0.93 (0.86-1.01)	0.94 (0.87-1.02)
	Mean (95% CrI†)	**Mean (95% CrI†)**
Spatial variance	0.48 (0.28-0.83)	0.63 (0.40-1.03)
Range of the spatial effect (km)	8.8 (4.9-15.8)	8.9 (5.2-14.6)

Statistically significant results are in bold.
*OR: Odds Ratio using the category between brackets as reference.
†CrI: Credible Intervals.
§210 observations were missing mother's education information and these were removed from model A.

to the beginning of the season of high malaria transmission, whereas the other maps produced either yearly average or average over the high transmission season.

Malaria parasitaemia risk has been shown to be spatially correlated over distances of about 9 km, a relatively short distance given that all households within a community were geo-referenced to the same location resulting in the loss of fine-scale heterogeneity in malaria risk. The highest risks were found in rural areas, while the lowest risk was in the urban areas (proxied by population density). Although the geo-statistical model's predictions proved to be relatively accurate, our prediction's RMSE

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http://www.parasitesandvectors.com/content/7/1/350

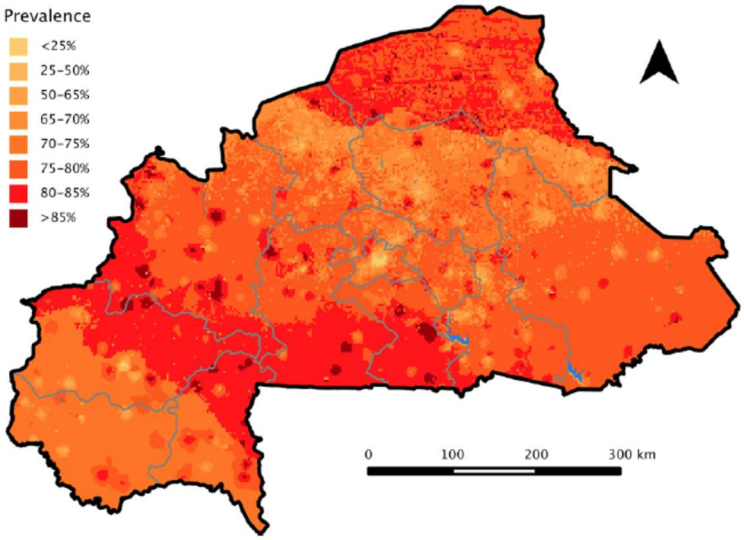

Figure 1 Geostatistical map of malaria parasitaemia risk in children under 5 years in Burkina Faso for August 2010.

was of 0.19. Some of the models' errors in the prevalence estimation could be due to important variables that were not accounted for in our risk maps such as coverage of indoor residual spraying (IRS) and ITN, and distribution and distances to mosquito breeding sites [41]. Unfortunately, no recent entomological studies were carried out in Burkina Faso that could provide more information on mosquito breeding sites and the vector layer of the country's main rivers and water bodies might have been too coarse to accurately represent smaller breeding habitats. Finally, the absence of information on coverage of malaria control interventions (e.g., IRS and ITN) has prevented the inclusion of related variables in the analysis.

The Burkinabé Ministry of Health set out the ambitious target to reduce the morbidity of malaria by 75% in 2015, using 2010 as a baseline, in its new 'National Control Program on Malaria from 2011 to 2015' [5]. The government aims to reach these targets by a series of prevention, treatment and support strategies. Prevention strategies include the two most important vector control measures: IRS, and long-lasting insecticidal net use (LLIN). IRS is recommended for populations in the regions of 'Sud-Ouest',

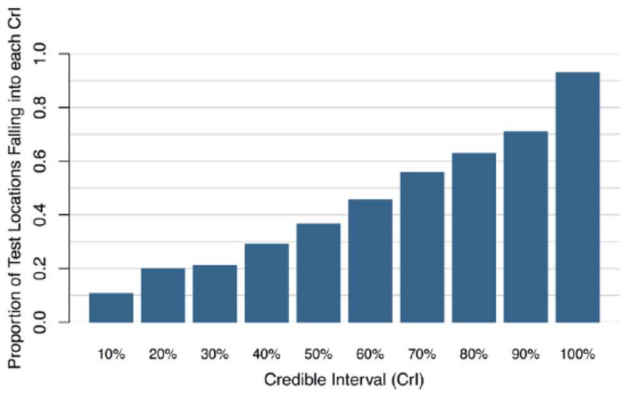

Figure 2 Proportion of observed prevalence at test locations falling into different coverage of the posterior predictive distribution.

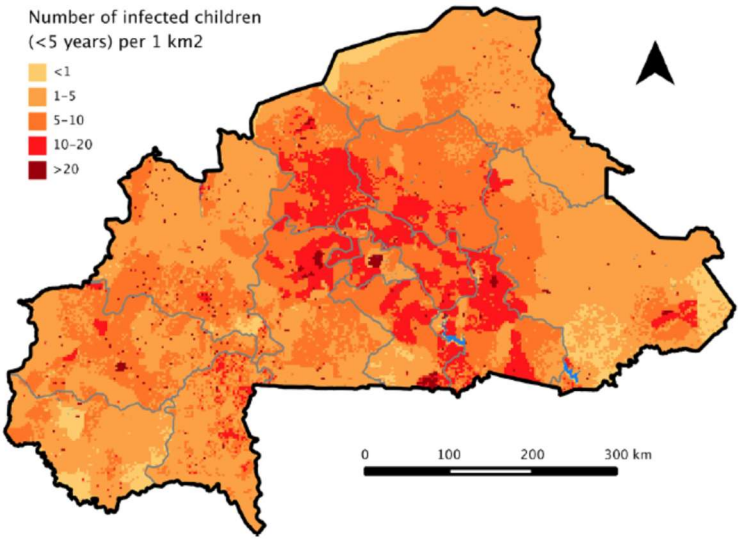

Figure 3 Geostatistical map of the estimated number of Bukinabé children under five that are infected with malaria in 2010.

'Cascades', 'Hauts-bassins', and 'Boucle du Mouhoun' (see Additional file 4: Figure S3 for a map of administrative regions). Larval source management is also considered for the mostly urban regions of 'Centrale' and 'Hauts Bassins'. Treatment strategies include early and adequate treatment of malaria with ACT and the prompt treatment of severe malaria cases in reference centers. Support strategies include better information, education and communication (IEC) campaigns and monitoring and evaluation of these programs [5]. Our malaria risk maps indicate that the first step of the target, i.e. IRS in the four regions mentioned above and larval control in two densely populated regions of 'Central' and 'Hauts Bassins' correspond to priority areas where interventions targeting malaria are more urgently required. However, given our estimated prevalence in the 'North' region, targeting hotspots in this area with LLIN and possibly IRS should also be considered.

This study has some limitations. First, because the survey does not differentiate between symptomatic and asymptomatic cases, our maps indicate where parasitaemia

Table 4 Prevalence of malaria (by microscopy) in children under five years from recent Demographic Health Surveys in sub-Saharan African countries

Country	Survey dates	Rainy season*	Malaria prevalence (%)
Benin	12/2011 to 03/2012	April-July & October-November	28.4
Ivory Coast	12/2011 to 05/2012	April-July & October-November	18.0
Gambia	02/2013 to 04/2013	June-Octoberber	0.8
Ghana	09/2011 to 12/2011	April-July & September-October	27.5
Guinea	06/2012 to 10/2012	May-October	43.9
Liberia	09/2011 to 12/2011	May-October	27.8
Mali	11/2012 to 02/2013	June-October	51.6
Nigeria	10/2010 to 12/2010	April-October	42.0
Senegal	10/2010 to 04/2011	June-October	2.9
Tanzania	12/2011 to 05/2012	January-April & November-December	4.1
Uganda	11/2009 to 01/2010	March-May & September-November	44.7
Burkina Faso	05/2010 to 01/2011	July-October	66.0

*Because of sometime important within country variations in the timing and duration of the rainy season, this climatic indicator is reported for the capital region of each country.

detected through microscopy was highest but not necessarily where treatment is most needed. The nature of the data also imposed important limitations in that individual households were not geolocated and only the centroid of the community was mapped. Further, to insure data confidentiality, random spatial error was added to the geographic locations of each cluster: 0.90 km on average for urban clusters and 2.26 km for the rural ones [42]. This random error could attenuate the strength of association between the climatic/environmental variables and parasitaemia risk by introducing some non-differential misclassification of exposures. The strengths of this study lie in its large sample size, rigorous variable selection, and the use of appropriate multilevel and geo-statistical models. An important advantage of Bayesian geostatistical analysis is that it takes into account the spatial correlation inherent to malaria transmission and properly models the effects of the covariates.

Conclusion

National prevalence of malaria in children under five years of age in Burkina Faso was one of the highest ever recorded by DHS surveys. High spatial variation in malaria risk was exhibited and children living in densely populated areas had the lowest risk of infection. The number of parasitemic children was, however, highest in such urban areas. The determinants of malaria infection described in this study as well as the maps of parasitaemia risk and number of infected children could be used by managers of malaria control programs to define priority intervention areas. Even though the environment plays an important role in malaria transmission, increasing coverage of malaria interventions and disease knowledge but also, improving socio-economic conditions will be key to achieving sustainable malaria burden decreases in Burkina Faso.

Additional files

Additional file 1: Text S1. Technical information related to the performed Bayesian Variable Selection and to the type of prior distributions used for fitting the multilevel and geo-statistical models.

Additional file 2: Figure S1. Map of surveyed clustered and observed prevalence of malaria parasitaemia in 540 clusters in Burkina Faso (2010).

Additional file 3: Figure S2. Maps of the posterior predictive distribution of the 2.5th and 97.5th percentiles of malaria parasitaemia risk in children under 5 years in Burkina Faso for August 2010.

Additional file 4: Figure S3. Map of the thirteen administrative regions of Burkina Faso.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SS developed the research question, performed the multilevel statistical analyses, interpreted the results and drafted the manuscript. MMG collected and arranged the environmental data, performed the geo-statistical analyses and the Bayesian variable selection, and contributed to the writing of the paper. FKS took part in the analysis of the data and participated in the redaction of the article. MDK helped with data management and edited the manuscript. MCC and AR contributed intellectual content, supervised the statistical analyses, and edited the manuscript draft. The final version of the manuscript was seen and approved by all authors.

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Additional File 1: Text S1

Technical information related to the performed Bayesian Variable Selection and to the type of prior distributions used for fitting the multilevel and geo-statistical models

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Introduction

The aim of this technical appendix is to provide the reader with further information on the Bayesian Variable Selection using Spike-and-Slab priors and the prior distributions used in fitting the multilevel and geo-statistical models through Integrated Nested Laplace Approximation (INLA).

Bayesian Variable Selection

In order to build parsimonious and well identifiable models, Bayesian variable selection was performed [1]. Specifically, we used a Gibbs variable

selection algorithm [2] that used spike and slab priors on the model's coefficients [3]. For the variable's coefficient k in the vector β, the spike and slab prior is given by:

$$\beta_k \sim Normal(0, \sigma_k^2)$$
$$\sigma_k^2 \sim I_k \Gamma^{-1}(a,b) + (1-I_k)\upsilon_0 \Gamma^{-1}(a,b)$$
$$I_k \sim Bernoulli(\pi_k)$$
$$\pi_k \sim Beta(1,1)$$

The hyperparameters (a, b) of the inverse Gamma were fixed to a=5 and b=25, and υ_0=0.00025, as proposed by Scheipl et al [4]. In addition, many of our variables were either categorical or polynomials. To enable simultaneous selection or deselection of block of coefficients pertaining to the same variable, we used parameter expansion on these scaled normal mixture of inverse Gamma [4] to avoid oversampling block of coefficients around zero [5]. This prior takes the following form for category h of variable β_k:

$$\beta_{kh} = \phi_k \xi_{kh}$$
$$\xi_{kh} \sim Normal(m_{kh}, 1)$$
$$m_{kh} = \gamma_{hk} - (1- \gamma_{kh})$$
$$\gamma_{kh} \sim Bernoulli(0.5)$$

where ϕ_k is given a spike and slab prior, as described above. The best set of predictors was identified using a model with independent random effect at the community level. Model selection was performed using Markov Chain Monte Carlo (MCMC) simulations implemented in JAGS [6]. An adaptive phase of 5,000 iterations and 5 chains of 35,000 iterations were used after discarding 5,000 iterations per chain as burn-in (inference was thus based on 150,000 iterations). The 'rjags' and 'CODA' libraries were used to run JAGS within the R statistical software [7] .

Prior distributions of the multilevel and geo-statistical models

The Bayesian model formulations described in the manuscript was completed using non-informative priors on all model hyperparameters and parameters. Specifically, all regression parameters were assumed to have Gaussian distributions with mean of zero and precision of 0.001. Priors for the hyperparameters of the random effect at the community level were defined on the logarithmic scale. That is, we assumed that the precision of the random effect followed a logGamma(shape=1, scale=1e-5) distribution. For the spatially-structured random effect of the geo-statistical model, the hyperparameters are the precision and spatial scale parameter (κ) of the Matérn model. Again, both hyperparameters are defined on the logarithmic scale and are given vague log-Normal prior distributions, where the prior medians for the hyperparameter are chosen heuristically to match the domain's spatial scale (see Lindgren 2012 for more information – [8])

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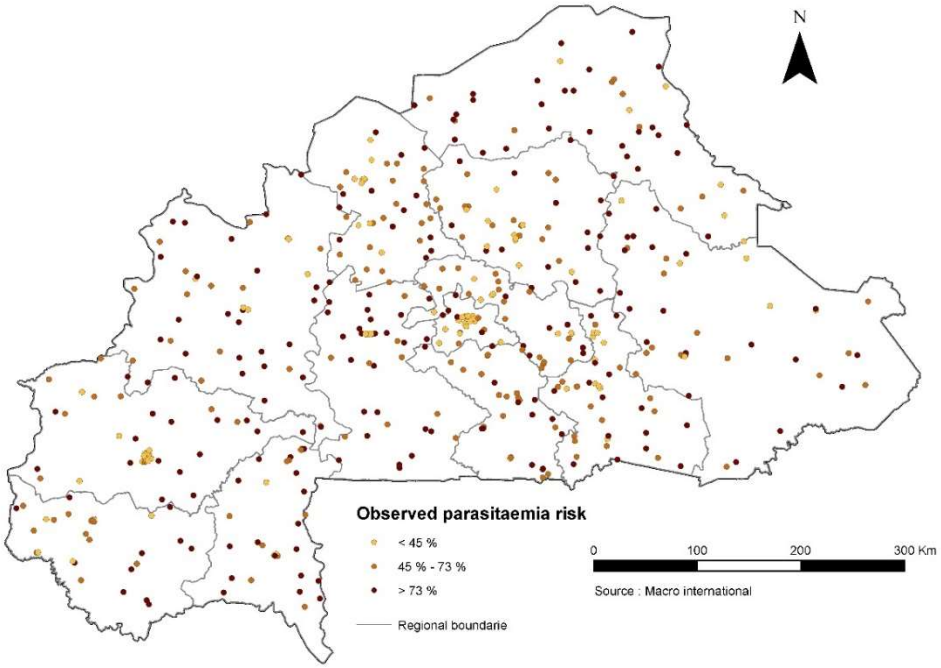
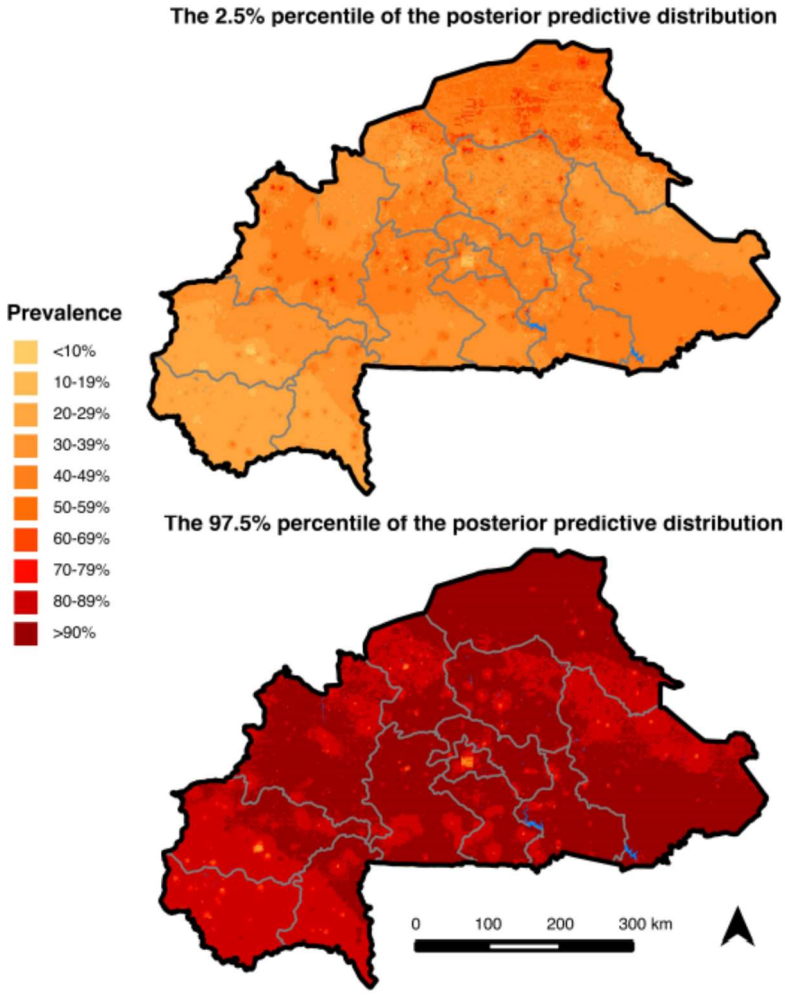
Additional file 2:

Figure S1: Map of surveyed clustered and observed prevalence of malaria parasitaemia in 540 clusters in Burkina Faso (2010).



Additional file 3:

Figure S2: Maps of the posterior predictive distribution of the 2.5thand 97.5th percentiles of malaria parasitaemia risk in children under 5 years in Burkina Faso for August 2010.



5.2. Accuracy of Paracheck® RDT for estimating Malaria Prevalence: does geographic location matter?

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Paracheck® rapid diagnostic test for detecting malaria infection in under five children: a population-based survey in Burkina Faso

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Abstract

Background: Over the past ten years, Rapid Diagnostic Tests (RDT) played a major role in improving the use of biological malaria diagnosis, in particular in poor-resources settings. In Burkina Faso, a recent Demography and Health Survey (DHS) gave the opportunity to assess the performance of the Paracheck® test in under five children nationwide at community level.

Methods: A national representative sample of 14,947 households was selected using a stratified two-stage cluster sampling. In one out of two households, all under five children were eligible to be tested for malaria using both RDT and microscopy diagnosis. Paracheck® performance was assessed using miscroscopy as the gold standard. Sensitivity and specificity were calculated as well as the diagnosis accuracy (DA) and the Youden index.

Results: The malaria infection prevalence was estimated at 66% (95% CI: 64.8-67.2) according to microscopy and at 76.2% (95% CI: 75.1-77.3) according to Paracheck®. The sensitivity and specificity were estimated at 89.9% (95% CI: 89.0-90.8) and 50.4% (95% CI: 48.3-52.6) respectively with a Diagnosis Accuracy of 77% and a Youden index of 40%. The positive predictive value for malaria infection was 77.9% (95% CI: 76.7-79.1) and the negative predictive value was 72.1% (95% CI: 69.7-74.3). Variations were found by age group, period of the year and urban and rural areas, as well as across the 13 regions of the country.

Conclusion: While the sensitivity of the Paracheck® test was high, its specificity was poor in the general under five population of Burkina Faso. These results suggest that Paracheck® is not suitable to assess malaria infection prevalence at community level in areas with high malaria transmission. In such settings, malaria prevalence in the general population could be estimated using microscopy.

Keywords: Malaria, Diagnosis, RDT, Microscopy, Paracheck

Background

In Burkina Faso, malaria is the main cause of consultations. In 2011, according to statistics from the ministry of health, this disease was responsible for 61.4% of consultations, 77.7% of hospitalizations, and more than three quarters (79.8%) of deaths occurring in health facilities among under five children [1]. Although routine data from health facilities include presumptive diagnosis and may be subject to reporting errors, malaria appears to be a huge burden for individuals, families, and communities in this country.

Early diagnosis and correct treatment are, therefore, a major public health need in this country in order to reduce morbidity and mortality due to malaria. However, the lack of laboratory equipment in primary health care facilities prevents the biological diagnosis of malaria using microscopy. Clinical diagnosis and presumptive treatment of fever are the rule, leading to a large proportion of over diagnosis due to the non-specific symptoms of malaria [2-5]. In rural Mozambique, in 2008, this proportion was estimated to range from 30% to 70% [6]. Improper use of

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anti-malarials increases the risk of adverse drug reactions and the evolution of drug resistance [7]. Drug resistance is a global issue requiring the development of new effective treatments [8,9]. Scaling up of artemisinin-based combination therapy, a more expensive anti-malarial treatment, also raises concern about the need for biological diagnosis of malaria.

In the last decade, there has been an increase in the number of companies manufacturing malaria Rapid Diagnosic Tests (RDT). A wide range of field and laboratory trials have been conducted to assess the accuracy and effectiveness of RDTs in order to establish their use in endemic areas [10]. Over the past ten years, these tests have played a major role in improving the use of biological malaria diagnosis, in particular in poor-resources settings [11].

In Burkina Faso, the performance of RDT has been largely documented in clinical settings [12-19], but no study has been undertaken nationwide at community level. A recent Demography and Health Survey (DHS) included for the first time the use of RDT to detect malaria infection in children under five years of age. Using these population data, the performance of one of the most widely used RDT has been assessed nationwide in the community.

Methods

2010-2011 Demography and Health Survey

Burkina Faso's fourth DHS was carried out from May 2010 to January 2011 [20]. A national representative sample of 14,947 households was selected using a stratified two-stage cluster sampling. In one out of two households, all under five children, either residents or visitors (i.e. present in the household the night before the survey), were eligible to be tested for malaria using both RDT and microscopy diagnosis. Absentees were revisited to recruit those missing at the first or second visit. Parents or guardians provided their consent for their child's participation.

Malaria diagnosis

At the day of the visit, fieldworkers tested children in their household using a RDT and thick and thin blood films were used by a laboratory technician to assess malaria infection prevalence by microscopy later.

In Burkina Faso, *Plasmodium falciparum* accounts for 95% of malaria infections in children less than five years old [21]. Paracheck® (Orchid Biomedical Systems, Goa, India), which detects a *P. falciparum*-specific HRP-2 protein (PfHRP-2), was used to detect infected children. This test requires approximately 5 μl of blood and is readable after 15 minutes.

Blood slides were labelled and air-dried horizontally in a slide tray. Thin films were fixed with methanol immediately after drying. Slides were stained with 2% Giemsa for 20 minutes in the field. Later, at the reference laboratory (Centre National de Recherche et de Formation sur le Paludisme) in Ouagadougou, two independent technicians read twice each blood slide and classified them as either negative or positive. Another reading was performed by a third microscopist in case of any discrepancy.

Statistical analysis

Analyses were performed using STATA 12. Prevalence was reported based on RDT results and microscopy. Paracheck® performance was assessed using microscopy as the gold standard. Sensitivity and specificity were calculated as well as the diagnosis accuracy (DA) and the Youden index. DA is the proportion of true results, either positive or negative, among RDT results. It measures the proportion of correct diagnoses and depends on the prevalence of the disease. The Youden index *(J)* is a function of sensitivity *(p)* and specificity *(q)* ($J = p + q - 1$), is not related to prevalence and is commonly used to measure diagnostic performance [22-24]. This index ranges between 0 and 1, with values close to 1 indicating that the performance is relatively large and values close to 0 indicating limited performance.

Results were calculated by age group, urban and rural areas, region, and month of data collection and period of the year. Three periods were defined according to the month of data collection: before the rainy season, in May and June, during the rainy season, from July to October, and after the rainy season, from November to January.

Survey procedures in STATA were used to account for the two-stage cluster sampling as well as the unequal probability of selection between children in rural and urban areas due to weighting. Proportions were compared using a Pearson chi-squared test or a Fischer Exact test. Means were compared using a Student test or Anova and the correlation between prevalence and sensibility or specificity was investigated by a Pearson correlation coefficient.

Results

6,102 children aged from 6 to 59 months were screened with both Paracheck® test and microscopy during the study period. There were no differences in the mean age ($p = 0.93$) and the sex distribution ($p = 0.98$) of recruited children across the 13 regions of the country (Table 1).

Overall, two thirds of the diagnostic tests (62.3%) were performed during the rainy season and slightly less than a third (31.8%) after the rainy season (Figure 1). In three regions – Central-North, Central Plateau and North - tests were mainly performed after the rainy season (87.3%, 76.4% and 82.4% respectively). Before the rainy season, only 5.9% of tests were performed, mainly in the Central region (73.2%).

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Table 1 Children mean age and sex distribution across the 13 regions of Burkina Faso

	Age (months)			Boy		Girl	
	Mean	±	SD	n	%	n	%
Central	32.5	±	15.3	246	50.0	246	50.0
Boucle du Mouhoun	31.3	±	14.9	384	51.1	367	48.9
Cascades	32.6	±	15.5	113	50.2	112	49.8
Central-East	32.3	±	15.3	252	51.7	235	48.3
Central-North	31.8	±	14.8	260	50.3	257	49.7
Central-West	32.9	±	15.5	252	51.7	237	48.5
Centre-South	32.4	±	15.2	141	53.2	124	46.8
East	32.7	±	15.4	362	52.6	326	47.4
Hauts Bassins	32.8	±	15.3	374	50.3	369	49.7
North	31.8	±	15.9	254	50.9	245	49.1
Central Plateau	31.7	±	15.4	142	49.7	144	50.3
Sahel	32.0	±	15.6	262	47.8	286	52.2
South-West	31.5	±	15.0	139	51.5	131	48.5
Burkina	32.3	±	15.3	3181	50.8	3079	49.2

Malaria infection prevalence

The overall malaria infection prevalence was estimated at 66% (95% CI: 64.8-67.2) according to microscopy and at 76.2% (95% CI: 75.1-77.3) according to Paracheck®. According to microscopy, the prevalence increased with age group, from 58.6% in 6 to 12 months old children to 69.7% in 48 to 59 months old children (Table 2). By period of the year, the prevalence was only 27.0% (95% CI: 22.0-31.0) before the rainy season while it increased to 69.9% (95% CI: 68.0-71.0) during the rainy season and remained similar after the rainy season, 65.0% (95% CI: 63.0-68.0). In rural areas the prevalence was higher than in urban areas: 73.0% in rural areas versus 18.1% in Ouagadougou.

The prevalence varied markedly between regions (Table 3). In the Central region, where tests were mainly performed before the rainy season, the prevalence was only 27.6%. Most of regions showed a prevalence ranging between 60 to 70%. The highest prevalence, around 75%, was estimated in five regions – Boucle du Mouhoun, Central-West, Central-South, South-West and Sahel.

Paracheck® sensitivity and specificity

Tables 2 and 3 summarize Paracheck® performance results. Overall, the sensitivity and specificity were estimated at 89.9% (95% CI: 89.0-90.8) and 50.4% (95% CI:

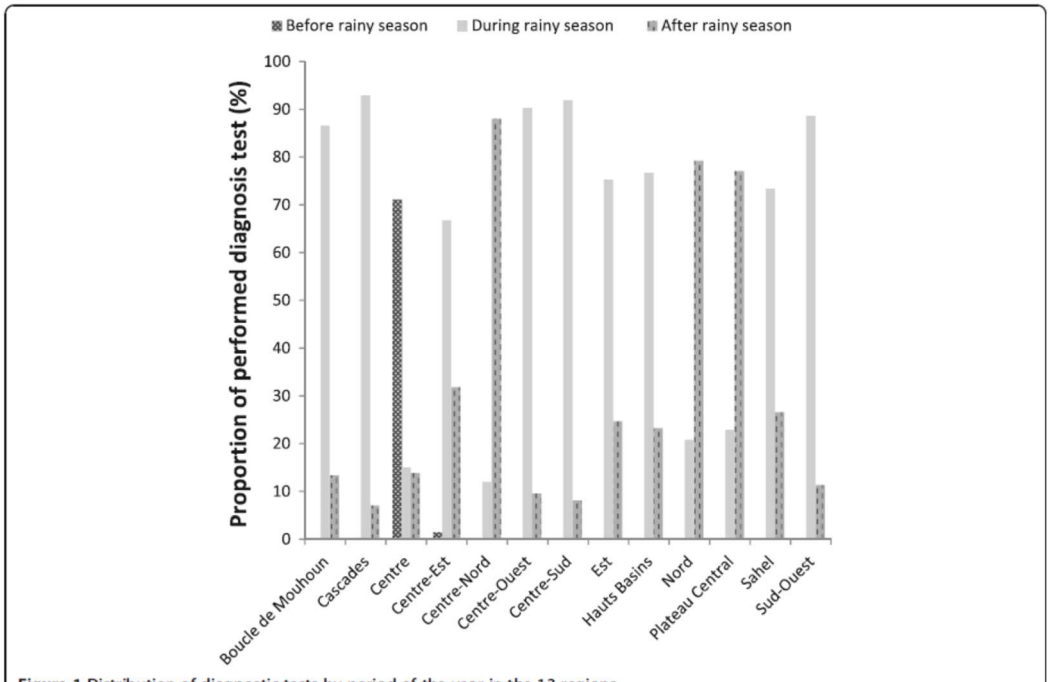

Figure 1 Distribution of diagnostic tests by period of the year in the 13 regions.

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Table 2 Prevalence and performance of Paracheck® by age group, month of data collection and area

		Microscopy prevalence	ST + (n)	Sensitivity (%)	ST- (n)	Specificity (%)	DA (%)	Youden index (%)
Area								
	Ouagadougou	18.1	68	80.9	308	73.7	75	55
	Small cities	37.2	242	88.0	408	63.7	73	52
	Rural areas	73.0	3823	90.2	1411	41.5	77	32
	p-value			0.024		<0.001		
Age group (months)								
	6 - 12	58.6	467	89.1	330	54.8	75	44
	13 - 23	61.9	775	89.0	478	52.1	75	41
	24 - 35	66.0	923	91.2	476	54.2	76	45
	36 - 47	70.4	1007	92.3	424	51.7	80	44
	48 - 59	69.7	961	87.4	417	49.2	76	37
	p-value			0.004		0.10		
Month of data collection*								
	May**	20.0	30	93.3	120	73.3	77	67
	June**	31.6	66	83.3	143	69.2	74	53
	July	74.0	376	89.6	132	36.4	76	26
	August	70.9	795	88.6	327	47.1	76	36
	September	73.3	869	88.3	317	44.2	76	32
	October	63.4	688	89.5	398	49.5	75	39
	November	66.3	838	91.8	426	44.6	76	36
	December	64.1	465	93.8	260	59.2	81	53
	p-value***			0.009		<0.001		

*Only seven children were tested in January, **Result for the Central region only, ***Comparison between July and December, ST+: positive blood smear test, ST-: negative blood smear test, DA: Diagnosis accuracy.

Table 3 Prevalence, sensitivity and specificity of Paracheck® across the 13 regions

	Microscopy prevalence	Paracheck prevalence	ST + (n)	Sensitivity (%)	ST - (n)	Specificity (%)
Central	27.6	44.1	136	83.8	356	71.1
Boucle du Mouhoun	77.4	90.7	581	95.4	170	25.3
Cascades	60.0	58.2	135	74.1	90	65.6
Central-East	66.9	76.2	326	90.8	161	53.4
Central-North	68.9	84.5	357	95.0	161	39.1
Central-West	76.3	86.1	373	92.5	116	34.5
Centre-South	75.1	92.8	199	97.5	66	21.2
East	69.1	79.3	475	85.9	212	35.4
Hauts Bassins	59.6	67.6	442	90.0	300	65.3
North	64.1	85.6	320	96.6	179	34.1
Central Plateau	61.0	73.8	175	90.3	112	52.7
Sahel	73.7	64.1	404	74.5	144	65.3
South-West	77.8	85.2	210	95.7	60	50.0
Burkina	66.0	76.2	4133	89.9	2127	50.4

ST+: positive blood smear test; ST-: negative blood smear test.

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48.3-52.6), respectively. The positive predictive value for malaria infection was 77.9% (95% CI: 76.7-79.1) and the negative predictive value was 72.1% (95% CI: 69.7-74.3).

By age group, the sensitivity ranged from 89.1% in 6 to 12 months old children to 92.3% in 36 to 47 months old children and slightly decreased to 87.4% in oldest children (Table 2). The specificity ranged from 49.2% to 54.8%.

Sensitivity was high during all of the periods of the study, from 88.3% (95% CI: 81.0-95.6) before the rainy season to 92.8% (95% CI: 91.3-94.3) after the rainy season. Sensitivity was slightly higher in rural areas compared to urban areas. By contrast, specificity did vary markedly by period of the year and area. The highest specificity was estimated to 71.3% (95% CI: 65.6-77.0) before the rainy season and decreased to 44.3% (95% CI: 41.4-47.2) and 51.9% (95% CI: 48.1-55.7) during and after the rainy season respectively. Specificity in urban areas was good but decreased drastically to 41.5% in rural areas.

A large variation across regions was found. The sensitivity ranged from 74.1% in the Cascades region to 97.5% in the Centre-South region (Table 3). While the specificity ranged from 21.2% in Centre-South region to 71.1% in the Central region. Figure 2 shows correlation between the sensitivity and specificity of Paracheck® and malaria infection prevalence in the 13 regions. No significant correlation was found.

Paracheck® diagnosis accuracy and Youden index

Overall the diagnosis accuracy was estimated at 77% and the Youden index at 40%. The DA did not vary by age group, period of the year or area (Table 2). By contrast, the Youden index was estimated at 71% before the rainy season and dropped to 44% and 52% during and after the rainy season respectively. By rural and urban areas, the Youden index was found higher in urban areas: 55% in Ouagadougou compared to 32% in rural areas.

A large variation across regions was found, the DA varying from 70% in the East region to 86% in the South-West region and the Youden index from 21% in the East to 55% in both Plateau Central and Hauts-Bassins regions (Figure 3).

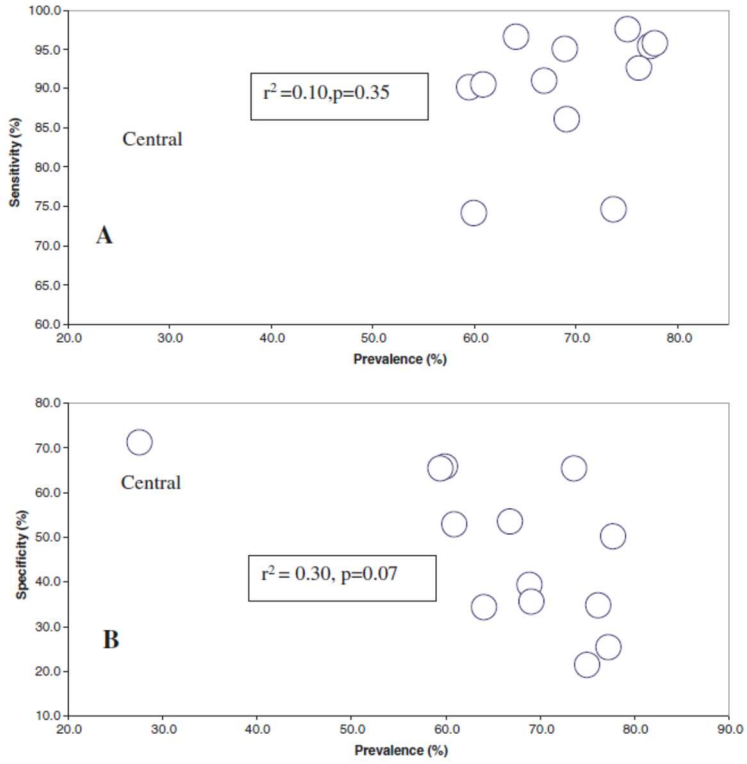

Figure 2 Correlation between sensitivity (A) and specificity (B) of Paracheck® and malaria infection prevalence (microscopy) in the 13 regions.

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Figure 3 Diagnosis accuracy (A) and Youden index (B) of Paracheck® in the 13 regions. The diagnosis accuracy (panel **A**) was quite similar across areas while the Youden index (panel **B**) showed large variations across regions.

Discussion

The 2010 DHS undertaken in Burkina Faso gave the opportunity to assess the performance of the Paracheck® test in under five children nationwide at community level. Overall, the test showed a high sensitivity (89.9%) with a low specificity (50.4%) for the detection of malaria infection. Malaria infection prevalence was high: 66.0% and 76.2% according to microscopy and Paracheck® respectively, reflecting an intense transmission of malaria in Burkina Faso, in particular during and after the rainy season.

In other countries, a few studies were undertaken at community level. In Tanzania, in an area of intense malaria transmission, Laurent *et al.* found similar results with a sensitivity and a specificity of the Paracheck® test estimated at 96.1% and 63.1% respectively [25]. However,

in Ethiopia [26] and Angola [27], while transmission of malaria was low, Pf.HRP-2 RDT showed a low sensitivity, 47.5% and 68.4% respectively, but a high specificity, 98.5% and 92.7% respectively. When the performance is assessed among symptomatic patients, various studies reported a higher specificity of Pf HRP-2 tests. A meta-analysis showed a mean sensitivity of 95% and a mean specificity of 95.2% [28]. In South-West of Burkina Faso, the Paracheck® sensitivity and specificity were estimated at 86% and 90% respectively during the dry season, and 94% and 78% respectively during the rainy season [13]. In the Central-West region, its sensitivity and specificity were estimated at 100% and 70.9% respectively [29].

Sensitivity results must be interpreted in relation to parasite density. Indeed, Tiono *et al.* showed that the sensitivity of HRP-2 tests increased with increasing parasite density, from 74.6% when the parasite density was low (0 to 99/μl) to 99.1% when the parasite density was higher (1,000 to 4,999/μl) [30]. This result is supported by other studies using OptiMAL RDT [16] as well as various other tests [10]. Although parasite densities were not available in the 2010 DHS dataset used in this study, these findings could explain why the Paracheck® sensitivity was found higher in rural areas, where transmission is higher than in urban areas, and slightly higher in younger children with no or a low level of acquired semi-immunity.

With 50% specificity for the Paracheck® test, about half of the children with a positive RDT result had a negative blood slide. This high proportion may be related to the well-known limitation of Pf HRP-2 tests which detect persistent HRP-2 antigenicity in the bloodstream for a few weeks after previous infections [17,25,31]. In addition, RDTs are known to detect low parasite densities (<100/μL) [32] which may not be detected by microscopy [33]. Low parasite densities in asymptomatic carriers are likely to be common at community level, in particular in endemic areas. In Senegal, among 8,636 cases of parasitaemia detected in the general population over a four-month follow-up period during the rainy season, only 4% suffered from fever [34]. In Burkina Faso, during the study period, an episode of fever during the two weeks prior to the interview was reported for 20.6% of children [26]. The malaria infection prevalence being estimated at 66%, this proportion may reflect a relatively large proportion of asymptomatic carriers. Before the rainy season or in Ouagadougou, while the proportion of asymptomatic carriers is likely to be lower, a highest specificity was found, estimated at 71.3% and 73.7% respectively. Laurent *et al.* also showed an increase in specificity with decreasing prevalence [25].

Specificity, as well as positive predictive value, results should however be interpreted bearing in mind one limitation of this study. Indeed, due to the capacity of the test to detect both low parasitaemia and persistent HRP2 antigenicity existing at community level, the discordant cases (positive RDT result/negative microscopy) could not be classified accurately in the absence of a second gold standard such as Polymerase Chain Reaction (PCR).

Variations in the sensitivity, specificity and Youden index were found across the 13 regions of Burkina Faso, whereas diagnosis accuracy was 70% or above. This is certainly due to the difference in the distribution of month of data collection and therefore differences in the transmission level, prevalence and parasite density. While tests were mainly performed before the rainy season in the Centre region, the prevalence was the lowest and the specificity the highest. In addition, under field condition, the performance of RDTs may vary from one user to the other and the quality of the tests may be affected by temperature, humidity, substandard transport or storage condition [35].

Conclusion

While the sensitivity of the Paracheck® test was high, its specificity was poor in the general under five population of Burkina Faso. These results suggest that Paracheck® is not suitable to assess malaria infection prevalence at community level in areas with high malaria transmission. In such settings, malaria prevalence in the general population should be estimated using microscopy. However, in other countries where elimination of malaria is targeted, detecting malaria infection at community level, even at very low parasite density levels, is certainly useful.

Abbreviations

DA: Diagnostic accuracy; DHS: Demography and Health Survey; Pf.HRP-2: *P. falciparum* specific HRP-2 protein; PCR: Polymerase chain reaction; RDT: Rapid diagnostic test; WHO/FIND: World Health Organization/ Foundation for Innovative New Diagnostics.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SS (first author) and FKS conceived the study, performed the statistical analysis and drafted the manuscript. SS (third author), HT, and FB contributed to the manuscript by giving substantial intellectual content. IN supervised the fieldwork and carried out microscopy diagnosis. AR contributed to intellectual content, supervised the statistical analysis and the writing up of the manuscript. All authors read and approved the final manuscript.

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5.3. Geographical Disparities in Coverage of Malaria Vector Control Interventions

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Progress in coverage of bed net ownership and use in Burkina Faso 2003–2014: evidence from population-based surveys

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Abstract

Background: Use of insecticide-treated bed nets (ITNs) is the cornerstone of malaria prevention. In 2010 and 2013, the Burkina Faso Government launched mass distribution campaigns of ITNs to increase coverage of ownership and use in the country. This study assessed the progress towards universal bed net coverage in Burkina Faso.

Methods: The authors used data from the Burkina Faso 2003 and 2010 Demographic and Health Surveys (DHS), the 2006 Multiple Indicator Cluster Surveys (MICS) and the 2014 Malaria Indicator Survey (MIS). For each survey, the authors computed key malaria prevention indicators in line with recommendations from the Survey and Indicator Task Force of the Roll Back Malaria Monitoring and Evaluation Reference Group. The trends over a decade was assessed by calculating percentage point change between 2003 and 2014.

Results: At national level, the proportion of households owning at least one ITN increased substantially from 5.6, 95% CI (4.7, 6.5%) in 2003 to 89.9% (88.5, 91.2%) in 2014, with low heterogeneity between regions. The proportion of households owning at least one ITN per two people increased significantly from 1.8% (1.4, 2.3%) in 2003 to 49.2% (47.3, 51.0%) in 2014. ITN use in the general population increased from 2.0% (1.6, 2.3%) in 2003, to 67.0% (65.3, 68.7%) in 2014. A similar trend was observed among children under the age of five years, increasing from 1.9% (1.5, 2.4%) in 2003 to 75.2% (73.2, 77.3%) in 2014, and among pregnant women, increasing from 3.0% (1.9, 4.2%) in 2003 to 77.1% (72.9, 81.3%) in 2014. The intra-household ownership gap was 67.0% (61.5, 72.4%) in 2003, but decreased significantly to 45.3% (43.6, 47.1%) in 2014. The behavioural gap, which was relatively low in 2013 with only 20.0% of people who had access to an ITN but were not using it, further decreased to 5.9% in 2014.

Conclusion: Burkina Faso made considerable progress in coverage of ITN ownership, access and use between 2003 and 2014, as a result of the two free mass distribution campaigns in 2010 and 2013. However, ITN coverage remains below the national targets of 100% for ownership and 80% for use. The results of 90% of ownership and 67% of use confirm that free mass distribution campaigns of ITNs are effective; however, there is room for improvement to reach and maintain optimal coverage of ITN ownership and use.

Keywords: Bed net, LLIN ownership gap, LLIN use gap, LLIN access gap, Behavioural failure, Malaria

Background

Insecticide-treated bed nets (ITNs) are effective tools for malaria control [1]. Meta-analyses have shown that ITNs are associated with an 18% reduction in child mortality [2], 51% decrease in uncomplicated malaria incidence and 17% reduction in parasite prevalence in children [3]. In the past decade, the rapid scale-up of bed nets in sub-Saharan Africa (SSA) contributed to the significant decline of malaria burden in the region [4, 5]. Sustaining high coverage of this intervention is critical to decrease further the burden of the disease and reach the long term-goal of malaria elimination. It is estimated that

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a minimum of 150 million ITNs per year are needed to maintain a constant pool of 450 million functioning ITNs to protect individuals at risk in SSA [6].

Increasing ITN coverage has been achieved using various distribution strategies, including social marketing [7–9], free distribution to target vulnerable groups (pregnant women and children under the age of five) through antenatal care (ANC) or immunization campaigns [7, 8, 10–12], and more recently, free, universal, population-based distribution campaigns targeting the general population [7, 8, 10, 12–18]. The World Health Organization (WHO) recommends to distribute free or subsidize bed nets as the best way to ensure full coverage [19].

In 2001, a nationwide survey in Burkina Faso estimated that only 12.4% of children under the age of five were sleeping under a net, compared to 23.2% in 2005. Among pregnant women this proportion was 10.0% in 2001 and 27.5% in 2005 [20]. To rapidly increase coverage of ITN ownership and use, particularly among vulnerable groups, the Government of Burkina Faso initiated a first national-scale, free distribution campaign of ITNs in 2010. The aim of the campaign was to ensure that households had access to at least one ITN for every two people through the distribution of about eight million long-lasting insecticidal nets (LLINs). Moreover, in 2013, the national malaria control programme (NMCP) launched the second free LLIN distribution campaign to scale-up the coverage of ITNs in the country. This campaign aimed to ensure that 100% of households owned at least one ITN, and reach 80% ITN use by 2015. In 2014, the Burkina Faso Government decided to conduct the first Malaria Indicator Surveys (MISs) to assess coverage and impact of scaled-up malaria interventions. MISs were developed by the Roll Back Malaria (RBM) Monitoring and Evaluation Reference Group (MERG) with the aim to help national ministries of health collect key and timely information on malaria control at national level [21]. As Burkina Faso aims to achieve universal coverage with LLINs, this paper assessed the progress and gaps in coverage of bed net ownership and use based on RBM/MERG-recommended indicators [21].

Methods

The authors analysed regional trends of ITNs ownership, access and use indicators in Burkina Faso over 11 years. These indicators were computed using data from the 2003 and 2010 Demographic and Health Surveys (DHS) [22, 23], 2006 Multiple Indicators Cluster Survey (MICS) [24] and the first national MIS 2014 [25]. At the time of these surveys, Burkina Faso was divided into 13 administrative regions.

Data from Demographic and Health Survey 2003 and 2010

DHS 2003 (between June and December 2003) and DHS 2010 (between May 2010 and January 2011) were conducted during the high transmission season. DHS was designed to obtain national and regional estimates for malaria indicators. The DHS surveys followed a two-stage selection process in which a random sample of clusters was first selected from the most recent national sample frame. In the second stage, all households were listed and the final list of households selected by systematic random sample. In the Burkina Faso DHS, the sample was selected in two stages, stratified by place of residence (urban and rural) with enumeration areas (EAs) as the first-stage sampling units, and households as the second-stage sampling units. Further details are provided in the DHS reports [22, 23].

Data from MIS 2014

The MIS data were collected from October to November 2014 (at the end of the high transmission season), using the standard malaria indicator questionnaires developed by the RBM and the DHS Program. The dataset consists of malariometric information, demographic characteristics and socio-economic status on a nationally representative sample of 6448 households from 252 clusters, of which 52 are in the urban areas. These clusters were derived from a stratified two-stage cluster design. A detailed description of the sampling strategies is documented in the final report of the 2014 Burkina Faso MIS [25].

Data from MICS 2006

Multiple Indicator Cluster Surveys are typically carried out by government organizations with the support and assistance of UNICEF to fill data gaps for monitoring the children and women wellbeing. The Burkina Faso MICS conducted from March to June 2006 used a two-stage stratified sample design. At the first stage of sampling, 198 census EAs (197 visited) were selected. The clusters in each region were selected using systematic sampling with probability proportional to their size. A complete household-listing exercise covering all EAs in the 2003 Burkina Faso DHS was carried out. At the second stage, a systematic sampling of households was selected based on this list. For the 2006 Burkina Faso MICS, 30 households per EA were selected per rural EA, 32 (in Ouagadougou, the capital city) to 36 households per urban EA. Due to the fixed sample size per EA, the disproportional number of EAs and different sample sizes selected per EA among regions, the household sample is not self-weighting at the national level. A more detailed description of the sample design can be found elsewhere [24].

Indicators

Ownership, access, use, and gap indicators were calculated from the datasets of households and individual household members, as recommended by MERG [21] (Table 1).

Statistical methods

Data was analysed using Stata version 14 software and the maps were made using the R software. Point estimates (in percentage) and 95% confidence intervals were computed for each indicator and data point. In addition the percentage point changes between the baseline (2003) and endline (2014) were computed to assess change in the indicator and statistical significance assess at 5% level. Change by region and socio-demographical factor of each indicator between 2003 and 2014 were explored using the difference between weighted proportions (with svy prop command for survey data analysis) in Stata version 14 followed by a Lincom command (Linear combination of estimators). The survey mean command followed by Lincom (to compute two-sample t-test for difference in means with sampling weights) was used for the continuous variable access. Using this approach, we were directly testing whether the observed difference was significantly superior to zero.

Results

ITN ownership at household level (referred to as percentage 1-P1)

Respectively, 9097, 6034, 14,424, and 6448 households were visited in the DHS 2003, MICS 2006, DHS 2010, and MIS 2014. Ownership of ITN at household level in Burkina Faso was 5.6, 95% CI (4.7, 6.5%) in 2003, 23.3% (19.8, 27.3%) in 2006, 56.9% (54.8, 59.0%) in 2010, compared to 89.9% (88.5, 91.2%) in 2014 (Fig. 1). Overall ownership of ITNs at household level increased significantly from 2003 to 2014 ($p < 0.001$, Fig. 1). Ownership of ITNs in rural areas increased from 3.2% in 2003 to 90.8% in 2014 ($p < 0.001$). In urban areas, a percentage point increase of 72.5 of ITN ownership by households was observed from 2003 to 2014 ($p < 0.001$). In 2003, the richest households had the highest level of ITN ownership (15.8 vs 1.8% for poorest households). In 2014, ITN ownership increased and reached 84.4% in the poorest quintile compared to 87.4% in the richest quintile (Table 2).

Insecticide-treated bed nets coverage also increased significantly in different regions from 2003 to 2014. The percentage point increases were consistently high across regions (from 76.9 to 94.5). Compared to 2003 and 2010, ITN ownership was rather stable across the country and displayed limited geographic heterogeneity in 2014 (Fig. 2).

ITN ownership at household level (P2: households with at least one ITN for every two people)

The proportion of households with enough ITNs for every household member, i.e., at least one ITN for every two people, was 1.8% (1.4, 2.3%) in 2003, 8.4% (6.1, 11.4%) in 2006, 18.5% (17.1, 20.0%) in 2010, compared to 49.2% (47.3, 51.0%) in 2014, indicating a substantial increase ($p < 0.001$). Household access to ITNs improved significantly from 2003 to 2014 in urban and rural areas, in all quintiles of wealth and in the different regions in Burkina Faso. The largest increases were observed in urban areas amongst the richest two quintiles, in smallest households and in the Hauts-Bassins and Central-South regions (Table 3). In these two regions, 62.5 and 60.4% households, respectively, owned at least one ITN for every two members in 2014 (Fig. 2).

Access to ITN at population level (P3)

Access to ITNs increased significantly from 2.5% (2.1, 3.0%) in 2003, to 13.4% (11.0, 15.9%) in 2006, 36.1% (34.1, 38.0%) in 2010, and reached 71.2% (69.6, 72.8%) in 2014 ($p < 0.001$) (Table 4; Fig. 1).

Use of ITN at individual level (P4)

In 2003, 2.0% (1.6, 2.3%) slept under a net. In 2010, the proportion of people who slept under an ITN was 31.5% (29.8, 33.2%) compared to 67.0% (65.3, 68.7%) in 2014, suggesting a considerable increase of 65.0% points from 2003 to 2014 ($p < 0.001$, Fig. 1). In urban areas, 5.6% of individuals used ITNs in 2003, a proportion that increased to 61.8% by 2014 ($p < 0.001$). In rural areas, a significant increase was also observed, with 1.2% of people who used an ITN in 2003 and 68.8% in 2014 ($p < 0.001$). The substantial increase in the proportion of people who slept under ITNs was observed across all quintiles of wealth. Use of ITNs increased significantly from 0.8% in 2003 to 63.7% in 2014 ($p < 0.001$) in the poorest wealth quintile. In the second poorest wealth quintile, ITN use increased from 0.8% in 2003 to 69.1% in 2014 ($p < 0.001$), compared to an increase of 54.9% points in the richest quintile (6.1–61.0%) (Table 5).

In terms of regions, the largest increase occurred in the Central-East and Central-South regions. The absolute increase in ITN use in the Central-East region was 75.9% points ($p < 0.001$), increasing from 2.6% in 2003 to 78.6% in 2014. The corresponding estimates for the Central-South region were 1.4% in 2003 and 75.4% in 2014 ($p < 0.001$) (Fig. 3).

Use of ITN among children under 5 years of age (P5)

In 2003, 1.9% (1.5, 2.4%) of children under 5 years of age were sleeping under an ITN, compared to 9.6% (7.6,

Table 1 RBM/MERG-approved indicators used

Indicator	Numerator	Denominator
Ownership		
Proportion of households in the survey with at least one ITN (P1)	Number of households owning at least one ITN	Number of households in the survey
Proportion of households with sufficient access to ITN (P2)	Number of households owning at least one ITN for every two household members	Number of households in the survey
Proportion of population with access to ITN within the household (P3)	Potential number of household members protected by the ITN (i.e., number of ITN owned multiplied by two), or number of de facto household members in the household, whichever was the lowest	Population in the survey
Proportion of households with at least one ITN for every two people among households owning any ITN (P7)	Number of households owning at least one ITN for every two household members	Number of households owning at least one ITN
Intra-ownership gap, the proportion of households owning less than one ITN for every two household members, is calculated as 1-P7		
Use		
Proportion of population sleeping under an ITN the previous night (P4)	Number of household members who slept under an ITN the night before the survey	Population in the survey
Proportion of children under 5 years sleeping under an ITN the previous night (P5)	Number of children under 5 years who slept under an ITN the night before the survey	Number of children under five years in surveyed households
Proportion of pregnant women sleeping under an ITN the previous night (P6)	Number of pregnant women who slept under an ITN the night before the survey	Number of pregnant women in surveyed households
Proportion of population sleeping under an ITN the previous night among those with access (P8)	Number of household members who slept under an ITN the night before the survey	Total number of people with access to an ITN, calculated as the sum of all access (P3) values
Behavioural gap, the proportion of household members who did not sleep under an ITN despite having access to one, is calculated as 1-P8		

11.6%) in 2006, 47.4% (45.3, 49.5%) in 2010, and 75.2% (73.2, 77.3%) in 2014 (Table 5). Overall, the use of ITNs among children under five years has increased significantly from 2003 to 2014 ($p < 0.001$) (Fig. 1).

Analysis of ITN use by age band showed a significant increase from 2003 to 2014. In children younger than 12 months, use of ITNs increased from 1.9% in 2003 to 77.0% in 2014 ($p < 0.001$). Among children aged 12–23 months, the proportion that used ITNs increased from 2.2% in 2003 to 76.7% in 2014, suggesting an absolute increase of 74.5% points between the two periods ($p < 0.001$). Substantial increases in the use of ITNs also were observed in older children (ages 24, 36 and 48 months) from 2003 to 2014 (Table 6).

In urban settings, 6.2% of children under five years slept under an ITN in 2003, compared to 69.9% in 2014, indicating an absolute increase of 63.7% points ($p < 0.001$). In 2003, 1.3% of children under 5 years living in rural areas slept under an ITN. This proportion increased significantly in 2014, reaching 76.8% in children under 5 years living in rural areas ($p < 0.001$).

In wealth quintiles, the smallest increases were observed in children under 5 years from the richest wealth quintile, with an increase from 7.0% in 2003 to 69.7% in 2014 (Table 6).

Marked increases in ITN use were also achieved in all regions over the specified period; however, the Centre-East and Centre-Nord regions displayed the greatest increase in ITN use compared to the other regions with an increase from 2.5 to 86.5% and from 0.5 to 82.1% (Table 6, Fig. 3).

Use of ITN among pregnant women (P6)

The use of ITNs by pregnant women in Burkina Faso was 3.0% (1.9, 4.2%) in 2003, 44.5% (41.2, 49.%) in 2010, and 77.1% (72.9%, 81.3%) in 2014, indicating a significant increase from 2003 to 2014 ($p < 0.001$) (Fig. 1). In urban areas, 7.5 and 69.6% of pregnant women used ITNs in 2003 and 2014, respectively, an increase of 62.1% points ($p < 0.001$, Table 7). The corresponding estimates in rural areas were 2.1% in 2003 and 78.8% in 2014, a significant improvement in ITN use among pregnant women between these periods ($p < 0.001$). A trend similar to that of ITN use in children under five years was found when analyses were performed by wealth quintile.

ITN ownership and use gaps

In 2003, 94.4% (93.5, 95.2%) of the study households did not possess an ITN (Fig. 1). Among those who owned at least one ITN, 67.0% (61.5, 72.4%) did not have sufficient

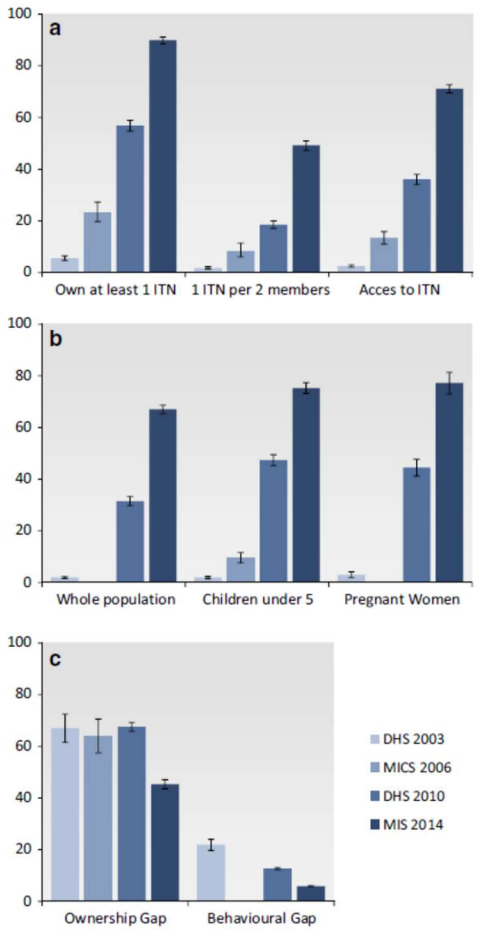

Fig. 1 Trends of main malaria prevention indicators between 2003 and 2014, Burkina Faso. *Panel A* (ITN ownership) represents the proportion of households owning at least 1 ITN, owning 1 ITN for 2 household members and the proportion of individuals with access to an IT. *Panel B* (ITN use) represents the proportion of people who slept under an ITN the night before the survey for the whole population, among children under five years old and among pregnant women. *Panel C* (gap indicators) represents the proportion of household onwing at least 1 ITN, but less than 1 for every 2 household members (intraownership gap), and the proportion of people having access to an ITN but who did not use it the night before the survey (behavioural gap). All indicators are *plotted* for the 2003, 2006, 2010 and 2014 surveys, along with their 95% confidence interval

bed nets to protect all members (intra-household net ownership gap). However, 19.4% (n = 94) of these households had excess ITNs (i.e., more than one ITN for every two people). A significant proportion (21.9%, n = 316) of the population with sufficient access to ITNs did not actually use them the night before the survey.

In 2010, 43.0% (41.0, 45.2%) of the study households did not have an ITN. The intra-household net ownership gap was 67.6% (65.8, 69.3%), indicating that about two-thirds of the households with at least one ITN did not have sufficient ITNs to protect all members. This gap is presented in Table 8 by background characteristics and shows that the gap was very high in large household size (93.4%) and rural areas (70.4%). However, 18.3% (n = 1475) of these households had excess ITNs (i.e., more than one ITN for every two people). A small proportion (12.7%, n = 3700) of the population with sufficient access to ITNs did not actually use them.

In 2014, only 10.6% (9.2, 12.0%) of the study households did not have an ITN. The intra-household net ownership gap was 45.3% (43.6, 47.1%), indicating that about half of the households with at least one ITN did not have sufficient ITNs to protect all members. This gap was 80.7% in large household size and well above the national average (Table 8). However, 34.5% (n = 1926) of these households had excess ITNs (i.e., more than one ITN for every two people). A small proportion (5.9%, n = 1562) of the population with sufficient access to ITNs did not actually use them. In contrast, this proportion was 13.1% in urban areas and only 3.4% in rural areas (Table 9).

Discussion

The Government of Burkina Faso set a national goal to increase ITN ownership, access and use. These data provide evidence of the remarkable increase in the coverage of ITN ownership, particularly in 2014 after the second free distribution campaign. Indeed, ownership, access and use indicators calculated following MERG's recommendations [21] dramatically increased between 2003 and 2014 and was particularly successful at reaching the poorest populations. The increasing trend in ITN ownership described here, is consistent with data from 19 SSA countries during a similar time period [26]. The data show that the two free distribution campaigns substantially increased ITN ownership and reduced inequity among populations in Burkina Faso. These findings are consistent with other free mass distribution campaigns that have been carried out in SSA [9, 27], demonstrating that this strategy can be used to rapidly scale-up ITN coverage in areas with low coverage and reduce social inequity. However, despite the significant progress, less than 50% of households own enough ITNs to protect every household members (Fig. 1). These campaigns should not represent the only mechanism by which ITNs are distributed to poorest communities and vulnerable populations [9]. In Burkina Faso, ITNs were provided for free to pregnant women and children under five years

Table 2 Proportion of households owning at least one insecticide-treated bed net

Background characteristic	DHS 2003		MICS 2006		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Residence									
Urban	14.8 (12.5–17.2)	2182	45.0 (38.6–51.4)	921	60.0 (56.9–63.0)	4391	87.8 (85.2–90.4)	1305	72.5 (69.0–76.0)
Rural	3.2 (2.4–4.0)	6868	14.9 (12.8–17.1)	4602	55.9 (53.3–58.5)	9997	90.8 (89.2–92.4)	5104	87.6 (85.8–89.4)
Household wealth quintiles									
Poorest	1.8 (0.7–3.0)	1880	8.4 (6.4–10.5)	1276	48.8 (44.9–52.7)	2620	84.4 (81.0–87.7)	1511	82.6 (79.0–86.2)
Poorer	2.6 (1.6–3.7)	1619	13.3 (10.5–16.1)	1276	53.4 (50.2–56.7)	2744	91.8 (90.2–93.4)	1385	89.0 (87.2–90.9)
Average	2.8 (1.8–3.8)	2023	14.1 (10.7–17.4)	1116	56.8 (53.7–60.0)	2777	93.8 (92.2–95.4)	1288	91.1 (89.2–92.9)
Richer	3.8 (2.4–5.2)	1407	23.5 (18.9–28.1)	1013	59.5 (56.4–62.7)	2922	94.0 (91.5–96.4)	1236	90.1 (87.3–92.8)
Richest	15.8 (13.3–18.3)	2121	52.1 (45.7–58.4)	842	65.1 (62.3–67.9)	3325	87.4 (84.9–89.9)	989	70.8 (67.1–74.4)
Size of the household									
Small (1–5 members)	6.0 (4.7–7.2)	4421	24.5 (19.4–29.7)	2345	53.3 (51.1–55.6)	8169	88.3 (86.6–90.0)	3362	82.0 (79.8–84.1)
Medium (6–8 members)	5.5 (4.1–6.8)	2401	22.7 (18.9–26.5)	1665	60.3 (57.8–62.8)	3911	91.4 (89.6–93.2)	1760	85.9 (83.6–88.2)
Lager (9+ members)	4.8 (3.7–5.9)	2228	21.9 (17.4–26.3)	1513	63.7 (60.8–66.7)	2308	92.6 (90.8–94.5)	1287	87.8 (85.7–89.9)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey, *N* number of households

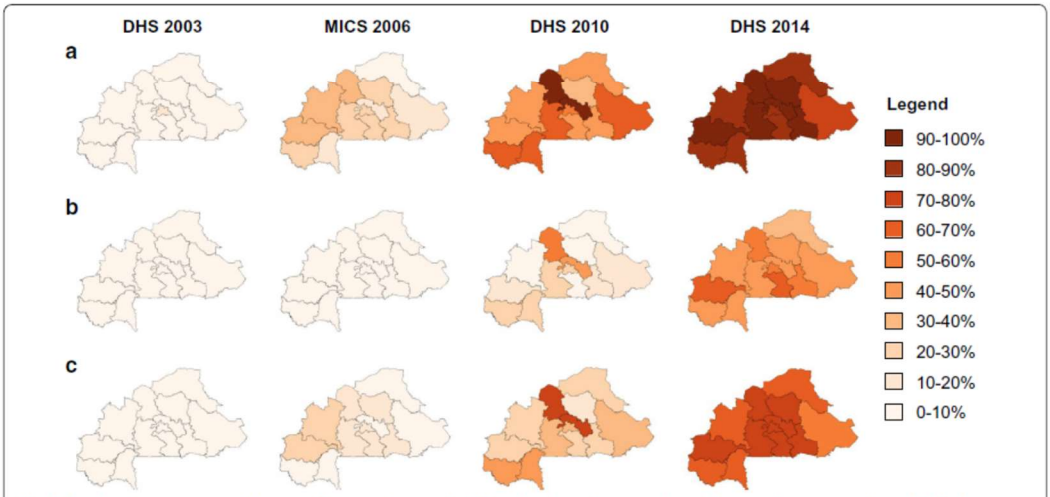

Fig. 2 Trends of main ownership indicators between 2003 and 2014, Burkina Faso. The proportion of households owning at least 1 ITN (**a**), owning at least 1 ITN for 2 household members (**b**) and the proportion of the population with access to an ITN (**c**) is indicated for each region, for 2003, 2006, 2010, and 2014, respectively

of age through routine channels, such as antenatal care and immunization campaigns. ITNs were also available for purchase in retail shops and stores. This could explain both the slight increase in bed net ownership (Fig. 1) and use (Fig. 3). However, the relative contribution of these distribution channels remains, to date, very limited. More than 90% of the ITNs were obtained during the free distribution campaign [25]. To reach and maintain high ITN coverage in Burkina Faso, there is a need to improve the contribution of the routine distribution through ANC and vaccination programs and develop alternative strategies, such as the continuous distribution of ITN in schools and by community health workers for replacement [28]).

Ownership and behavioural gap analyses provide complementary information regarding ITN ownership and use. The results reveal geographical and sociogeographic

Table 3 Proportion of households owning at least one insecticide-treated bed net for every two members

Background characteristic	DHS 2003		MICS 2006		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Residence									
Urban	5.8 (4.2–7.4)	2182	20.9 (16.2–25.7)	921	24.8 (22.5–27.1)	4391	55.6 (52.4–58.8)	1305	49.0 (45.4–52.6)
Rural	0.8 (0.5–1.1)	6868	3.6 (2.7–4.4)	4602	16.4 (14.6–18.1)	9997	46.5 (44.4–48.5)	5104	45.4 (43.3–47.5)
Household wealth quintile									
Poorest	0.6 (0.1–1.1)	1880	1.5 (0.8–2.2)	1276	12.4 (10.3–14.5)	2620	41.1 (37.0–45.1)	1511	40.3 (36.3–44.4)
Poorer	0.2 (0.0–0.5)	1619	2.4 (1.3–3.4)	1276	15.4 (13.2–17.7)	2744	47.4 (44.2–50.7)	1385	47.0 (43.8–50.2)
Average	0.5 (0.2–0.9)	2023	3.7 (2.3–5.0)	1116	17.0 (14.7–19.2)	2777	45.6 (42.3–48.8)	1288	44.8 (41.5–48.1)
Richer	0.8 (0.3–1.3)	1407	5.3 (3.5–7.0)	1013	17.7 (15.4–20.0)	2922	52.2 (48.7–55.6)	1236	51.0 (47.6–54.5)
Richest	6.5 (4.8–8.1)	2121	25.8 (21.0–30.6)	842	28.6 (26.2–31.0)	3325	58.3 (55.0–61.6)	989	50.9 (47.2–54.5)
Size of the household									
Small (1–5 members)	3.3 (2.5–4.0)	4421	14.4 (10.2–18.6)	2345	26.7 (24.7–28.7)	8169	65.7 (63.6–67.9)	3362	61.5 (59.3–63.8)
Medium (6–8 members)	0.7 (0.1–1.2)	2401	5.3 (3.6–7.0)	1665	9.8 (8.5–11.2)	3911	37.2 (34.1–40.2)	1760	36.5 (33.3–39.7)
Large (9+ members)	0.1 (0.0–0.3)	2228	1.2 (0.6–1.7)	1513	4.2 (3.1–5.3)	2308	17.9 (15.3–20.4)	1287	17.8 (15.2–20.3)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey; *N* number of households

Table 4 Proportion of population having access to an insecticide-treated bed net

Background characteristic	DHS 2003		MICS 2006		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Residence									
Urban	8.1 (6.6–9.6)	12,313	28.8 (23.4–34.1)	5691	40.2 37.3–43.0)	21,758	71.1 (6 7.8–74.4)	6733	63.0 (59.4–66.7)
Rural	1.3 (0.9–1.7)	46,530	8.5 (7.1–9.9)	32,813	34.9 (32.6–37.2)	58,774	71.2 (69.4–73.0)	31,660	69.9 (68.0–71.8)
Household wealth quintiles									
Poorest	0.7 (0.3–1.2)	10,802	4.3 (3.1–5.5)	8734	29.5 (26.4–32.6)	15,243	63.0 (59.7–66.4)	8380	62.3 (58.9–65.7)
Poorer	0.9 (0.5–1.2)	11,113	7.8 (5.8–9.7)	8072	33.5 (30.8–36.3)	15,389	72.3 (70.2–74.3)	8495	71.4 (69.3–73.5)
Average	1.1 (0.4–1.8)	14,345	8.2 (6.2–10.3)	8685	35.8 (33.0–38.5)	16,306	74.0 (72.0–76.0)	8520	72.8 (70.7–75.0)
Richer	1.5 (0.8–2.2)	10,056	12.0 (9.2–14.8)	7702	37.5 (34.8–40.2)	16,989	74.8 (72.4–77.3)	8165	73.3 (70.7–75.9)
Richest	8.3 (6.8–9.7)	12,527	34.9 (29.5–40.2)	5311	44.1 (41.4–46.7)	16,605	71.8 (68.1–75.6)	4833	63.5 (59.5–67.6)
Size of the household									
Small (1–5 members)	4.2 (3.2–5.1)	14,278	19.1 (15.0–23.2)	8166	42.2 (40.0–44.4)	27,130	79.7 (77.9–81.4)	11,250	75.5 (73.5–77.5)
Medium (6–8 members)	2.7 (1.9–3.5)	16,500	14.1 (11.4–16.7)	11,415	36.2 (34.0–38.3)	26,634	73.1 (71.0–75.2)	12,025	70.4 (68.1–72.7)
Large (9+ members)	1.5 (1.0–1.9)	28,065	10.2 (7.9–12.5)	19,434	29.8 (27.6–32.1)	26,768	62.7 (60.4–64.9)	15,118	61.2 (58.9–63.5)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey, *N* number of individuals

discrepancies of ITN ownership and use. Gap decreased (>10% point change) in all regions, with highest decreases in the Hauts-Bassins and, in the Sud-Ouest half of the country (zones where malaria transmission is permanent with a peak during the rainy season). Sahel, Nord and Centre-Est (where malaria transmission is seasonal) display lower gap reduction, but the ownership gap was already low in 2003. Change in malaria transmission may explain this difference. In 2014, geographical discrepancies in the ownership gap were minimum. Remarkably, the ownership gap increased in Centre-Nord. This increase can be attributed to the 2003 gap value, which is clearly an outlier: 35.8% gap, while the gap in all other regions fell between 59 and 90 (Fig. 4).

By contrast with ownership gap, behavioural gap remained stable across the country. However, significant decrease was observed in Boucles de Mouhoun, Centre, Centre-Sud, and Centre-Est. All four regions displayed higher-than-average behavioural gap in 2003. In this respect, Centre consistently displayed higher behavioural

Table 5 Proportion of population who slept under an insecticide-treated bed net the night before the survey

Background characteristic	DHS 2003		MICS 2006[a]		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Residence									
Urban	5.6 (4.4–6.7)	12,313	–	–	31.2 (28.0–34.5)	21,758	61.8 (58.8–64.8)	6733	56.2 (53.0–59.4)
Rural	1.2 (0.8–1.5)	46,530	–	–	31.6 (29.5–33.6)	58,774	68.8 (67.0–70.6)	31,660	67.6 (65.8–69.5)
Household wealth quintiles									
Poorest	0.8 (0.3–1.2)	10,802	–	–	25.9 (23.4–28.5)	15,243	63.7 (60.5–66.8)	8380	62.9 (59.7–66.1)
Poorer	0.8 (0.4–1.1)	11,113	–	–	30.2 (27.7–32.7)	15,389	69.1 (66.9–71.3)	8495	68.3 (66.1–70.5)
Average	0.9 (0.4–1.5)	14,345	–	–	32.7 (30.2–35.1)	16,306	71.2 (68.8–73.5)	8520	70.2 (67.8–72.7)
Richer	1.3 (0.7–1.9)	10,056	–	–	34.5 (31.8–37.1)	16,989	70.1 (67.6–72.6)	8165	68.8 (66.2–71.4)
Richest	6.1 (4.8–7.3)	12,527	–	–	34.2 (31.1–37.3)	16,605	61.0 (57.8–64.2)	4833	54.9 (51.5–58.3)
Size of the household									
Small (1–5 members)	3.1 (2.5–3.8)	14,278	–	–	37.3 (35.2–39.3)	27,130	72.3 (70.3–74.4)	11,250	69.2 (67.0–71.3)
Medium (6–8 members)	2.1 (1.4–2.8)	16,500	–	–	31.0 (29.0–33.0)	26,634	69.5 (67.4–71.6)	12,025	67.4 (65.2–69.7)
Large (9+ members)	1.2 (0.8–1.7)	28,065	–	–	26.2 (24.1–28.4)	26,768	60.6 (58.1–63.0)	15,118	59.4 (56.8–61.9)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria Indicator Survey, *N* number of individuals

[a] Data not available

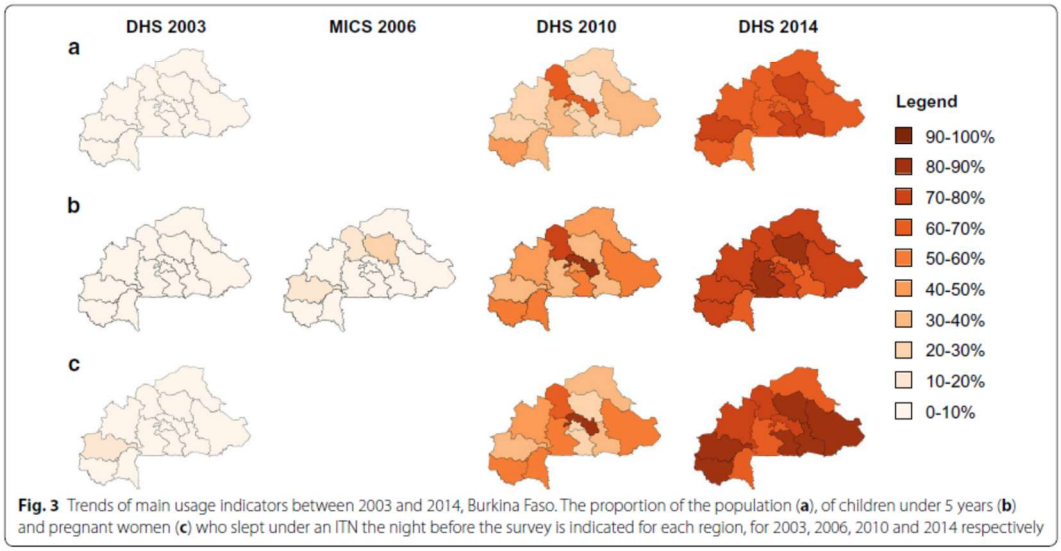

Fig. 3 Trends of main usage indicators between 2003 and 2014, Burkina Faso. The proportion of the population (**a**), of children under 5 years (**b**) and pregnant women (**c**) who slept under an ITN the night before the survey is indicated for each region, for 2003, 2006, 2010 and 2014 respectively

gap values for all years studied, most likely because the population in this region is concentrated in urban habitat (Ouagadougou). This result could be explained by higher population dynamics in the capital region. Interestingly also, the change in behaviour is very recent in this region (in 2010, behavioural gap was 40%). In 2014, the behavioural gap was uniformly low across the country (0–15%). This reduction is probably a result of the health promotion programmes initiated by the Government of Burkina Faso to improve awareness concerning malaria prevention methods [25].

Household size is the main factor associated with ownership gap in this study. Large households with at least one bed net lacked additional bed nets to protect all family members (vs 25.5% for small households). Conversely, households in urban settings and from the richest

Table 6 Proportion of children under 5 years old who slept under an insecticide-treated bed net the night before the survey

Background characteristic	DHS 2003		MICS 2006		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Age group (months)									
0–11	1.9 (1.2–2.6)	2153	11.3 (8.6–13.9)	1209	55.6 (52.4–58.8)	1517	77.0 (73.8–80.2)	1412	75.1 (71.8–78.4)
12–23	2.2 (1.5–2.9)	1892	8.1 (5.7–10.4)	1069	54.6 (51.1–58.1)	1427	76.7 (73.8–79.5)	1314	74.5 (71.6–77.4)
24–35	2.3 (1.4–3.2)	1819	10.2 (7.6–12.9)	1149	46.3 (42.7–49.9)	1426	74.7 (71.9–77.5)	1408	72.4 (69.5–75.3)
36–47	1.9 (1.1–2.7)	2091	10.0 (5.0–15.0)	1060	45.4 (42.1–48.7)	1447	75.5 (72.7–78.3)	1419	73.6 (70.7–76.6)
48–59	1.4 (0.7–2.1)	1867	7.7 (4.5–10.8)	796	45.2 (42.9–47.5)	8407	72.4 (69.1–75.7)	1369	70.9 (67.5–74.3)
Gender									
Male	1.8 (1.3–2.3)	5061	10.2 (7.5–12.9)	2677	47.9 (45.7–50.2)	7223	75.5 (73.3–77.8)	3506	73.7 (71.4–76.0)
Female	2.1 (1.5–2.6)	4761	9.0 (6.9–11.2)	2604	46.8 (44.4–49.1)	7001	75.0 (72.5–77.4)	3416	72.9 (70.3–75.4)
Residence									
Urban	6.2 (4.4–7.9)	1631	23.8 (17.8–29.9)	573	45.5 (41.5–49.6)	3167	69.9 (64.8–75.1)	1051	63.7 (58.3–69.2)
Rural	1.3 (0.9–1.8)	8191	6.2 (4.7–7.8)	4710	47.8 (45.4–50.1)	11,057	76.8 (74.7–78.8)	5871	75.5 (73.4–77.6)
Household wealth quintiles									
Poorest	1.2 (0.3–2.2)	1810	4.4 (2.5–6.4)	1255	41.2 (37.4–45.0)	2756	72.3 (68.4–76.3)	1528	71.1 (67.0–75.3)
Poorer	0.7 (0.2–1.3)	2011	6.0 (3.7–8.3)	1100	46.4 (43.0–49.8)	2923	76.1 (73.1–79.0)	1570	75.3 (72.3–78.3)
Average	0.8 (0.3–1.2)	2582	6.0 (3.8–8.2)	1306	49.2 (46.0–52.3)	3109	78.5 (75.4–81.6)	1604	77.7 (74.6–80.9)
Richer	1.6 (0.6–2.6)	1748	9.4 (6.2–12.7)	1091	51.5 (48.1–54.9)	3086	78.3 (74.4–82.2)	1508	76.7 (72.7–80.7)
Richest	7.0 (4.9–9.1)	1671	26.2 (21.5–30.9)	531	48.8 (45.1–52.6)	2350	69.7 (64.3–75.1)	712	62.7 (56.9–68.5)
Size of the household									
Small (1–5 members)	2.9 (1.9–3.9)	2365	15.4 (9.8–21.0)	1039	53.5 (51.1–55.9)	4853	77.9 (74.5–81.4)	2135	75.1 (71.5–78.7)
Medium (6–8 members)	2.2 (1.4–3.1)	2633	10.0 (6.6–13.5)	1590	46.4 (43.6–49.1)	4634	78.2 (75.4–81.1)	2048	76.0 (73.0–79.0)
Large (9+ members)	1.3 (0.7–1.9)	4824	6.5 (4.8–8.3)	2654	42.0 (39.0–45.1)	4737	70.7 (67.9–73.5)	2739	69.4 (66.6–72.3)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey, *N* number of children

Table 7 Proportion of pregnant women who slept under an insecticide-treated bed net the night before the survey

Background characteristic	DHS 2003		MICS 2006[a]		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Residence									
Urban	7.5 (4.0–10.9)	219	–	–	38.3 (30.7–45.9)	378	69.6 (57.5–81.8)	6733	62.1 (49.6–74.7)
Rural	2.3 (1.1–3.6)	1056	–	–	45.8 (42.2–49.4)	1310	78.8 (74.5–83.1)	31,660	76.5 (72.0–80.9)
Household wealth quintiles									
Poorest	1.1 (−0.4–2.7)	221	–	–	44.0 (37.5–50.5)	297	69.0 (60.8–77.2)	161	67.9 (59.6–76.2)
Poorer	0.7 (−0.4–1.7)	269	–	–	42.5 (36.4–48.6)	369	78.5 (71.4–85.6)	8495	77.8 (70.7–84.9)
Average	3.2 (0.4–5.9)	343	–	–	43.2 (37.1–49.2)	365	79.8 (72.9–86.8)	8520	76.7 (69.3–84.1)
Richer	1.5 (−0.4–3.3)	216	–	–	49.1 (42.4–55.7)	358	87.8 (82.1–93.6)	8165	86.4 (80.4–92.4)
Richest	9.4 (4.9–14.0)	226	–	–	43.9 (36.2–51.6)	299	65.5 (50.8–80.3)	4833	57.4 (42.2–72.5)
Size of the household									
Small (1–5 members)	4.3 (2.3–6.3)	442	–	–	47.0 (42.6–51.4)	813	75.8 (69.7–81.9)	11,250	71.5 (65.1–77.9)
Medium (6–8 members)	2.0 (0.0–4.0)	350	–	–	42.1 (36.9–47.2)	463	78.3 (71.5–85.2)	12,025	76.3 (69.2–83.4)
Large (9+ members)	2.5 (0.3–4.7)	483	–	–	42.2 (36.3–48.1)	412	78.4 (71.3–85.6)	15,118	75.9 (68.5–83.4)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey, *N* number of pregnant women

[a] Data not available

Table 8 Proportion of households owning at least one insecticide-treated bed net but with fewer than one net for every two household members (intra-ownership gap)

Background characteristic	DHS 2003		MICS 2006		DHS 2010		MIS 2014		Percentage point change (2003–2014)
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	
Residence									
Urban	60.8 (53.8–67.8)	2182	53.5 (45.1–62.0)	921	58.7 (56.0–61.3)	4391	36.7 (33.5–39.8)	1305	23.9 (15.8–31.9)
Rural	74.4 (66.8–81.9)	6868	76.2 (72.8–79.6)	4602	70.7 (68.5–72.9)	9997	48.9 (47.0–50.7)	5104	25.9 (18.2–33.7)
Household wealth quintiles									
Poorest	67.0 (51.0–82.9)	1880	82.5 (75.0–90.1)	1276	74.6 (71.4–77.8)	2620	51.3 (47.4–55.2)	1511	15.4 (−0.8–31.6)
Poorer	90.5 (79.6–101.4)	1619	82.2 (76.0–88.5)	1276	71.1 (67.9–74.3)	2744	48.3 (45.1–51.5)	1385	42.1 (30.3–53.8)
Average	80.4 (67.7–93.2)	2023	74.0 (67.1–80.9)	1116	70.2 (67.2–73.2)	2777	51.4 (48.1–54.7)	1288	28.7 (15.6–41.9)
Richer	79.4 (66.6–92.2)	1407	77.6 (71.9–83.3)	1013	70.2 (67.2–73.3)	2922	44.5 (41.1–47.9)	1236	35.2 (22.7–47.8)
Richest	59.2 (52.8–65.6)	2121	50.4 (42.9–57.9)	842	56.1 (53.4–58.8)	3325	33.3 (30.2–36.4)	989	26.0 (18.8–33.2)
Size of the household									
Small (1–5 members)	45.2 (38.2–52.2)	4421	41.2 (34.9–47.5)	2345	49.9 (47.8–52.1)	8169	25.5 (23.7–27.4)	3362	20.4 (13.3–27.5)
Medium (6–8 members)	87.9 (78.3–97.5)	2401	76.6 (69.7–83.6)	1665	83.7 (81.7–85.7)	3911	59.3 (56.2–62.5)	1760	28.6 (18.0–39.2)
Large (9+ members)	97.5 (94.5–100.5)	2228	94.7 (91.8–97.6)	1513	93.4 (91.7–95.1	2308	80.7 (78.0–83.4)	1287	16.8 (12.9–20.8)

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey, *N* number of households

Table 9 Proportion of individuals with access to an insecticide-treated bed net who did not use them the night before the survey (behavioural gap)

Background characteristic	DHS 2003		MICS 2006[a]		DHS 2010		MIS 2014	
	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N
Residence								
Urban	31.0 (27.9–34.1)	12,313	–	–	22.2 (21.2–23.2)	21,758	13.1 (12.3–13.9)	6733
Rural	9.6 (7.3–11.9)	46,530	–	–	9.6 (9.2–10.0)	58,774	3.4 (3.1–3.7)	31,660
Household wealth quintiles								
Poorest	0.0[b] (0.0–1.2)	10,802	–	–	12.0 (11.1–12.9)	15,243	0.0[b] (0.0–0.0)	8380
Poorer	8.9 (3.2–14.6)	11,113	–	–	9.9 (9.1–10.7)	15,389	4.4 (3.9–4.9)	8495
Average	17.8 (11.9–23.7)	14,345	–	–	8.6 (7.9–9.3)	16,306	3.8 (3.3–4.3)	8520
Richer	16.9 (10.9–22.9)	10,056	–	–	8.1 (7.4–8.8)	16,989	6.4 (5.8–7.0)	8165
Richest	26.6 (23.8–29.4)	12,527	–	–	22.5 (21.5–23.5)	16,605	15.0 (14.0–16.0)	4833
Size of the household								
Small (1–5 members)	24.6 (21.2–28.0)	14,278	–	–	11.7 (11.1–12.3)	27,130	9.2 (8.6–9.8)	11,250
Medium (6–8 members)	23.0 (19.1–26.9)	16,500	–	–	14.3 (13.6–15.0)	26,634	4.9 (4.4–5.4)	12,025
Large (9+ members)	16.3 (12.7–19.9)	28,065	–	–	12.1 (11.4–12.8)	26,768	3.3 (2.9–3.7)	15,118

All estimates take into account sample weights

CI Confidence intervals, *DHS* Demographic and Health Survey, *MICS* Multiple Clusters Indicator Survey, *MIS* Malaria indicator Survey, *N* number of individuals

[a] Data not available

[b] Negative gap values were set to zero

quintile of the population more frequently owned enough bed nets than households located in rural settings or with a lower wealth index. This result is consistent with the findings of other studies showing that ITN coverage is lower in urban areas because mass distribution campaigns usually focus on rural communities [29, 30]. Therefore, future strategies for ITN distribution should pay partiuclar attention to urban areas.

Overall, the behavioural gap was very low in 2014. However, households located in urban settings and from the richest quintile of wealth index have higher gaps, because they might have other alternative prevention

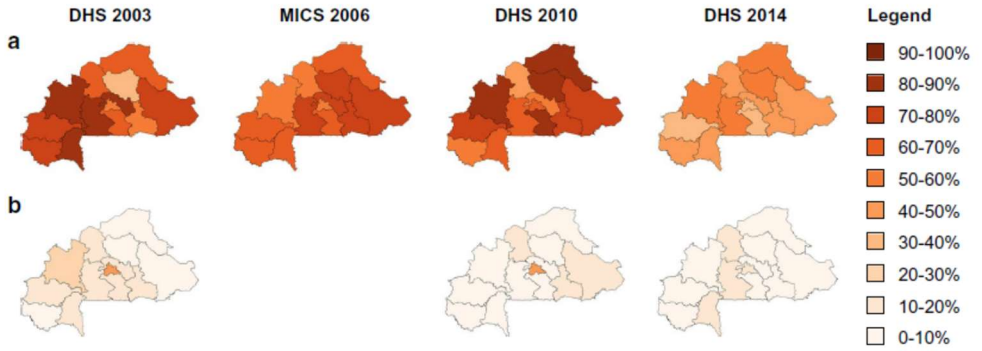

Fig. 4 Trends of ownership and behavioural gaps between 2003 and 2014, Burkina Faso. The proportion of households owning at least 1 ITN but less than 1 for every 2 members (**a**) and the proportion of people with access to ITN but who did not use it the night before the survey (**b**) is indicated for each region, for 2003, 2006, 2010 and 2014 respectively

methods, such as better housing. Also, behavioural gap was significantly lower for large households which could result from large households having more family members (especially children) sleeping under the same bed net. The results showed that only a few large households possessed enough bed nets to protect all family members.

This study has a few limitations, however, they do not affect the validity of the results. This study was based on exiting data, and was limited by available data. Survey data were collected during different seasons of the year. MIS data were collected during the high transmission period while DHS data were collected during the end of the transmission period. This difference could potentially affect the trends analysis and may have under- or overestimated the effect size, as ITN use can be seasonal depending on the perceived nuisance of mosquitoes [31]. Furthermore, the measures presented in this paper were self-reported and therefore susceptible to social desirability biases.

Conclusion

Following the two free mass distribution campaigns in 2010 and 2013, Burkina Faso has made considerable progress in coverage of ITN ownership, access and use between 2003 and 2014. However, bed net coverage remains below national targets of 100% for ownership and 80% for use. To reduce significantly the malaria burden in Burkina Faso, the NMCP needs to increase further and sustained ITN ownership and use in the general population. The free mass distribution campaigns contributed effectively to increase INT ownership and use in Burkina Faso. The NMCP should continue implementing these campaigns to reach the universal coverage target. In addition, these campaigns should be complemented by other bed net distribution mechanisms (through antenatal care, immunization) to identify and replace nets that are worn, damaged or lost between free mass distribution campaigns. Furthermore, NMCP should have an effective behaviour change communication component in all distribution mechanisms to ensure that the population use bed nets consistently.

Abbreviations

ANC: antenatal care; RBM: Roll Back Malaria; BBC: behaviour change communication; DHS: Demographic and Health Surveys; EA: enumeration areas; LLINs: long-lasting insecticidal nets; MERG: Monitoring and Evaluation Reference Group; MICS: Multiple Indicator Cluster Surveys; MIS: Malaria Indicator Survey; ITNs: insecticide-treated bed nets; NMCP: national malaria control programme; SSA: sub-Saharan Africa; WHO: World Health Organization.

Authors' contributions

FKS and SS conceived the study. SS and MP performed the statistical analysis. SS, FKS and MP drafted the manuscript. FKS and YY contributed to the manuscript by giving substantial intellectual inputs. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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Table 2 : Factors associated with bed net use in univariate and multivariate analysis for households owning at least 1 ITN for every 2 household members: Burkina Faso 2014 Malaria Indicator Survey.

Variable	*N* (Use%) [1]	Crude OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Age group					
U5 (<5 years old)	5206 (82.7%)	1	-	1	-
Child (5-14 years old)	7315 (66.0%)	0.53 [0.43-0.65]	$p < 0.001$ ***	0.52 [0.42-0.65]	$p < 0.001$ ***
Adult (15-34 years old)	6997 (71.6%)	0.57 [0.48-0.69]	$p < 0.001$ ***	0.60 [0.49-0.73]	$p < 0.001$ ***
Older (35+ years old)	6212 (81.3%)	0.73 [0.59-0.90]	$p = 0.003$ **	0.73 [0.59-0.91]	$p = 0.005$
Gender					
Male	11812 (70.2%)	1	-	1	-
Female	13918 (77.5%)	1.35 [1.20-1.51]	$p < 0.001$ ***	1.39 [1.24-1.56]	$p < 0.001$ ***
Household wealth index					
Poorest	5246 (74.2%)	1.17 [0.90-1.52]	$p = 0.25$	0.94 [0.74-1.21]	$p = 0.65$
Poorer	5805 (74.8%)	0.77 [0.61-0.96]	$p = 0.02$ *	0.72 [0.57-0.90]	$p = 0.004$ **
Average	5957 (75.0%)	1	-	1	-
Richer	5696 (73.8%)	0.94 [0.69-1.28]	$p = 0.68$	0.99 [0.74-1.34]	$p = 0.97$
Richest	3026 (70.3%)	0.60 [0.45-0.81]	$p = 0.001$ **	0.82 [0.53-1.28]	$p = 0.389$
Location of cluster					
Urban	4239 (70.5%)	1	-	1	-
Rural	21491 (74.7%)	1.50 [1.19-1.89]	$p = 0.001$ **	1.14 [0.78-1.67]	$p = 0.482$
Size of the household					
Small (1-5 members)	8229 (82.3%)	1	-	1	-
Intermediate (6-8 members)	8384 (76.4%)	1.03 [0.85-1.24]	$p = 0.76$	1.04 [0.86-1.27]	$p = 0.68$
Big (9+ members)	9117 (66.0%)	0.84 [0.65-1.09]	$p = 0.19$	0.87 [0.66-1.15]	$p = 0.33$

[1] Effectives are un-weighted.

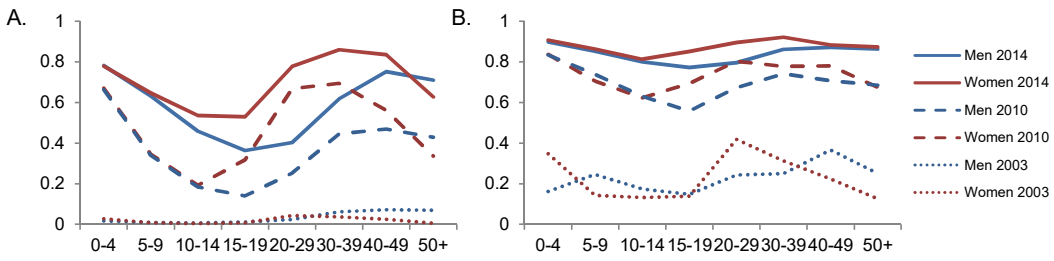

Figure 155 : ITN use by age and gender. Weighted proportions are plotted in red for women, blue for men in (A) households with less than 1 ITN for 2 members (if any ITN) and (B) households with at least 1 ITN for 2 members for 2003, 2010 and 2014

6. DISCUSSION

In this work, we have performed a number of analyses to assess the current malaria burden among children under 5 years old in Burkina Faso following the implementation of malaria control measures. We used the prevalence of malaria infection (proportion of *Plasmodium* infected individuals diagnosed by microscopy or rapid diagnostic test) as the indicator to evaluate malaria burden. This work consisted in the evaluation of: i) the spatial distribution of malaria burden and associated factors, ii) the performance of malaria burden assessment tools, and iii) the proportion of population that used LLINs, the main strategy to reduce malaria burden.

This exploratory analysis is the first to estimate the burden of malaria in Burkina Faso from a population level survey, using data from the first survey in which children under five years old were tested for *Plasmodium sp* infections. These results come at the right moment when Burkina Faso's National Malaria Control Program (NMCP) is looking for up-to-date information on malaria epidemiological patterns, its burden and factors influencing mosquito nets use across the country [1]. The results provide some responses to these questions.

Spatial distribution of malaria infection among children in Burkina Faso and its implication for effective prevention

The epidemiological study of *P. falciparum infection*, using data from the 2010 Demographic and Health Survey was presented in Chapter 5. Results demonstrated that in a context of endemic transmission, despite the national overall prevalence of malaria (66%), significant heterogeneity remains between the 13 regions, and also between villages and districts within the same region.

In 2010, regional level prevalence varied between 28% to 78%. Geostatistical models were used to show that prevalence varied between 11% and 92% among communities. Low risk areas were concentrated in major urban centers such as the capital Ouagadougou. The northern part of the country and the horizontal band between the cities of Bobo-Dioulasso and Ouagadougou had the highest risk of malaria. Communities with high malaria infection prevalence represent important infectious reservoirs that substantially contribute to transmission.

Other studies also reported a high heterogeneity in malaria transmission [2-6]. This heterogeneity is likely to reduce the effectiveness of malaria prevention programs [3, 4, 7], and should therefore be considered as key element in planning these programs [7-9]. Malaria transmission risk is usually localized in space and time [9]. Only a small proportion of the population bears most of the burden of malaria and contributes disproportionately to subsequent transmission [2, 10]. Research suggests, therefore, that optimal interventions should target high-risk areas [2, 7, 9, 11, 12]. Although targeting

seems an attractive strategy, its implementation is complex. In endemic areas, it is difficult to delineate high-risk areas of malaria with adequate accuracy [13].

Explanatory factors of the spatial heterogeneity of malaria distribution in Burkina Faso

A number of factors could explain the heterogeneity of malaria infection in endemic areas [14, 15]. Particularly they include variation in vector density, temperature and humidity [6, 16], household characteristics [17-20], population genetic susceptibility [21, 22], and behavioral factors [23]. The combination of these factors creates areas of high risk of malaria or "hot spots" [7]. By intervening on these factors, control interventions could reduce transmission.

Our results, like many other studies conducted in Burkina Faso [24, 25], confirmed significant associations between malaria and a number of environmental factors (the NDVI index, rainfall, temperature). Malaria infection was also associated with age, mother's educational level, socio-economic status and health facility attendance.

However, there was no significant association between malaria infection in children and bed net use. Studies conducted in similar contexts, however, have reported significant associations[4, 26]. The effect of net use is likely to vary with the level of malaria endemicity and geographical scale [4, 27]. Some interventions may not produce an effect when implemented at the

national level while they could be protective at sub-national levels [28]. Using DHS data, Diboulo et al [28], found that the use of LLINs had a protective effect against malaria infection only in Ouagadougou (the capital) and in three other health districts of Burkina Faso [28].

What "modifiable factors" can be targeted immediately in order to reduce the parasitic reservoir of malaria in Burkina Faso?

Based on our results, improving health facilities attendance is the main factor the NMCP could influence to reduce malaria burden. Children living in communities with an average yearly attendance at health centers greater than 2 visits per year were significantly less at risk of malaria infection.

This could be related to the fact that health centers are the principle source of access to malaria prevention and treatment measures. In addition, these centers carry out information, education and communication (IEC) activities that could improve people's knowledge, attitudes and practices towards malaria prevention. It is reported that in Burkina Faso this type of intervention significantly improves the prevention of malaria [29, 30].

Studies in Côte d'Ivoire [31] and Kenya [32] reported that risk of malaria infection decreases following the distance to health centers. Improving physical accessibility of populations to health centers could reduce the burden of malaria in Burkina Faso. An alternative strategy could be that Burkina Faso’s health authorities implement prevention and case management

activities (mosquito nets distribution, prompt diagnosis, awareness, and adequate treatment of uncomplicated cases) within the community.

Can microscopy be replaced by RDTs in estimating malaria burden in Demographic and Health Surveys (DHS)?

DHS surveys are the main tools for monitoring malaria morbidity and the impact of anti-malarial interventions in sub-Saharan Africa. RDT use to detect malaria infection during these surveys remains problematic. Although RDTs offer many advantages in resource-constrained settings, several studies suggest that they may bias the estimation of malaria burden. They overestimate malaria prevalence by about 1.5% to 10% [33-35]. In contrast, microscopy, which is method of reference in most sub-Sahara African countries, is often not available in rural settings [36, 37].

Our results in Chapter 6 represent the first countrywide assessment of RDT performance in Burkina Faso. The overall sensitivity ranged from 74% in the Cascades region to 98% in the South Central region and the specificity from 21% in the Central-South region to 71% in the Central region. Sensitivity increased from 88% during the dry season to 93% during the rainy season. The results also suggest that RDT specificity is higher in urban areas and in younger children. This important variation in sensitivity and specificity according to region, rural or urban area, age group and season underlies the need to consider the influence of such variation in approaches aiming to

estimate the prevalence of malaria infection. Statistical models could be proposed to adjust RDT estimated prevalence.

The RDT Paracheck Pf® used in this survey is *P. falciparum* HRP-2 antigen specific. The low specificity of this RDT could be explained by the persistence of HRP-2 antigen over several days during which smear results remain negative [38, 39]. Also, false negative results have been reported in asymptomatic carriers indicating the existence of non-secretory HRP-2 protein *P. falciparum* strains [40]. The following question then arises: What methods should be used to screen malaria infection during community surveys in Burkina Faso?

Our results suggested that for community-based surveys such as the DHS that primarily target asymptomatic carriers the use of Paracheck Pf® RDT should be coupled with the microscopy, or with novel techniques such as the Loop mediated isothermal amplification assay of DNA (LAMP) [41].

Can Paracheck Pf® RDT's specificity and spatial variability affecting the effectiveness of the "Test and Treat" policy in Burkina Faso?

Early diagnosis and adequate treatment of uncomplicated malaria cases will help reduce the severity of the disease, its associated mortality, and the transmission intensity. In Burkina Faso, following with WHO recommendations, all malaria suspected cases should be confirmed parasitologically (by microscopy or rapid diagnostic test) prior to the administration of treatment. This is the so-called « test and treat » strategy.

This approach rationalizes the use of antimalarials compared to the presumptive diagnosis strategy [42]. It also helps prevent the emergence of antimalarial resistance and reduces the costs associated with repeat patient visits to health care facilities [43].

Although this study (Chapter 5) was not conducted in a context of malaria clinical diagnosis, our results indicate that the performance of Paracheck Pf® RDT varies significantly by region. This variability suggests that the effectiveness of the "test and treat" approach may not be similar throughout the year or throughout the regions. This approach may be adequate for some contexts and unacceptable for others, given the large proportion of false negatives. Further investigations are needed to propose malaria diagnostic algorithms and case management that account for regional context.

Could bed net ownership or its use partly explain spatial heterogeneity of malaria prevalence as certain areas are more at risk than others ?

Vector control is the main approach of preventing and reducing malaria transmission in Burkina Faso. It is assumed that protection against malaria through LLINs is effective if utilization rate by the population reaches at least 80%.

An evaluation using data from four national population level surveys conducted in 2003, 2006, 2010 and 2014 has helped describe the geographical heterogeneity of the ownership and use of mosquito nets in Burkina Faso (Chapter 5). In terms of prevention, household level net ownership increased

from 6% in 2003 to 90% in 2014 with low regional disparity. Similarly, the use of ITNs in children under five years old increased from 2% (2003) to 75% (2012). Our report also shows that the gap between ownership and use of mosquito nets has decreased between 2003 and 2014 in Burkina Faso, with the largest reduction reported in the southwest part of the country, particularly in the Hauts Bassins regions. Changes in the gap between net possession and use have slight geographical heterogeneity. The Sahel, the North and the Central East presented a smaller gap reduction. These results could partly explain the high prevalence of malaria in these regions.

Despite progress made in Burkina Faso, the rates of LLIN possession and use remain below the respective national targets of 100% and 80%. Although the majority of households possess LLINs, about half of them do not have a sufficient number to protect all household members. Also, one in two regions has a gap between LLIN possession and use of up to 10%. Similar results have been from multiple countries have been published elsewhere [44-46]. Increased involvement of communities during LLIN distribution and promotion campaigns could remove some of these associated barriers. In particular, it may be useful to take into account the population’s preferences (size, color, shape) in the choice of LLINs. Finally, an incentive should be put in place (financial or in-kind) to avoid the "malaria trap" [47] which results in the use of nets for other purposes (resale to a parallel market, fishing activities), particularly by the poorest populations.

7. CONCLUSION AND PERSPECTIVES

7.1.Conclusion

In this thesis, we sought to generate new evidence in the understanding of the spatial distribution of malaria in children under 5 years old in Burkina Faso. To answer our research question, we used the fourth Demographic and Health Survey (DHS) conducted in 2010 in Burkina Faso. This was the first national survey in which children were tested for *Plasmodium sp*. Results from this study include the high variability of malaria prevalence in the country. The North-South gradient of malaria observed since 2003 seems to no longer guide transmission. The challenge of controlling malaria resides now at the community level. Recent climate change, rapid urbanization, development projects (dams, roads) and legislative changes may have contributed to changes in the pattern of malaria distribution in Burkina Faso. Improving health care access and educating mothers (mainly through raising community awareness campaigns) could reduce the prevalence of malaria in children according to this study.

This thesis brings to light evidence that malaria prevalence estimates using Paracheck® RDT vary according to region, season, place of residence, and age of the subject. RDT use in community surveys should be compared to other screening technique (microscopy or PCR) to validate results. This work also reveals that a unique algorithm based on RDT may be ineffective due to the geographical variation in the number of false negative tests. Further investigations are needed to propose RDTs that are suited to different areas of malaria transmission in Burkina Faso. Finally, there is a need for optimal coverage of LLIN access and use to reduce the burden of malaria. According

to the observed trends between 2003 and 2014, LLIN possession and use increased sharply in all regions of Burkina Faso. This progress is still, however, below the NMCP target in Burkina Faso.

Currently, people acquire LLINs mainly through free distribution campaigns. The contribution of other distribution mechanisms of mosquito nets (vaccination campaigns and antenatal care visits) should be improved to ensure the adequate protection of vulnerable populations, including children.

This exploratory work paves the way towards new research questions, and produces findings that could contribute to reducing malaria burden and to better addressing current NMCP weaknesses.

7.2.Perspectives

What was the contribution of antimalarial interventions in reducing the risk of malaria in Burkina Faso between 2010 and 2014?

Average malaria prevalence decreased from 66% in 2010 to 46% in 2014 [48, 49]. It is necessary to compare prevalence variation estimates using a fine spatial resolution to quantify the effects of antimalarial interventions both at national and subnational levels. These estimates are valuable tools to identify priority areas where interventions appear less effective in order to reinforce malaria control. Similar studies conducted in Angola, Liberia, Mozambique, Senegal, Rwanda, Tanzania and more recently in Ouagada reported that interventions' effects vary among regions and villages [4, 50]. To mitigate malaria burden, the authors suggest that areas in need of additional resources should be targeted as well as areas where interventions are more likely to produce the greatest impact [4].

Given the endemic context of malaria in Burkina Faso, could spatial analysis accelerate progress in malaria control and lessen the waste of resources in Burkina?

In the context of high heterogeneity in malaria prevalence, targeting highly affected communities appears complex. Heterogeneity implies diversity of needs in terms of intervention strategies against malaria. In urban areas, for example, although malaria prevalence seems low, there are areas of high prevalence. These areas should be targeted with specific activities such as the destruction of larva breeding sites and the promotion of indoor residual insecticide spraying.

However, in areas of high malaria prevalence it could be possible to achieve the NMCP goal of reducing malaria mortality rate by at least 40% by 2020 [1]. In a near future, the NMCP could achieve this objective through a spatial identification of health districts (operational entity of the Burkinabè health system), which report most of the malaria severe cases. Cases occur mainly between August and October according to our spatio-temporal analysis of severe malaria distribution in Burkina Faso (Appendix 1). Risk of severe malaria is significantly higher than the NMCP target in several districts of the South West between June and July (Appendix 2). During September, the highest burden of severe cases is reported in the northern part of the country (Appendix 2).

Is Burkina Faso's work accomplished in terms of population mosquito net coverage?

Coverage of mosquito net ownership and use has sharply increased in Burkina Faso between 2003 and 2014. Nonetheless, malaria burden in children remains high with a high heterogeneity at the community level. Progress seems unevenly distributed among communities. In Burkina Faso, mosquito net use increases when populations have access to sufficient quantity of nets, (Figure 15). The high level of coverage of malaria control interventions at regional level may overlook important disparities at sub-regional level [51, 52]. It is important to estimate coverage indicators for these interventions on a fine geographic scale and at a household level. Individuals from large households were less likely to sleep under a net (Table 2). Finally, some studies suggest that improving housing conditions could contribute to more effective vector control. Understanding the relationship between the probability of malaria infection and housing characteristics (roofing, interior walls and floors) is essential to optimize vector control in Burkina Faso.

Our results also confirm that understanding the factors that influence malaria distribution is key to optimizing malaria intervention strategies. In order to reduce number of new P. falciparum infections, it appears necessary to identify the areas and populations for focused intervention efforts including prevention activities, access to care and treatment. In Burkina Faso, our results suggest that malaria control activities should be particularly strengthened in the north of the country and in the horizontal band between the cities of Bobo-Dioulasso and Ouagadougou. Regarding household and regional characteristics, efforts should focus on high-risk groups, such as

children over one year of age, households with low socio-economic status and children with low access to health care.

Finally, our results indicate that the prevalence of malaria, during the high transmission season, does not follow a North-South gradient. Within the same region, there are often significant variations between villages and districts. This finding recommends that malaria control strategies target communities for a more effective impact.

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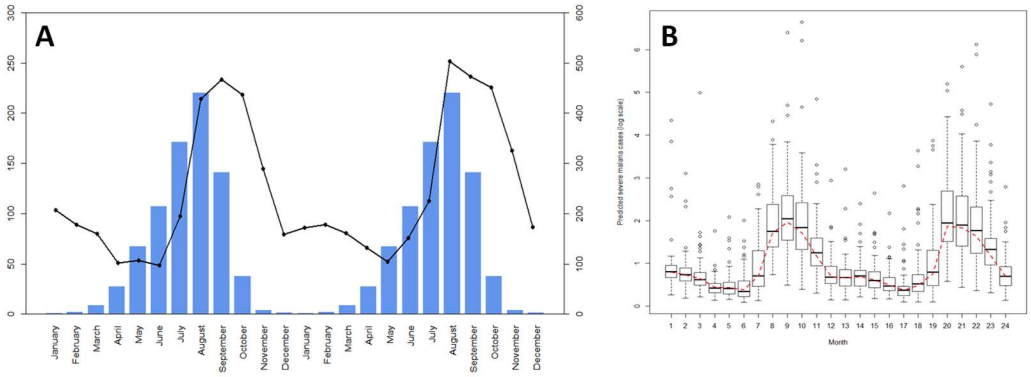
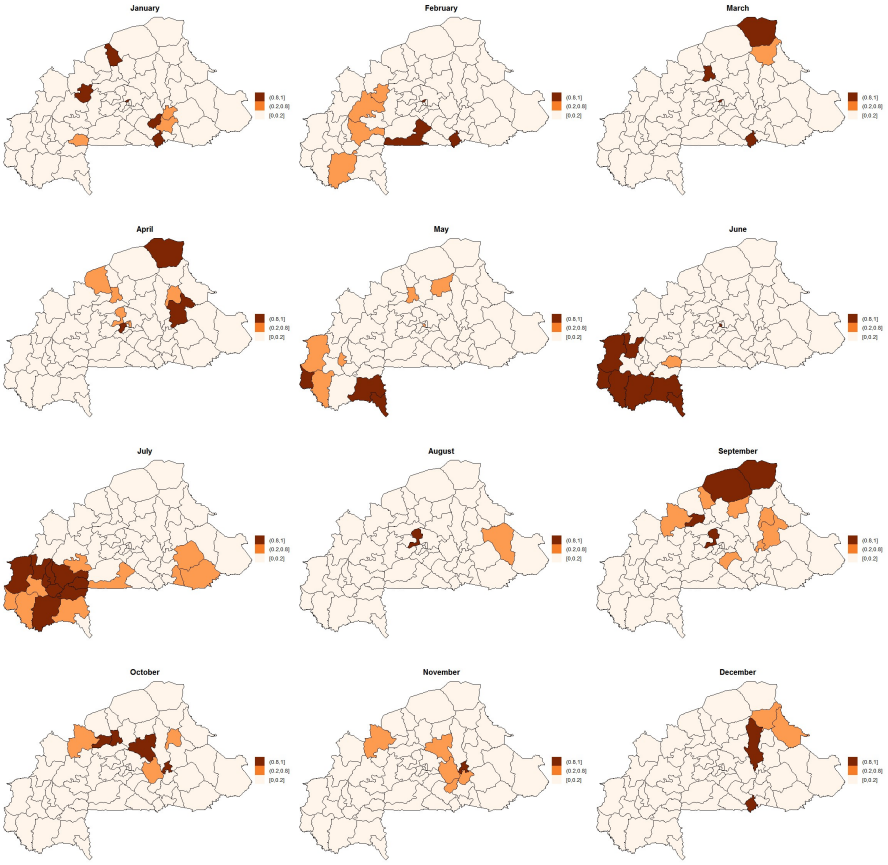
8. APPENDICES

8.1. Heterogeneity of severe malaria among children in Burkina Faso: a spatio-temporal analysis.



Appendix 1: Figures showing A) showing the average monthly rainfall (line) and malaria cases for Burkina Faso (2013-2014) (bars) and B) A box plot of predicted rate by month for the two-year period. The red dashed line is a loess smooth based on the median.



Appendix 2: Figures showing space-time interaction term for probability of incidence density ratio >1.6, spatiotemporal model of Burkina Faso (2013-2014).

8.2.Scientific Curriculum Vitae

Expériences professionnelles

- Assistant d'enseignement et de recherche - Université Catholique de Louvain, 15/09/2012–14/09/2018

Education

- PhD - Sciences médicales, Université catholique de Louvain, IREC , EPID. Belgium 2018.
- Certificat universitaire en statistique, Université catholique de Louvain, Institute of Statistics, Biostatistics and Actuarial Sciences. Belgium 2016.
- Master bioingénieur, Université catholique de Louvain, Faculty of bioscience engineering. Belgium 2010.
- Master en sciences et gestion de l'environnement, Université catholique de Louvain, Faculty of bioscience engineering. Belgium 2008.
- Diplôme d'Etudes Approfondies (DEA) en sciences biologiques appliquees, option: biochimie et microbiologie appliquées, Université de Ouagadougou, Unité de formation et de recherche Sciences de la Vie et de la Terre. Burkina Faso 2004.

Publications

- **Samadoulougou S**, Pearcy M, Ye Y, Kirakoya-Samadoulougou F: Progress in coverage of bed net ownership and use in Burkina Faso 2003-2014: evidence from population-based surveys. Malar J 2017, 16:302.
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Communications

- **Samadoulougou S**, Sawadogo K C, Robert A: Regional disparities of late entry to antenatal care and associated socio-demographic barriers in Burkina Faso. European Congress of Epidemiology. Lyon, France, 2018.
- **Samadoulougou S**, Pearcy M, Robert A: Spatial patterns of anaemia among young children in Burkina Faso: a Bayesian Geo-Additive Modelling. GeoMed 2017: International Conference on Spatial Statistics, Spatial Epidemiology & Spatial Aspects of Public Health. 2017. Porto, Portugal,

- **Samadoulougou S,** Kirakoya-Samadoulougou F, Robert A: Geographic disparities in bednet ownership and usage: an analysis of Burkina Faso 2010 Demographic and Health Survey data. Tropical Medicine & International Health 2015, 20:74. Bâle, Suisse.
- **Samadoulougou S**, Kirakoya-Samadoulougou F, Robert A: Spatial distribution of anemia in children under five in Burkina Faso. Tropical Medicine & International Health 2015, 20:290. Bâle, Suisse.
- **Samadoulougou S**, Valéa I, Tinto H, Kirakoya-Samadoulougou F, D'alessandro U, Robert A: Incidence of malaria infection and related risk factors among pregnant women in rural Burkina Faso. Tropical Medicine & International Health 2013, 18:150. Copenhague, Denmark.
- **Samadoulougou S**, Pearcy M, Robert A: Geographic Geographical patterns of severe anaemia among young children in Burkina Faso. Young Researchers' Overseas Day - Royal Academy for Overseas Sciences 2016.
- **Samadoulougou S**, Kirakoya-Samadoulougou F, Robert A: Spatial modelling of malaria incidence in Burkina Faso. Public health Seminar from the Public Health Faculty of UCL 2016.

Activités d'enseignement réalisées

- Logiciels d'épidémiologie et de Statistique (UCL), Advanced epidemiology (UCL), Introduction à la statistique descriptive et aux probabilités (UCL), Statistiques en sciences de la santé (UCL), Statistique Médicale Avancée (UCL), Modèles linéaires multi-prédicteurs appliqués aux sciences de la santé (UCL), Epidémiologie génomique (UCL), Séminaire de méthodes avancées en santé publique (épidémiologie spatiale - UCL).
- Encadrement de mémoires de fin d'études

Formations continues suivies

- Acquisition et traitement statistique de données - niveau 3. École Pratique des Hautes Études, Montpellier, 2018.
- Modelling spatial and spatio-temporal areal unit data in R with CARBayes, Université Porto, 2017.
- Spatial and Spatio-Temporal Analysis Training Course, University of Cambridge, 2016.

- Applied Spatial Statistics with R, Katholieke Universiteit Leuven, 2016
- Modèle de régression pour données corrélées, Association Epiter France, 2015
- GIS for Public Health Short Course, Imperial College London, 2016
- Hierarchical modelling of spatial and temporal data, University of Southampton, 2015
- Introduction to Bayesian Analysis and MCMC, University of Southampton, 2015
- Introduction à la modélisation et au calcul bayésien Gembloux, Gembloux Agro-Bio Tech, Université de Liège, 2015
- Bayesian Analysis of Follow-up Studies, International Biometric Society, Florence Italy, 2014
- Introduction aux modèles multi-niveaux avec SPSS, Université catholique de Louvain, 2013

Bourses

- Fellowship of the FNRS of Tropical Medicine for attending the 9th European Congress on Tropical Medecine and International Health (ECTMIH). September 2015.
- Study grant of Unversity of Cambridge for Advanced Training Courses – Spatial and Spatial-temporal Data Analysis – June 2016.