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Spatial malaria distribution and, insecticide-treated nets and artemisinin-based combination therapy usage among children under-five years in Cameroon, 2018

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FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

SPATIAL MALARIA DISTRIBUTION AND, INSECTICIDE-TREATED NETS AND ARTEMISININ-BASED COMBINATION THERAPY USAGE AMONG CHILDREN UNDER-FIVE YEARS IN CAMEROON, 2018

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology in the field of Implementation Science.

Johannesburg 2021

Declaration

I hereby declare that this research report is my work. It is being submitted in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology in the field of Implementation Science at the University of the Witwatersrand, Johannesburg. The contents of this research report are original and have not been submitted for any other degree or qualification in this, or any other university.



November 18th 2021

Sylvie Ngum Njong

ABSTRACT

Background

Malaria is highly endemic in Cameroon with children under five years being the most vulnerable despite the widespread provision of preventative and curative interventions. These include, insecticide-treated nets (ITN) and artemisinin-based combination therapy (ACT) respectively. This study examined the spatial distribution of malaria prevalence, ITN and ACT use among children under five years in Cameroon.

Methods

A cross-sectional design was used to study malaria data from the 2018 Cameroon Demographic and Health survey. The observed prevalence, hot and cold spots, and spatial autocorrelations among Cameroon's 58-second administrative divisions were determined. Multilevel logistic regression modelling was used to determine the relationship between malaria and the use of ITN, ACT and the combined usage of ITN and ACT, adjusting for sociodemographic and climatic factors. Conditional autoregressive modelling was used to adjust for spatial random effects and to map predicted malaria risk

Results

Of the 4,733 children in the study, 1,161 (24%) had malaria in 2018. The observed malaria prevalence was highest in Mayo-Louti, Faro-et-Deo, Djerem, Haute-Sanaga, Nyong-et-Kelle, Lekie, Nyong-et-Mfoumou, Mbam-et-Inoubo, Nkam, Boumba-et-Ngoko and Vallee-du-Ntem divisions. There was a significant spatial autocorrelation (Moran's I 0.457; $p<0.00001$) indicating a clustering pattern of malaria infections. Malaria hot spots were identified in some divisions of the Centre, East, Adamawa and South regions of Cameroon. ITN usage was 58% (n=2,824) and was highest in the divisions of Far-north and North regions. ACT usage among children with fever

two weeks before survey was low (n=48, 5.5%). ITN and ACT use were not significant but the odds of malaria were increased for some children who neither used any of the two interventions (AOR 2.30, 95%CI 1.09, 4.84). Increasing age, history of fever, and living in rural areas significantly increased the odds of malaria (AOR 2.97, CI 2.18, 4.03; AOR 2.64, CI 2.03, 3.43 and AOR 1.86, CI 1.32, 2.63 respectively). Conversely, Altitude, tertiary levels of maternal education and higher socioeconomic status significantly lowered the odds (AOR 0.16, CI 0.09, 0.29; AOR 0.48, CI 0.26, 0.90 and AOR 0.29, CI 0.15, 0.55 respectively). High malaria risk was predicted in some divisions of the Far-North, Adamawa and Centre regions. Whereas, malaria risk was predicted to be low in the most division of the northern and coastal regions. Climatic and environmental factors had no significant effect

Conclusion

High malaria prevalence among children under five years in 2018 indicates a need for targeted intervention measures, particularly in the Center, East and South regions. Conjugated efforts is required to increase the coverage and use of ITN and ACT in order to effectively reduce prevalence and transmission as these provide a synergetic effect

Keywords:

Spatial analysis, malaria prevalence, interventions

Dedication

This research is dedicated to my loving husband Henry and my beautiful daughter Eliora-Audrey.

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I would like to heartily thank my supervisors Dr Ntombizodwa Ndlovu and Professor Eustasius Musenge for their unconditional support, guidance, patience and encouragement during this study. This research project could not have been possible without you. You were so understanding, available and determined to see that I succeed even when I felt overwhelmed and wanted to leave out part of the work, you stood by me. God bless you all.

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Abbreviations

ACT: Artemisinin-based Combination Therapy

AIC: Akaike Information Criterion.

BCI: Bayesian credible interval

BIC: Bayesian Information Criterion

CDHS: Cameroon Demographic and Health Survey

CI: Confidence Interval

DHS: Demographic and Health Survey

GIS: Geographic Information System

GPS: Global Positioning System

ICC: Intra-class correlation coefficient

ICF: Inner City Fund

INLA: Integrated nested Laplace approximation

IRS: Indoor residual spraying.

ITNs: Insecticide-treated nets

KR: Kids Recode

LR: Likelihood ratio

MCMC: Markov Chain Monte Carlo

MIS: Malaria Indicator Survey

OR: Odds Ratio

PMI: United States President's Malaria Initiative

PR: Persons recode

RDT: Rapid Diagnostic Test

UNFPA: United Nations Population Fund

USAID: United States Agency for International Development

WHO: World Health Organization

Definition of terms

- An insecticide-treated net (ITN) as defined in the guide to DHS statistics [reference 54] is a factory-treated net that does not require any further treatment. Prior to 2018, this definition was formerly ascribed to a long-lasting insecticidal net (LLIN), and an ITN was either (1) a factory-treated net that does not require any further treatment (LLIN) or (2) a net that has been soaked with insecticide within the past 12 months.
- Artemisinin-based combination therapies (ACTs) are the best anti-malarial drugs available for treating uncomplicated malaria

CHAPTER ONE

INTRODUCTION

This chapter presents a background of malaria beginning with the aetiology. It continues to describe the global burden of malaria with focus on Cameroon. It describes the impact of malaria among children under five years. The literature review covers the epidemiology of the disease, malaria interventions and the application of spatial techniques to study disease burden. This leads to the problem statement which highlights the burden of malaria and the state of interventions in Cameroon. This is followed by justification for the study, research question, aim and objectives.

1.1 Background

Malaria is a tropical disease caused by the unicellular protozoan *Plasmodium*. There are four human species: *P. ovale, P. falciparum, P. vivax* and *P. malariae* (1). In addition, the zoonotic specie *P. knowlesi* has been found to also infect humans (2). Two of the species; *P. falciparum* and *P. vivax* are most common. *Plasmodium falciparum* is responsible for about 99% of malaria infections especially in children under five years (3).

The main vector responsible for transmission is the female *Anopheles* mosquito (1,2). Figure 1.1 illustrates the malaria parasite lifecycle. While taking a blood meal, a mosquito infects the human host by releasing sporozoites into the blood. These migrate to the liver and develop into schizonts which later ruptures to release trophozoites, some of which differentiate to gametocytes. The gametocytes are ingested by another mosquito during a blood meal. The gametocytes undergo developmental stages within the mosquito to become sporozoites. The sporozoites are inoculated

when the mosquito bites an uninfected host thus transmitting the parasite from one person to another.

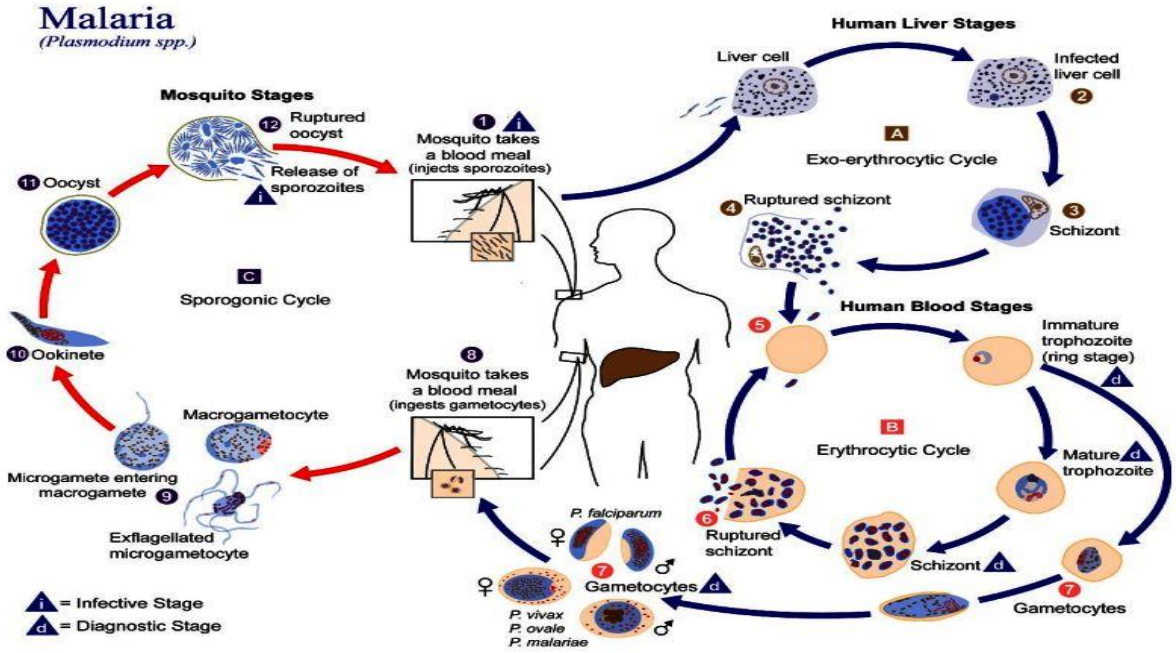


Figure 1.1 Life cycle of malaria parasite
Source: https://www.ncbi.nlm.nih.gov/books/NBK5951/figure/malaria_LifeCycle/

Approximately 3.4 billion people worldwide are at risk of malaria (4). In 2019, 229 million cases of malaria were recorded globally with sub-Saharan Africa contributing about 70% of the global malaria burden (5). Most of the cases (215 million) and deaths (384,000) were in the World Health Organization (WHO) African Region, accounting for about 94% of the mortalities globally (5). The majority of the deaths (67%) in 2019 were recorded in children under five years (5). However, the other WHO Regions such as South East Asia, West Pacific, East Mediterranean, the Americas and parts of Europe are also affected.

Cameroon being in sub-Saharan Africa and in the tropics has a high malaria burden as all of its population is at risk for malaria (5,6). Details of Cameroon are described in the methods section. The country has ten administrative regions belonging to different epidemiologic zones of malaria transmission (7). The Far-North and North regions are hyperendemic malaria zones with three months of seasonal transmission and entomological inoculation rate of 2.4 to 36.5 infective bites/person/month. The Adamawa region is a mesoendemic zone with seven to 12 months of perennial transmission and an inoculation rate of 100 infected bites/person/year. The West and Northwest regions located at altitudes > 1,000 m above sea level are hypoendemic with an inoculation rate of 2.24 to 11 infective mosquito bites/person/year. The Centre, East and South regions experience stable transmission. The coastal regions (Littoral and South-West) are holoendemic with inoculation rates ranging from zero to 100 infective bites/person/year (7–9).

In Cameroon, from 2017, there has been a steady increase in the burden of malaria as the number of cases and deaths continue to rise (6). It is one of the 11 countries labelled by WHO in 2018 as high burden to high impact (HBHI) as they account for 70% of the global estimated case burden (4,5). It is said that 6.3 million malaria cases and 12,000 deaths occurred in Cameroon in 2019 contributing 3% of the global malaria cases recorded (5). All four *Plasmodium* species are found in the country with *P. falciparum* responsible for 95% of the cases (7). In addition, 17 of the 20 *Anopheles*' species known to transmit malaria are present. The five common vectors being (*An. funestus, An gambiae, An. nili, An. arabiensis and An. moucheti*) (8).

Malaria is primarily responsible for illness and death in children under five years in Cameroon (9). The 2018 Cameroon Demographic Health Survey (CDHS) reported an average malaria prevalence

of 24% in children under five years (10). There were 390,180 malaria related hospitalizations and 39,6% malaria deaths among children under five years in 2019 (11). It is known to be responsible for 26% school and work absences and 40% household expenditures in Cameroon (9)

Interventions recommended by the WHO to control malaria like insecticide-treated nets (ITNs) as a vector control method, case management with artemisinin-based combination therapies (ACTs) have been implemented in Cameroon (9,12,13). Other strategies include; intermittent preventive treatment for pregnant women, indoor residual spraying (IRS) using pyrethroids insecticides in 15 districts in Yaounde and seasonal malaria chemoprevention for children three – 59 months in the two northern regions of the country (6,7).

1.2 Review of Literature

1.2.1. Risk factors for malaria infections in children under five years

There are various factors known to influence the transmission of malaria among children under five years. These factors are both intrinsic and extrinsic factors. Intrinsic factors are host/human, parasite and vector factors. Extrinsic factors are socioeconomic, climatic, environmental and malaria control efforts which influence the ability of parasites and their vectors to coexist favoring transmission (14,15).

Intrinsic factors

The risk of malaria is high in children as their immune system is still under-developed and as such they suffer from severe infections (1,14). Younger children acquire antibodies from their mothers during pregnancy and breastfeeding. It is only later in childhood as children grow older that they

develop their own immunity (14,15). Immune suppressive conditions like malnutrition also predispose children to severe infections including malaria (14).

Genetic factors influence susceptibility to malaria infection. Children with sickle cell trait have altered red blood cell structure that limits parasite multiplication thus protecting them against malaria (15). Glucose-6-phosphate deficiency and Thalassemia syndromes have also been associated with decreased malaria susceptibility. In contrast, the presence of the Duffy blood factor facilitates *P. vivax* entry into red blood cells increasing the risk of infection (15).

The different parasite species cause varying degrees of disease severity. *Plasmodium falciparum* is the most virulent resulting in over 90% cases of severe malaria (14,15). *Plasmodium vivax* and *P. ovale* are responsible for relapse months after the initial infection although they cause less severe infections. *Plasmodium malariae* is associated with renal complications and recrudescence (15). Vector factors such as the biting frequency, inoculation rate, density and longevity all influence malaria transmission (15)

Extrinsic factors

Socioeconomic factors have been demonstrated to influence malaria transmission. Houses constructed with cement and bricks tend to limit the entry of mosquitoes and thus reduce infection (16,17). Availability of electricity decreases the risk of malaria as opposed to households with no electricity where occupants spent more time outside thereby exposing themselves to mosquitoes (17). The risk of malaria is lower for children whose mothers have an education. These educated mothers tend to have better health seeking behavior (18). Socioeconomic status has been shown

to be associated with malaria. Poor people tend to have reduced access and affordability to health care. Also they live in poorly constructed houses and in dirty environments which further increases the risk (16,18). Malaria risk is also related to the area of residence. It was demonstrated in a meta-analysis that malaria transmission was lower in urban than rural areas (19). The increased risk in rural areas can be attributed to poor access to health care and low knowledge of control strategies(20).

Climatic factors such as rainfall with resulting stagnant water and temperatures between 25°C to 30°C favor the breeding and survival of malaria vectors (18,21,22). The development of sporozoites within the mosquito is not completed at temperatures below 16°C to 18°C and so cannot be transmitted (15). Environmental factors are also said to influence the transmission of malaria. For instance, low altitude causes poor drainage resulting in pools of water that serve as breeding sites for mosquitoes (23). In addition, temperatures are said to be higher at lower altitudes favoring the survival of vectors and development of *Plasmodium* within the vectors (22–24). Rivers and forests found around homes are potential breeding sites for mosquitoes which increase the risk for developing malaria (22). Bushes, swamps or garbage are breeding sites for mosquitoes and so houses located around these sites are at risk of being infested by these malaria vectors (21). A study found vegetation index to be significantly associated with malaria transmission (25). Another study showed malaria varied in season and geography (land cover and use) (26).

1.2.2. Malaria control interventions (ITN and ACT)

Amongst the strategies to control malaria is vector control with insecticide-treated mosquito nets and case management with artemisinin-based combination therapy (3,27). The WHO recommends

sustained provision and universal access to quality vector control measures, diagnostics and antimalarial medicines (2). Especially for countries with high or moderate malaria transmission to ensure maximal reduction of morbidity and mortality. Thus, the WHO has called for the reinvigoration of progress in control so as to meet the global technical strategic milestone of reducing the 2015 level of malaria morbidity and mortality by 90% in 2030 (2,5). The Cameroon government has considered the fight against malaria an important priority in its 2019 to 2023 national strategic plan with mission to guarantee universal access to effective and affordable malaria preventive and curative interventions (6). These interventions are vector prevention using ITN and IRS; chemoprevention with IPTp for pregnant women, SMC for children 3 to 59 months; case management with ACT; behavioral change interventions, research and surveillance (6).

Insecticide-treated nets

ITNs are the main method for malaria vector control in sub-Saharan Africa with 68% of households having at least one ITN in 2019 (5). The proportion of under-five children in sub-Saharan Africa who slept under ITNs was 52% in 2019 (5). However, it has been shown that the distribution, ownership, and use of ITNs are still inadequate and thus limits their effectiveness (1). In addition, the increase in insecticides resistance over the years has presented challenges with ITN use as a tool in the malaria elimination effort (28).

Sleeping under an ITN is effective in preventing the transmission of malaria. Malaria prevalence in children under five years who slept under ITNs was shown to decrease in randomized trials conducted across sub-Saharan Africa. For example, studies in Burkina Faso and Kenya showed that children who used ITNs were less prone to malaria with a significant decrease in all-cause

morbidity and mortality (29–31). However, some studies did not find any protective effect. A study in Ghana on the impact of interventions on malaria among children under five was non-significant for ITN use (32). The non- protective of ITN use observed in this study could be explained by insecticide resistance and inconsistent use due to perceived heat increase and fear of suffocation attributed to sleeping under ITN (32).

The Abuja declaration on rollback malaria partnership called on a committed and coordinated action towards malaria elimination. As such the government of Cameroon became committed to fighting malaria (9,33). Since 2003, together with partners like the Global Fund, the government has sponsored the free distribution of ITNs. In 2011, distribution was scaled up through mass nationwide campaigns done every three years to achieve universal coverage (9,13). Coverage of ITNs in Cameroon is estimated at 70% with about 60% of children under five years having slept under an ITN in 2018 (10). Studies were done in communities within the regions of Cameroon after the roll out of ITNs and they demonstrated its effectiveness in reducing malaria prevalence (13,20,34,35). However, assessments of ITN use and its protective effects nationwide have been limited.

Artemisinin-based combination therapy

Given their effectiveness, fast action and gametocyte clearing ability, treatment with ACTs is considered as the first-line for uncomplicated malaria in sub-Saharan Africa especially for *P. falciparum* infections (1,2). Oguche and colleagues in Nigeria were able to show that using ACTs significantly reduced the level of malaria parasite in blood one day after treatment in children under five years (36). This reduction was greater with the artesunate-amodiaquine regimen

compared with artemether-lumefantrine. They also demonstrated the efficacy of ACT to be 96.3% (36).

Other studies have shown the treatment of simple malaria to be very effective when any of the ACTs are used especially for *P. falciparum* infection (36,37). For instance, a study used surveys from 2003 to 2015 in 33 countries across sub-Saharan Africa. The study found that generally, overtime, ACT coverage had increased across the region even though utilization rates have remained low in many countries (37). Also in Benin, a study in under-five children found the utilization of ACT to be sub-optimal as alternative more readily available and less expensive medicines were preferred compared to ACT (38).

Artemisinin-based combination therapy has been the first-line treatment of uncomplicated malaria in Cameroon since 2004 (8). From 2011, the government and partners have been subsidizing the cost of treatment of uncomplicated malaria providing free ACTs for children under five years (9,12). In 2018, the prevalence of children under five years with fever treated with ACT was 21% (6,10). Two formulations of ACT were recommended for use as first line. These are artesunate-amodiaquine and arthemeter-lumefantrine (mostly for the North and Far-North regions) as children in these regions usually recieve amodiaquine as seasonal malaria chemoprevention (6).

Combination of ITN and ACT

It has been said that the burden of malaria can be reduced with the scale-up of combinations of control strategies (1). Bhatt et al found that *Plasmodium falciparum* prevalence halved and clinical disease reduced by 40% from 2000 to 2015 with combination of ITNs, IRS and ACTs use across

Africa (39). Also they showed that these interventions averted 663 million malaria cases with ITN being the largest contributor. However, the ACTs were important in preventing disease severity and mortality (39).

The effect of combining ITN and ACT has been demonstrated in other studies. For example the combined benefit in both ITNs and ACTs dramatically reduced malaria morbidity and mortality by 10 fold within two years in children under five years in Zanzibar (40). Another study in Uganda found a parasite reduction of 19%, 78% and 34% with ITN, IRS and ACT respectively from 2009 to 2014 (41). However, studies in Cameroon on the combined effects of interventions are limited.

1.2.3. Conceptual framework

Based on the risk factors and malaria interventions described above an analytical conceptual framework can be developed. This is illustrated in figure 1.2 showing how the explanatory variables are related to malaria (outcome). Availability and usage of interventions will have a direct influence on the malaria prevalence. Also access and use of malaria interventions will be impacted by the socioeconomic and environmental factors. Likewise, Sociodemographic, environmental and climatic factors are related and have direct impacts on malaria morbidity. On the other hand, malaria causes a social burden related to household income, education (school and work absences), economic growth and development.

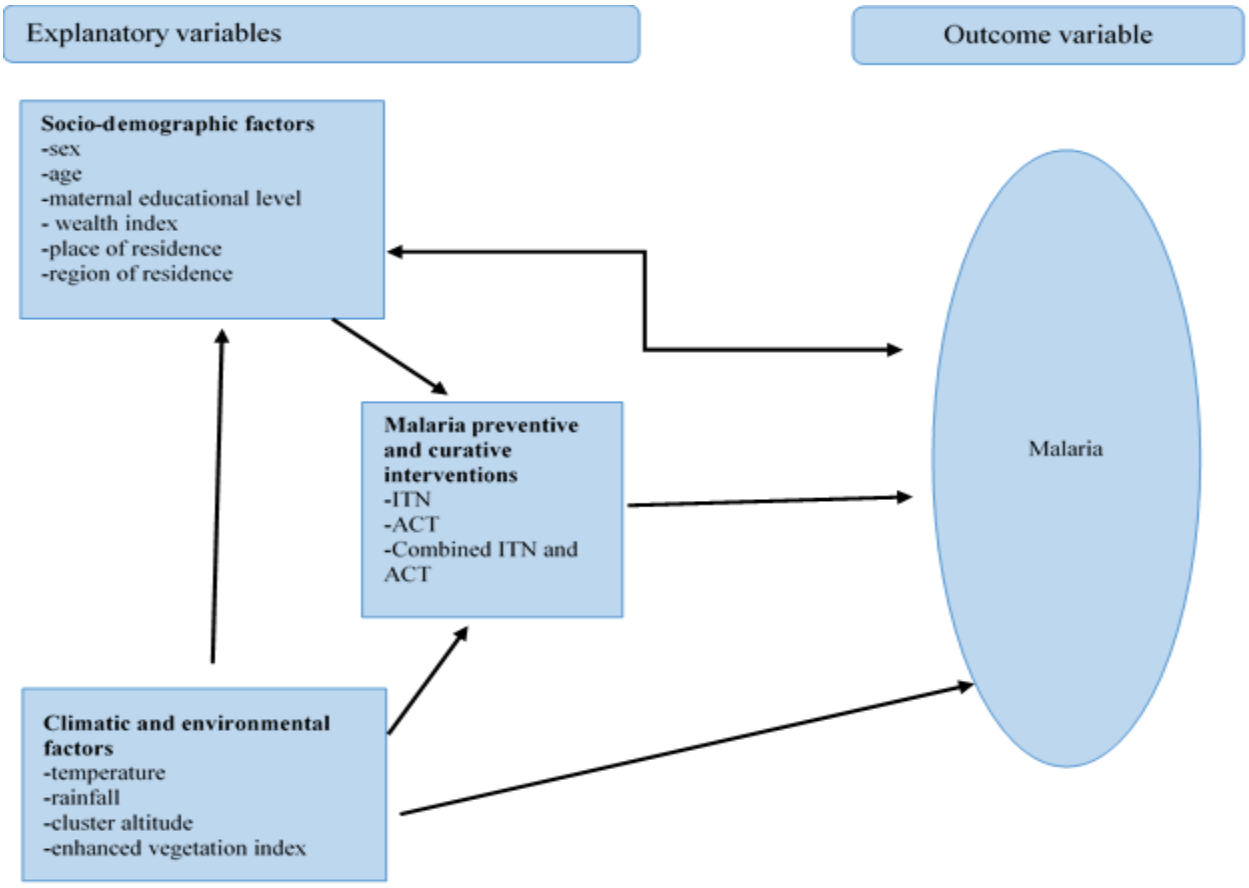


Figure 1.2 Conceptual framework of associated factors of malaria

1.2.4. Spatial distribution of malaria and malaria interventions

The application of geographic information systems (GIS) in health has been useful in studying the burden of emerging infectious diseases like malaria (42). The use of interventions targeting malaria have also been shown to vary in space as their effects are related to the geographical endemicity of malaria (43)

Spatial malaria distribution

Spatial analysis have been applied to study disease burden especially malaria using health surveys (44). Spatial case data can be aggregated according to geographic areas and mapped to estimate

the relative risk of cases while adjusting the effects of other variables (42). Malaria is characterized by spatial variability that poses a challenge for control programs.(1). This variability is related to the endemicity of the disease within geographic locations and among households (45,46). The spatial epidemiology of malaria considers the geographic distribution in terms of demographic, socio-economic, behavioral, genetic, environmental and other risk factors (25).

Several studies used spatial statistics to analyze health survey data describing malaria distribution in sub-Saharan Africa (22,25,47–49). These studies employed different spatial methods to describe varying degree of malaria risk. For example, a study in Equatorial Guinea used the Getis-Ord Gi and spatial scan statistics to identify malaria hot spots (22). Two studies in Burkina-Faso and Cameroon used the Moran Indexes to identify spatial autocorrelation in survey data (25,47). In addition, Bayesian methods were also applied in some studies to predict malaria risk in different settings (48–51). For instance, Adigun and colleagues in Nigeria used Markov Chain Monte Carlo (MCMC) simulation to predict malaria risk (51). Other studies used the integrated nested Laplace approximation (INLA) to model the probability of malaria (47,49). A Zambian study used penalized and basis spline (P- and B-splines) curves and kriging to predict malaria risk which showed high variability nationally(48).

Spatial analysis of malaria interventions

Spatial statistical models were used to estimate the effectiveness of interventions on malaria risk at high spatial resolution using national surveys in different countries in sub-Saharan Africa. (43,45,52). Most studies used Bayesian geostatistical modelling and had varying degree of intervention effects with some protective at national levels while others at sub-national levels. For

instance, two studies used spatiotemporal Bayesian geo-statistical models to evaluate ITN, ACT and IRS effects on malaria risk (39,41). One showed that Interventions were responsible for the decline of parasitaemia risk in Uganda from 2009 to 2014 (41).The other found that widespread reductions in malaria prevalence occurred across Africa from 2000 to 2015 due to malaria control interventions (39). Contrarily, a study in Nigeria found no effects for the role of interventions (51).

Another study conducted in Cameroon also applied Bayesian geo-statistical modelling to estimate the geographic distribution of malaria risk and interventions effects. The study used both 2011 Cameroon Demographic and Health survey (CDHS) and Malaria indicator survey (MIS) data (50). The CDHS data showed ITN use had a statistically significant effect on parasite risk.

1.3 Problem Statement

Malaria is a highly endemic disease in Cameroon and children under five years are most vulnerable (9). It is caused by the *plasmodium* parasite. In Cameroon, malaria is responsible for significant morbidity and mortality in the general population. The prevalence of malaria among children under five years in 2018 was 24%. In 2019 there were 390,180 hospitalizations and 39,6% of the registered malaria deaths were in children under five years (10,11). The persistent rise in infections is due to the uneven scaling-up of malaria interventions

The geographical distribution of malaria varies by zones of endemicity that challenges the implementation of control measures (7–9). There are four main zones of endemicity; hyper, meso, hypo and holo-endemic zones across regions. The implementation of interventions tends to be determined by the existence of health facilities. Whereas, implementation should be based on the

epidemiologic distribution of malaria (9). Government efforts to cut down the spread of malaria include the free distribution of ITNs and ACTs (12,13). Despite the scale-up of these strategies, the burden of malaria remains high (53).Thus, the burden of malaria has not been adequately addressed in the formulation of national strategies from the epidemiological profile.

Previous studies on malaria prevalence and the use of interventions were limited to local communities in Cameroon. Earlier researched examined single interventions with varied study populations (12,13,20,34). In contrast, there has been no study known to the author that addresses the combined effects of interventions. In addition, few assessments of the national malaria risk and the use of interventions among children under five years have been made (25). As far as can be ascertained, few studies used spatial methods and thus, there is a paucity of data on the application of these techniques (25). The current study will apply both non spatial (multilevel mixed effects) and spatial (spatial autocorrelation and Bayesian) statistical methods, to give reliable estimates of the distribution of malaria and malaria intervention using the most recent CDHS data. These methods accounts for cluster random effects and correlation of malaria in space due to common exposures affecting neighbouring areas (spatial random effects).

1.4 Justification

The utilization of robust spatial statistics to examine malaria prevalence and use of interventions are understudied in Cameroon (25). An understanding of the spatial distribution of malaria prevalence and use of interventions is crucial for effective distribution of interventions. Maps are necessary tools to guide the malaria control program as this mapping method identify disease hotspots for possible targeted interventions distribution (25,45).

The impact of interventions has only been assessed in specific localities in the South west and North west regions for example (12,13,20,34,35). However, there exists a knowledge gap in the assessment of interventions nationally. An assessment of the combine effects of interventions is also lacking. Therefore, knowledge on the association of malaria and use of interventions on a national scale will assist in evaluating the progress of interventions. `

1.5 Research Question

What is the spatial malaria distribution and its association with using ITN and ACT, among children under five years in Cameroon in 2018?

1.6 Aim

To determine the spatial distribution of malaria and its association with ITN and ACT use among children under five years in Cameroon in 2018.

1.7 Objectives

1) To describe the spatial distribution of malaria prevalence in children under five years in Cameroon during 2018.
2) To examine the association between ITN usage and malaria prevalence among children under five years in Cameroon during 2018.
3) To examine the association between ACT usage and malaria prevalence in children under five years in Cameroon during 2018
4) To estimate the association between the combined ITN and ACT usage and malaria prevalence among children under five years in Cameroon during 2018

CHAPTER TWO

METHODOLOGY

2. Introduction

The chapter describes the study setting and design of the primary study (Cameroon Demographic and Health Survey) carried out in 2018. Next, details regarding the secondary study such as study population, power computation, study variables, data management and analysis procedures are provided. It ends with the ethical considerations of the study.

2.1 Study Setting

The primary data was obtained from Cameroon situated in Central Africa, within latitude 2º and 13° North and longitude 9º and 16° E (7,8) [see Appendix I]. Cameroon's surface area is 475,440 km² and its population is approximately 25,492,353 inhabitants (6). The country is bordered by Equatorial Guinea, Gabon, Congo at the south, Central African Republic at the East, Nigeria at the west and Chad at the North (figure 2.1) (6,7). There are ten administrative regions as shown in figure one above, which are further divided into 58 divisions or departments (table 2.1). The capital city is Yaoundé and Douala is the economic capital. The Demographic and Health Survey (DHS) program considered these two large cities as regions. As such there are 12 DHS regions.



Figure 2.1 Map of Cameroon showing the ten administrative regions and their regional capital

Source: https://www.mapsofworld.com/cameroon/cameroon-political-map.html

Table 2.1 Administrative regions and divisions of Cameroon

Regions	Divisions
Far North (6)	Logone-et-Chari, Diamare, Mayo-Kani, Mayo-Danay, Mayo-Sava, Mayo-Tsanaga
North (4)	Mayo-Louti, Benoue, Mayo-Rey, Faro,
Adamawa (5)	Mayo-Banyo, Djerem, Mbere,,Faro-et-Deo, Vina
Centre (10)	Mfoundi, Haute-Sanaga, Mbam-et-Kim, Lekie, Mbam-et-Inoubou, Mefou-et-Afamba, Nyong-et-Mfoumou, Mefou-et-Akono, Nyong-et-Kelle, Nyong-et-So'o
East (4)	Haut-Nyong, Boumba-et-Ngoko, Kadey, Lom-et-Djerem
South (4)	Dja-et-Lobo, Mvila, Ocean, Vallee-du-Ntem
Littoral (4)	Moungo, Sanaga-Maritime, Nkam, Wouri
Northwest (7)	Donga-Mantung, Boyo, Bui, Ngo-ketunjia Menchum, Mezam, Momo,
Southwest (6)	Fako, Meme, Koupe-Manengouba, Lebialem, Ndian, Manyu,
West (8)	Bamboutos, Noun, Haut-Nkam, Menoua, Hauts-Plateaux, Nde Koung-Khi, Mifi,

Cameroon is commonly referred to as "Africa in miniature" because of its rich culture and geographic diversity comprising deserts, coastal, mountains, rainforests and savannas lands all present in one (8). It has tropical and equatorial climates with subtypes varying across regions (8). For example, the Far North is characterized by a hot and dry Sahelian climate, long (≥7 months) dry season, short rainy season and rainfall averaging 400 - 900 mm.

The North and Adamawa regions have the Sudanese tropical (dry and humid savannah climate respectively), short dry season and longer rainy season with rainfall averaging 900 -1,500 mm. Meanwhile, the Southern, South West, Littoral, Central and Eastern regions which extend from the Atlantic coast to the Equatorial evergreen forest are characterized by the equatorial climate, two dry and rainy seasons with rainfall ranging from 1,500 -2,000 mm. Debuncha in the South-west region has an average rainfall of 10,300mm and has been described as the wettest place on

earth (6–8). The last decade has been characterized by an increase in temperature of about 0.4 °C and a 10-20% decrease in rainfall (7).

Increase demographic growth, deforestation and urbanization have further compounded the malaria transmission risk (8). Recently the North-West and South-West regions have suffered a sociopolitical crisis with displaced populations, and which have influenced the malaria epidemiology and control efforts in these regions (7).

2.2 Primary Study

The CDHS is carried out every 5 years involving the entire nation. Data is obtained to monitor indicators of health, population and nutrition. The survey was conducted by the Health Ministry together with the National Institute of Statistics, the DHS programme-Inner City Fund (ICF) International. Funding was provided by the state and partners like the U.S. Agency for International Development (USAID), United States President's Malaria Initiative (PMI), the United Nations Population Fund (UNFPA), and the World Bank (10).

2.2.1 Primary study design

The CDHS was a cross-sectional study carried out from June 16, 2018 to January 19, 2019

2.2.2 Primary study aim

To collect data in order to provide reliable estimates of indicators on maternal and child health, nutrition, marriage, fertility and domestic violence. These are used for policymaking and evaluation of existing programs (10).

2.2.3 Primary study sampling method

Stratified probability sampling was done in two stages. First, 470 clusters were systematically drawn from enumeration areas enlisted during the 2014 cartographic works of the fourth household census survey. Second, 28 households were systematically sampled from each cluster resulting in 6,860 households in 245 urban clusters and 6,300 households in 225 rural clusters. The sample was distributed so as to ensure adequate representation of urban and rural areas within the 12 DHS administrative regions: The Far-North, North, Adamawa, Center (without Yaoundé), Yaoundé, Littoral (without Douala), Douala, Northwest, Southwest, West, South and East.

In each area of study (except the cities of Yaoundé and Douala which are considered to have no rural part), two strata were created: the urban strata and the rural strata. Of the 13,160 households initially planned to be surveyed, 11,986 households were actually selected and among these, 11,776 were identified at the time of the survey. Among them, 11,710 were surveyed successfully, giving a response rate of 99%. From the 11,710 households surveyed a 50% sub-sample of 5,993 was selected to interview women aged 15 to 49 years who usually lived there or had spent the night there before the survey. Of these 5,872 were found to be occupied and, 5,839 households were interviewed successfully. Within these households 4,733 children aged six to 59 months were tested for malaria (10).

2.2.4 Primary data collection

Data was collected using the household questionnaire and woman questionnaire after obtaining informed consent from the interviewee. The household questionnaire contained information on

household location (region, urban or rural), household assets, use of ITN by household members. The woman questionnaire was for women who were between 15 to 49 years old in the household and their children. For example, information on the woman's education, age and sex of all her children, whether a child had fever two weeks before the survey and treated with ACT were found in the woman questionnaire (10).

A malaria rapid diagnostic test (RDT) was done for children aged six to 59 months. The health worker sought and obtained informed consent from the parent. Then blood was obtained from the finger of these children and placed on the RDT strip (SD BIOLINE Malaria Antigen P.f / Pan). The biomarker sheet was used to record the results of the RDT after 15 minutes and also the parents were informed of the outcome. If the child was positive with uncomplicated malaria, Artesunate-Amodiaquine was offered to the parents to give the child. For children with severe malaria, and those with a positive RDT who had recently been treated with antimalarials prescribed by community health workers, no treatment was offered but the child was referred immediately to the nearest health facility (10).

2.3 Secondary study

2.3.1 Secondary study design

A cross-sectional design was used for secondary analysis of the 2018 CDHS data.

2.3.2 Secondary data source

Survey data: The 2018 CDHS data contained the malaria RDT results for children under five years and their socio-demographic characteristics. These variables were captured from the household members or persons recode (PR) file which had biomarker data and information from the household questionnaire, and from the children recode (KR) file which had children data from the

woman questionnaire. Both files were merged as recommended by the DHS programme that different files could be combined to obtain the variables needed for analysis (54).

Global Positioning System (GPS) data: Geo-referenced cluster coordinates were obtained using recreational GPS receivers during the survey sample listing process (55). The GPS longitude and latitude positions for each cluster were randomly displaced in order to ensure confidentiality. Rural urban clusters were displaced five and two kilometers respectively with 1% of rural clusters displaced up to ten kilometers (https://dhsprogram.com). The data was in the form of a point shape file meanwhile the second administrative level polygon shape file was downloaded from diva GIS (https://www.diva-gis.org/gdata).

Geospatial covariate data: Environmental and climatic predictors were obtained from the geospatial covariate dataset at the measure DHS website. They were extracted from raster and vector data available in varied public sources and standardized by the DHS program for easy linkage to DHS datasets (56). In particular variables obtained were; Enhanced Vegetation Index (EVI) year, rainfall year, and mean temperature year. The covariates were listed for five yearly intervals (e.g. 2000, 2005, 2010, 2015). The variables selected were for the most recent year preceding the 2018 survey (2015).

2.3.3 Secondary data power computation

There was no sampling as all the data provided were analysed. A power computation was performed using clustersampsi synthax which accounts for clustering (57). In a study carried out using the 2011 CDHS data, malaria prevalence was 33% (50). Also, a prevalence of 24% was

obtained from positive malaria RDT results from the 2018 CDHS (10). Using the ado file synthax, power was calculated to be 90% at 0.05 level of significance (see appendix B.2).

2.3.4 Inclusion criteria

All children aged six to 59 months who were tested for malaria were included in the study.

2.3.5 Exclusion criteria

Children less than 6months because they were not tested for malaria. Also children aged six to 59 months in sampled households for whom their caretakers did not consent to parasitemia testing of their child. Finally, children aged six to 59 months who don't usually stay in the sampled household.

2.3.6 Secondary study population

The study involved 4,733 children who had a malaria test result and were in 50% of sampled households within sampled clusters in Cameroon in 2018. The selection of study participants is illustrated in figure 2.2 below.

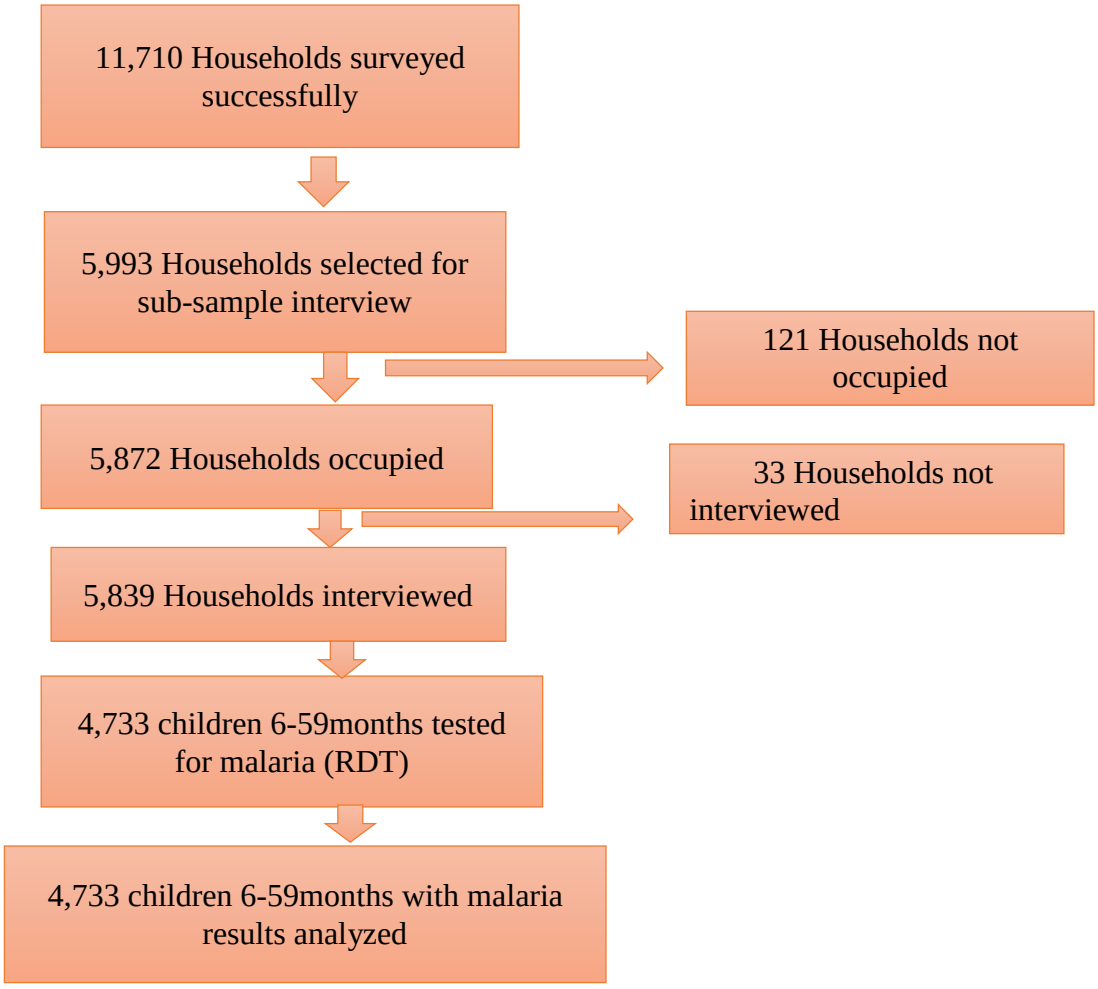


Figure 2.2 Households and participants selected for study.

2.4 Data management

There were four data files in Stata format (. dta): the household persons' file (CMPR71FL), the children's file (CMKR71FL), the geospatial covariates (CMGC72FL) and GPS file (CMGE71FL). The household persons and children's files were merged using the variables; cluster number (hv001), household number (hv002) and child's line number (hvidx) in a one-to-one relationship. The Geospatial covariates containing the environmental variables were also merged with the survey dataset in a many to one relationship using DHS cluster for matching (figure 2.3).

The cluster GPS points (centroid) were geographically linked to the second administrative level (Admin_2) polygon shape file map in ArcGIS based on spatial locations. This joined data was imported to Stata and merged with survey data in a many-to-one relationship based on primary sampling unit id.

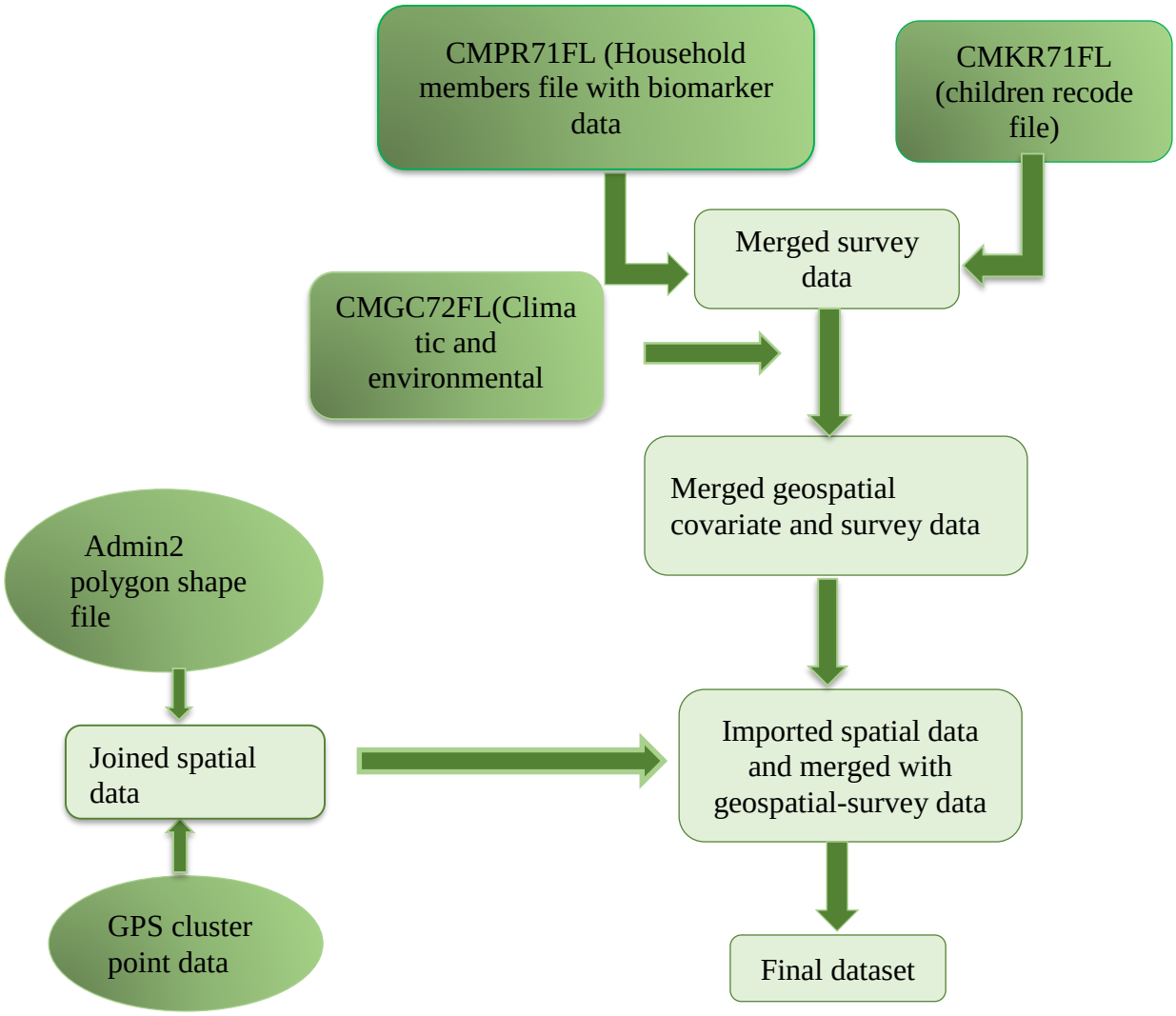


Figure 2.3 Data management approach

The geospatial covariate file was cleaned by removing all observations with missing data (-9999) and keeping just the needed variables and categorizing them. The household and children's files were cleaned by dropping all children that were not tested, extracting the required variables, recoding, renaming and generating variables. For instance, the ages of children and environmental covariates were recoded into categories because they did not meet the conditions of normality.

Data was stored safely in a password-secured computer and backed in a CD drive and Google Drive. The data was survey set before analysis in order to take into account the characteristics of survey design which include sample weighting and stratification (58). The sample weight was calculated by dividing the household sample weight (hv005) by 1,000,000.

2.5 Variables and their measurement

The variables as well as their description based on the DHS recode are described in table 2.2 below.

Table 2.2 Variables and their scale of measurement

Variable name	Description	Type of variable	Categories based on DHS recode manual
Child's age in months	Calculated from subtracting the date of birth from the date of survey	Categorical	<six months, six to 11 months, 12 to 23 months, 24 to 35 months, 36 to 47 months and 48 to 59 months
Child's gender	Sex of the child	Binary	Male, Female
Region of residence	First administrative level in the country where the household is located.	Categorical	Far-north, North, Adamawa, East, South, Center without Yaoundé, Littoral without Douala, Yaoundé, Douala, West, North West and South West
Place of residence	The location of the cluster where the household resides	Binary	Urban, Rural
Mother's education	Highest educational level the child's mother attained	Categorical	No education, Primary, Secondary and Higher
Household wealth index	Computed from data on various household assets, (television,	Categorical	Poorest, Poorer, Middle income, richer, richest

	bicycle, household construction material)		
Malaria (Outcome)	Result of malaria RDT	Binary	Positive, Negative
Fever in the last two weeks	Children with fever two weeks before the survey	Binary	No, Yes
Net use	Children who slept under any type of mosquito net the night before survey	Categorical	No children, all children, some children
Net type	Specific type of mosquito net| child slept under	Binary	None or untreated net and treated net
ACT use	Children with fever two weeks before the survey, treated with ACT	Binary	No, Yes
Combined variable (generated variable)	Combination of Net use, Net type and ACT use	Categorical	None; no & untreated & ACT; All children & untreated & no ACT; All children & untreated & ACT; All children & ITN & no ACT; All children & ITN & ACT; Some children & untreated & no ACT; Some children & untreated & ACT; Some children & ITN & no ACT; Some children & ITN & ACT
Cluster altitude (in meters)	Placement above sea level in which the cluster is located	Binary	<1,000 meters, >1,000 meters
Rainfall 2015 (in millimeters per year)	Average rainfall within 10 km (rural) or 2 km (urban) buffer surrounding cluster location in 2015	Categorical	Low rainfall (400mm-999.99mm), Moderate rainfall (1,000mm-1,999.99mm), Abundant rainfall (>2,000mm)
Mean temperature 2015 (in degrees Celsius)	Average temperature within 10 km (rural) or 2 km (urban) buffer surrounding cluster location in 2015	Binary	Below room temperature (<25◦C), Above room temperature (>25◦C)
Enhanced vegetation index 2015 (value between zero and 10000)	Average vegetation within10 km (rural) or 2 km (urban) buffer surrounding the cluster in 2015	Categorical	Least vegetation (zero to 1,999.99), Much Vegetation (2,000 to 2,999.99), Abundant vegetation (3,000 to 3,999.99), Most vegeta-tion (4,000 and beyond)

2.6 Data analysis

Data analysis was done using Stata 16, ArcGIS10.6 and R studio 4.0.5 soft wares. Stata was used to perform descriptive analysis and fit multilevel logistic regression models. Spatial statistical

applications in ArcGIS were used to produce maps of the observed malaria prevalence, hotspots analysis and to identify spatial autocorrelation. Conditional autoregressive models were fitted in R to adjust for spatial random effects and produce a malaria predicted risk map.

2.6.1 Descriptive analysis

The description of categorical variables was done using contingency and frequency distribution tables with survey and sample weights adjustment. Survey adjusted bivariate analysis was done using Pearson's chi-square test. Results were stratified by malaria (positive or negative).

2.6.2 Mapping of observed malaria prevalence, ITN and ACT usage

The survey data were collapsed to the country's second administrative level shape file which are divisions. This was done using the unique identifier of that administrative level (id_2). The collapsed data was then exported to ArcGIS and added to the attribute table of the shape-file. To map the malaria prevalence, the properties function of the shape-file was open. Under symbology, the quantities feature was selected as graduated colors. The value field was entered as the variable of interest to be mapped (positive malaria or Treated nets or ACTusage). Normalization specified as percent of totals and the number of classes selected to be four classes.

2.6.3 Spatial autocorrelation

The presence of a clustering pattern was examined using the global spatial autocorrelation (Morans I) test located under the spatial statistics toolbox in ArcGIS. In spatial autocorrelation, the null hypothesis of spatial randomness is tested (42). The Moran I test required an input feature class

which was the shapefile used; an input field which was variable to assess autocorrelation (positive malaria results); specification of spatial relationship as inverse-distance; distance method as Euclidean-distance [1].

The result produced comprised of the Moran's I Index, z-score, p-value, variance. The z-score and p-value were important to determine if the null hypotheses should be rejected (59). A positive and significant Moran's I Index value meant there was a clustering pattern of disease or like values. A negative and significant Moran's I meant dispersion or spatial heterogeneity whereas a value close to zero indicated spatial randomness (42,59).

2.6.4 Hotspot analysis

For hotspot analysis, the local spatial autocorrelation (Getis-Ord Gi statistic) tool in ArcGIS was used [2]. The test also involved specifying an input feature class which was the second level adminstrative shape file. The input field was malaria positive results. The spatial relationship distance was a fixed distance band which is the default and the distance method being the Euclidean distance. The Output feature class creates the confidence level and a choropleth map with red coded (hot) and blue coded (cold) areas.

[1] ArcMap 10.6 (2018) Spatial Autocorrelation (Global Moran's I) available at https://desktop.arcgis.com/en/arcmap/10.6/tools/spatial-statistics-toolbox/spatial-autocorrelation.htm. Accessed July 25, 2021.

[2]ArcMap 10.6 (2018) Hot Spot Analysis (Getis-Ord Gi*) available at https://desktop.arcgis.com/en/arcmap/10.6/tools/spatial-statistics-toolbox/hot-spot-analysis.htm. Accessed July 25, 2021.

2.6.5 Multilevel mixed effects modelling

Multilevel mixed-effect logistic regression models in Stata 16 (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC) were used to investigate the relationship between malaria and each of the primary exposure variables (ITN use, ACT use and Combined ITN and ACT usage). These models were fitted adjusting for socio-demographic and environmental factors. The multilevel model was preferred for clustered data as it provides an efficient estimate of regression coefficients modelling the way children within households are nested within urban and rural clusters of the second administrative divisions in Cameroon.

For the three models fitted, model A included the use of a net, type of net used and fever two weeks before as primary predictors while socio-demographic, climatic/environmental variables were control variables. Model B was only for children without missing information on ACT use and included the use of ACT and fever in the previous two weeks as main predictors while socio-demographic, and environmental variables were controls. Finally, model C included the newly generated combined variable and fever two weeks before as primary predictors. Meanwhile the socio-demographic and environmental variables were controls.

To determine which variables to include in the model, univariate analysis using survey adjusted logistic regression was done for each independent variable and the outcome of malaria. In addition to the primary predictors, the control variables added in the model were those with a p-values less than or equal to 10%. The liberal p-value of 0.1 permitted many variables to be included in the model

After identifying the significant variables, a base random intercept model was fitted with just the outcome variable to examine variation attributable to the location of study (divisions). The primary predictors were added followed by significant control variables being added progressively one at a time and comparing with the preceding model using the likelihood ratio (LR) test. A p-value ≤ 0.05 LR test would indicate the control variables to include in the model. The post-estimation test using the estat icc was used to estimate intra-class correlation (ICC) among children within the households whereby an ICC threshold of <0.05 signified lesser clustering in the data.

Finally, the Akaike and Bayesian Information Criterion (AIC and BIC) were performed to examined the fit of the model by computing 'estat ic'. A substantial reduction in the AIC and BIC indicated a good model. The AIC, BIC, ICC were computed adjusting the sampling weight but not the survey design because the Stata syntax used (estat ic, estat icc) does not support the use of survey design commands. A random intercept was adjusted for at the second administrative level (id_2) referring to the subnational divisional level. For all models, the unstructured covariance between the random effects was specified. The results were presented as adjusted odds ratios (AOR) with 95% confidence intervals (CIs).

2.6.6 Conditional autoregressive modelling

Multilevel logistic modelling adjusts for the correlation between individual data in a geographic area by modelling the data in a hierarchical multilevel structure. However, multilevel models consider only vertical dependence and not horizontal or spatial dependence (interaction of neighbouring areas due to their geographic boundaries) (60). This spatial dependence if not accounted for results in unreliable estimates of regression coefficients in multilevel modelling.

Conditional autoregressive (CAR) modelling is an approach of incorporating spatial dependence effect into the multilevel models (60). Thus CAR models were fitted to adjust for spatial random effects. In addition, these models assess spatial correlation in data and adjust population-associated variability while considering the predictive effect of the neighbors as a first-order dependency (61). The CAR models were fitted using the same variables from the multilevel logistic regression except for the region variable as this would be accounted for in the spatial modelling The second administrative level shape file was used and the models fitted using the INLA package in R. This is an alternative of the MCMC method and provides the posterior marginal distribution for latent Gaussian models as a Bayesian method (62).

In fitting the model, first, an INLA integrated map was generated from the shape file followed by the generation of the adjacency matrix in order to identify the neighbors surrounding each polygon. Next, the structured and unstructured priors were defined together with the model formula. The two priors were identifiers of the location (id_2) and the Besag, York, and Mollie (BYM) convolution which specifies the model type (62). The model was fitted and after extracting the marginal of the random effects, the marginal posterior probabilities estimates were added to the data frame and merged with the shape file. The probability estimates were then plotted on a map. The model was fitted with data from a random sample of 88% of the locations (51 divisions instead of 58). This was because data for 7 divisions were not available as these areas were not surveyed in 2018 due to socio-political unrest.

2.7 Ethical consideration

Permission to use the dataset was obtained from Measure DHS website (https://dhsprogram.com) (Appendix A.3). The study was approved by the Human Research Ethics Committee (Medical) of the University of Witwatersrand (certificate no M21027) (Appendix A.2).

CHAPTER THREE

RESULTS

3. Introduction

This chapter presents the results of data analysis. It begins with description of the socio-demographic, malaria-related and climatic/environmental characteristics of children under five years in Cameroon in 2018. It also describes the characteristics of children stratified by malaria RDT positive or RDT negative. It also describes the spatial malaria prevalence using a thematic map. This is followed by results of spatial autocorrelation (global Moran I) and hotspot analysis. In addition, a map showing the use of ITN is presented. Next are results of univariable and multivariable analyses of primary predictors (ITN, ACT and COMBINED usage) adjusted for control variables, random and spatial random effects. Finally, it shows a map of the predicted malaria risk from the first multivariable model.

3.1 Socio demographic, malaria related and environmental/climatic characteristics of children under five years in Cameroon in 2018.

The characteristics of study participants are summarised in table 3.1. There were slightly more males (n=2,392; 50.5%) than females. Children had a median age of 32 months (IQR 19 to 46 months). There were more children whose mothers attained secondary education (n=1,481; 31.3%). Majority of children were from poorer households (n=1,123; 23.7%). The highest number of children were from the Far-North region (n=605; 12.8%) and lowest number from the South-west region (n=100; 2.1%). Over half of children lived in rural areas (n=2,603; 55.0%) and about two-third slept under a mosquito bed net the night before the survey (n=3105; 65.6%). Among these children, over half slept under an ITN (n=2,603; 55.0%). About one-sixth of children were

reported to have fever two weeks before survey (n=717, 15.1%) and amongst these, very few were given ACT as antimalarial (n=42; 5.0%). Majority of households were located at altitude less than 1,000 meters below sea level (n=3,824; 80.8%). More than one-third of households were located in areas with most vegetation (n=1,913; 40.4%) and two-thirds located in areas with moderate rainfall (n=3,152; 66.6%).

Table 3.1 Description of socio demographic, environmental and malaria related characteristics of children under five years in Cameroon, 2018

VARIABLES	n (%)
SOCIO-DEMOGRAPHIC VARIABLES	
Child's sex	
Male	2,392 (50.5)
female	2,341 (49.5)
Child's age in months (median(IQR)*)	32 (19, 46)
Child's age in category (months)	
6-11	510 (10.8)
12-23	1,029 (21.7)
24-35	1,026 (21.7)
36-47	1,084 (22.9)
48-59	1,084 (22.9)
Mother's educational level	
no education	919 (19.4)
Primary	1,388 (29.3)
Secondary	1,481 (31.3)
Higher	198 (4.2)
Missing	747 (15.8)
Household wealth index	
Poorest	872 (18.4)
Poorer	1,123 (23.7)
Middle	1,081 (22.8)
Richer	974 (20.6)
Richest	683 (14.4)
Region	
Adamawa	354 (7.5)
Centre (excluding Yaoundé)	552 (11.7)
Douala	263 (5.6)
East	501 (10.6)
Far-north	605 (12.8)
Littoral (excluding Douala)	307 (6.5)
North	524 (11.1)
North-west	234 (4.9)
West	494 (10.4)
South	436 (9.2)
South-west	100 (2.1)
Yaoundé	363 (7.7)
Place of residence	
Urban	2,130 (45.0)
Rural	2,603 (55.0)
MALARIA RELATED VARIABLES	
Children < 5 that slept under mosquito net last night	
No children	1,558 (32.9)
All children	2,253 (47.6)
Some children	852 (18.0)

Missing	70 (1.5)
Type of net child slept under	
None&untreated	2,130 (45.0)
Only treated (ITN)	2,603 (55.0)
Child had fever last 2 weeks before survey	
No	3,269 (69.1)
Yes	717 (15.1)
Missing	747 (15.8)
Child received ACT(n=845)**	
No	803 (95.0)
Yes	42 (5.0)
Combined variable **(n=841)	
None	291 (34.6)
no & untreated & ACT	15 (1.8)
All children & untreated & no ACT	8 (1.0)
All children & untreated & ACT	1 (0.1)
All children & ITN & no ACT	359 (42.7)
All children & ITN & ACT	20 (2.4)
Some children & untreated & no ACT	59 (7.0)
Some children & untreated & ACT	4 (0.5)
Some children & ITN & no ACT	82 (9.8)
Some children & ITN & ACT	2 (0.2)
ENVIRONMENTAL/CLIMATIC VARIABLES	
Cluster altitude (in meters)	
<1,000m above sea level	3,824 (80.8)
>1,000m above sea level	909 (19.2)
Enhanced vegetation index 2015	
Least vegetation	200 (4.2)
Much vegetation	1,237 (26.1)
Abundant vegetation	1,371 (29.0)
Most vegetation	1,913 (40.4)
Missing	12 (0.3)
Mean temperature 2015 (in degrees Celsius)	
<room temp	2,628 (55.5)
>room temp	2,066 (43.7)
Missing	39 (0.8)
Rainfall 2015 (in millimetres)	
Low rainfall	921 (19.5)
Moderate rainfall	3,152 (66.6)
Abundant rainfall	660 (13.9)

Key: IQR = Interquartile range.

3.2 Description of the characteristics of children under five years stratified by malaria positive or negative

The characteristics of children under five were also described by stratifying into malaria positive and negative. Weighting was applied to adjust for the differences in probability of selecting households across strata so that survey estimates are representative of the population. The weighted results are shown on table 3.2.

There were 4,733 children under five years for the unweighted results and after survey setting, the weighted results involved 4,866 children. Of these, 1,161 (24%) had malaria. There was no significant difference in malaria prevalence between males (n=604, 52.0%) and females (n=557, 48.0%; p 0.4415). The highest prevalence of malaria was found among children aged 36 to 59 (n =311, 26.8%) while children aged six to 11 months were least affected (n=68, 5.9%; p<0.0001). The highest proportion of malaria was reported among children whose mothers had primary school education (n=355, 30.5%) while the lowest proportion of malaria was among children whose mothers had higher education (any certificate above secondary school) (n=15, 1.3%; p<0.0001).
A higher proportion of children with malaria was among those from poorer households (n=354, (30.5%) and the lowest was reported among children from rich households (n=64, 5.5%; p<0.0001). The Centre region had the highest proportion of children with malaria (n=262, 22.5%) unlike the Southwest region with the least (n=8, 0.7%; p <0.0001). Most children with malaria lived in rural areas (n=844, 72.7%) compared to urban areas (n=317, 27.3%; p<0.0001).

A total number of 2,824 (58.1%) children slept under an ITN the night before survey. There was no difference in malaria prevalence for those who used ITN (n=640, 55.1%) and those who did not (n=521, 44.9%; p=0.1119). Overall, 749 children had fever two weeks preceding the survey. Of these 283 (24.4%) had malaria. The proportion of children with fever two weeks before survey who received ACT was low (n=48, 5.5%). Malaria prevalence was not significantly different among children with fever treated with ACT (n=15, 4.9%) compared to those not treated with ACT (n=284, 95.1%; p=0.6576)

Malaria prevalence was higher among children who lived in houses located less than 1,000 meters above sea level (n=1,073, 92.4%) compared to those living in houses located greater than 1,000 meters above sea level (n=88, 7.6%; p<0.0001). Malaria was most prevalent among children living in areas with high vegetation coverage (n=515, 44.4%) and less prevalent among children living in areas with low vegetation coverage (n=55.11, 4.75%; p=0.001). The highest proportion of malaria was observed among children living in areas that had moderate rainfall (n=762.2, 65.64%) compared to children living in areas with low rainfall (n=303, 26.1; p=0.001).

Table 3.2 Description of children under five years in Cameroon in 2018 stratified by malaria positive and negative (N=4733)

Variables	Malaria Positive n (%)	Malaria Negative n (%)	(p-value)
Number	1161 (23.9%)	3705 (76.1%)	
DEMOGRAPHIC/SOCIOECONOMIC VARIABLES			
Child's Sex			
Male	604 (52.0)	1871 (50.5)	(0.4415)
Female	557 (48.0)	1834 (49.5)	
Child's age in months			
6 – 11	68 (5.9)	458 (12.4)	(<0.0001)
12 – 23	239 (20.6)	825 (22.3)	
24 – 35	232 (20.0)	809 (21.8)	
36 – 47	311 (26.8)	809 (21.8)	
48 – 59	311 (26.7)	804 (21.7)	
Mother's educational level			
No education	324 (27.9)	802 (21.6)	(<0.0001)
Primary	355 (30.5)	1050 (28.3)	
Secondary	277 (23.8)	1145 (30.9)	
Higher	15 (1.3)	200 (5.4)	
Missing	191 (16.4)	508 (13.7)	
Wealth Index			
Poorest	345 (29.7)	764 (20.6)	(<0.0001)
Poorer	354 (30.5)	750 (20.3)	
Middle	244 (21.0)	708 (19.1)	
Richer	155 (13.3)	798 (21.5)	
Richest	64 (5.5)	684 (18.5)	
Region			
Adamawa	69 (6.0)	152 (4.1)	(<0.0001)
Center (excluding Yaounde)	262 (22.5)	298 (8.0)	
Douala	34 (2.9)	350 (9.4)	
East	122 (10.5)	226 (6.1)	
Far-north	202 (17.4)	722 (19.5)	
Littoral (excluding Douala)	36 (3.1)	140 (3.8)	
North	181 (15.5)	513 (13.9)	
Northwest	28 (2.4)	263 (7.1)	
West	84 (7.3)	456 (12.3)	
South	74 (6.4)	154 (4.2)	
Southwest	8 (0.7)	75 (2.0)	
Yaounde	61 (5.3)	355 (9.6)	
Place of residence			
Urban	317 (27.3)	1868 (50.4)	(<0.0001)

Rural	844 (72.7)	1837 (49.6)	
MALARIA RELATED VARIABLES			
Children < 5 that slept under mosquito net last night			
No children	336 (29.0)	1091 (29.5)	(0.009)
All children	541 (46.6)	1926 (51.9)	
Some children	265 (22.8)	632 (17.1)	
Missing	19 (1.6)	56 (1.5)	
Type of net child slept under			
None&untreated	521 (44.9)	1520 (41.0)	(0.1119)
Only treated (itn)	640 (55.1)	2184 (59.0)	
Child had fever last 2 weeks before survey			
No	687 (59.2)	2731 (73.7)	(<0.0001)
Yes	283 (24.4)	466 (12.6)	
Missing	191 (16.4)	508 (13.7)	
Child received ACT(n=845)**			
No	284 (95.1)	542 (94.3)	(0.6576)
Yes	15 (4.9)	33 (5.7)	
Combined variable **(n=841)			
none	89 (30.0)	177 (31.0)	(0.0902)
no & untreated & ACT	3.6 (1.2)	12 (2.1)	
All children & untreated & no ACT	1.7 (0.6)	8.5 (1.5)	
All children & untreated & ACT	0.75 (0.3)	0 (0.0)	
All children & ITN & no ACT	124 (41.5)	271 (47.4)	
All children & ITN & ACT	7.7 (2.6)	18 (3.1)	
Some children & untreated & no ACT	31 (10.4)	26 (4.6)	
Some children & untreated & ACT	2.5 (0.8)	1.5 (0.3)	
Some children & ITN & no ACT	38 (12.7)	56 (9.9)	
Some children & ITN & ACT	0 (0.0)	1.4 (0.2)	
ENVIRONMENTAL/CLIMATIC VARIABLES			
Cluster altitude (in meters)			
<1,000m above sea level	1073 (92.4)	2947 (79.6)	(<0.0001)
>1,000m above sea level	88 (7.6)	757 (20.4)	
Enhanced vegetation index 2015			
Least vegetation	55 (4.7)	234.2 (6.3)	(0.0001)
Much vegetation	341 (29.3)	1382 (37.4)	
Abundant vegetation	250 (21.5)	1054 (28.5)	
Most vegetation	515 (44.4)	1028 (27.8)	
Missing	0 (0)	7.14 (0.2)	
Mean temperature 2015 (in degrees Celsius)			
<room temp	546 (47.0)	1787 (48.2)	(0.6959)
>room temp	609 (52.5)	1890 (51.0)	
Missing	5 (0.5)	28 (0.8)	
Rainfall 2015 (in millimetres)			
Low rainfall	303 (26.1)	1008 (27.2)	(0.0013)
Moderate rainfall	762 (65.6)	2074 (56.0)	
Abundant rainfall	96 (8.3)	623 (16.8)	

Key: ** = subsample of 845 participants analyzed

3.3 Spatial distribution of malaria prevalence

The map below (Figure 3.1) describes the observed prevalence of malaria in children under five years in the various divisions of Cameroon in 2018. The highest prevalence of malaria was observed in the Mayo-Louti, Faro-et-Deo, Djerem, Haute-Sanaga, Nyong-et-Kelle, Lekie, Nyong-et-Mfoumou, Mbam-et-Inoubou Nkam, Boumba-et-Ngoko and Vallee-du-Ntem divisions. These divisions are in the North, Adamawa, Centre, Littoral, East and South regions respectively. The lowest prevalence was observed in the Bui, Noun, Menoua and Meme divisions of the Northwest, West and Southwest regions respectively. Other divisions had a moderate malaria prevalence.

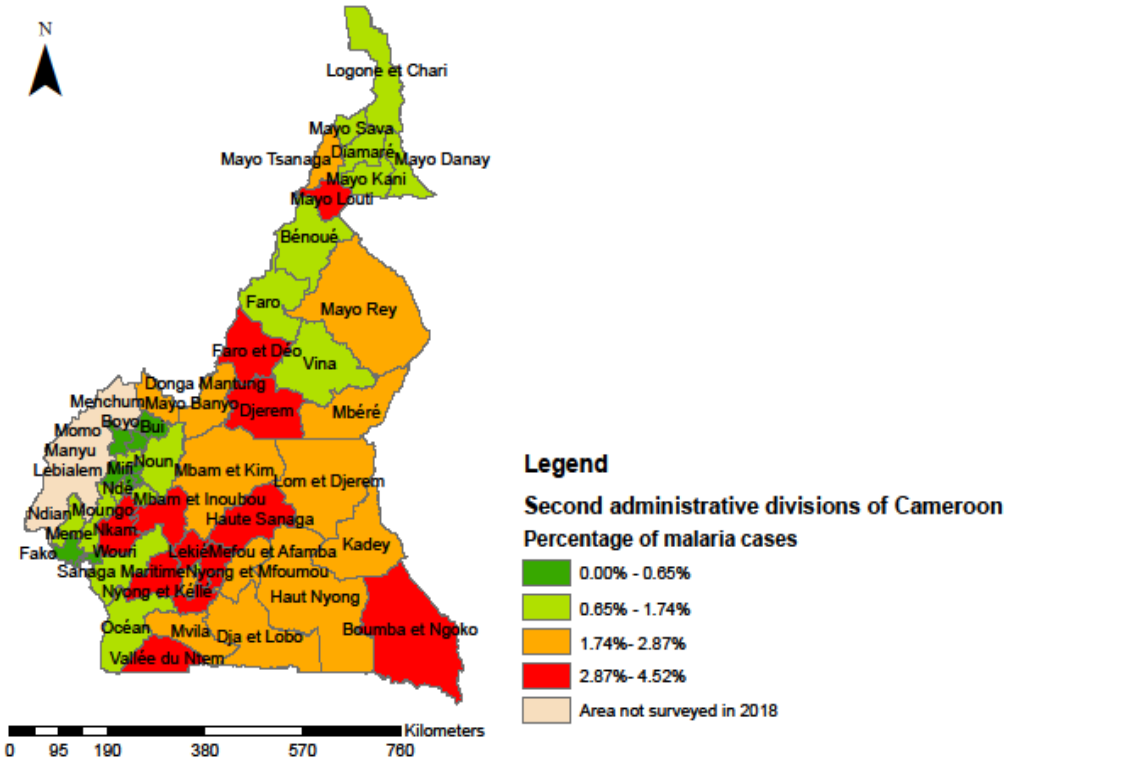


Figure 3.1 Thematic map of the distribution of malaria

3.4 Spatial autocorrelation

Spatial autocorrelation was to assess the distribution of malaria RDT positive data in space whether they were closely related or independent within the area of study. The results of the global Moran index were positive and significant (0.457; $p<0.00001$). There was a clustering pattern of malaria cases as highlighted in red in the square box on the right lower end of figure 3.2. Given the z-score of 8.25939309479, there is a less than 1% likelihood that this clustered pattern could be the result of random chance.

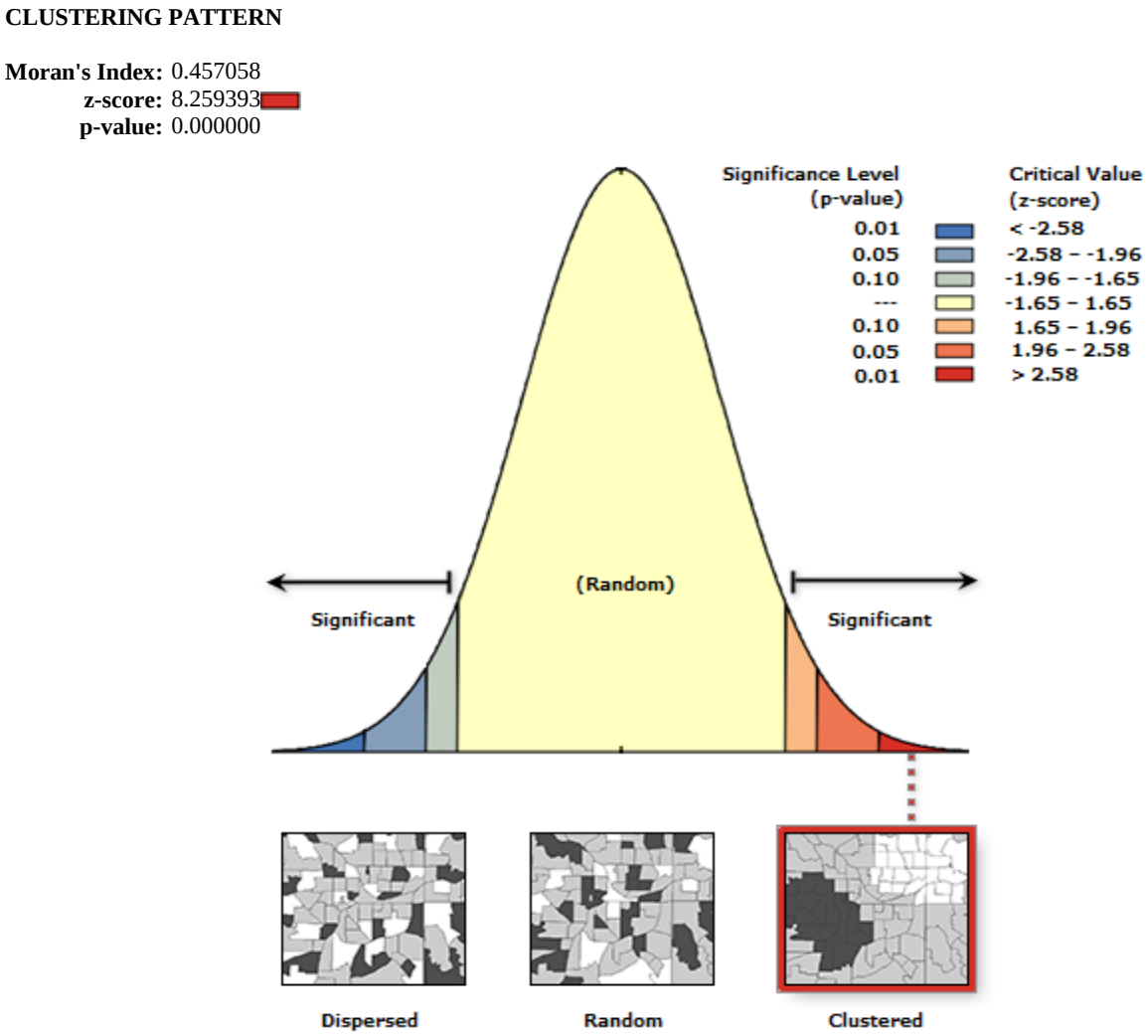
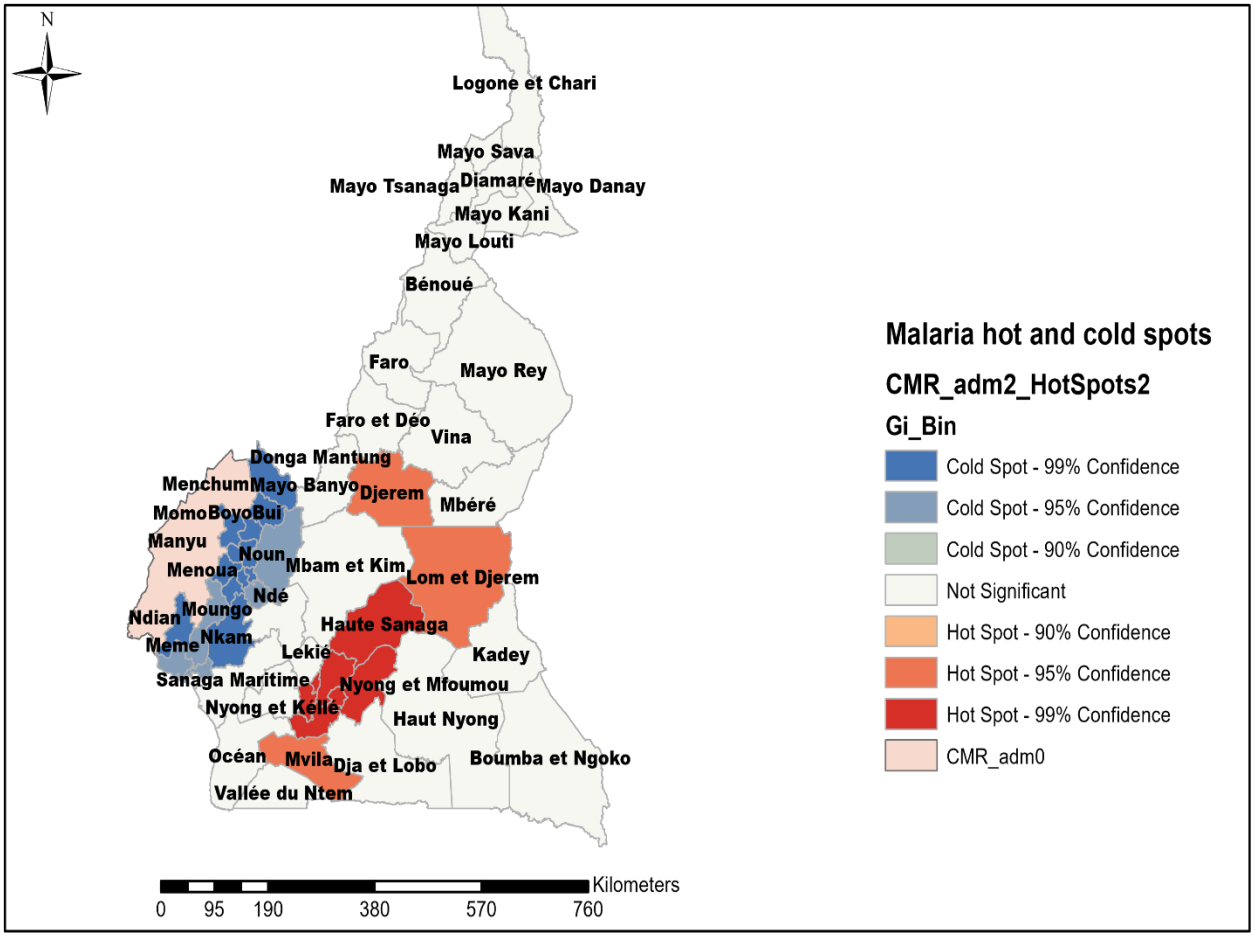


Figure 3.2 Global Moran's Index analysis (spatial autocorrelation).

3.5 Hotspot analysis

Given the clustered pattern of malaria infections observed from the global Moran's index, a hotspot analysis was done in order to identify the location of the malaria clusters. Statistically significant malaria cold and hot spots with 90, 95, and 99% confidences are shown in the figure 3.3 below. The hotspots were identified at the Djerem, Lom-et-Djerem, Haute-Sanaga, Nyong-et-Kelle, Lekie, Nyong-et-Mfoumou and Mvila divisions in the Adamawa, East, Center and South regions. The cold spots were found in Donga Mantung, Bui, Noun, Nde, Menoua, Moungo, Nkam and Meme divisions of the Northwest, West, Littoral and Southwest regions.

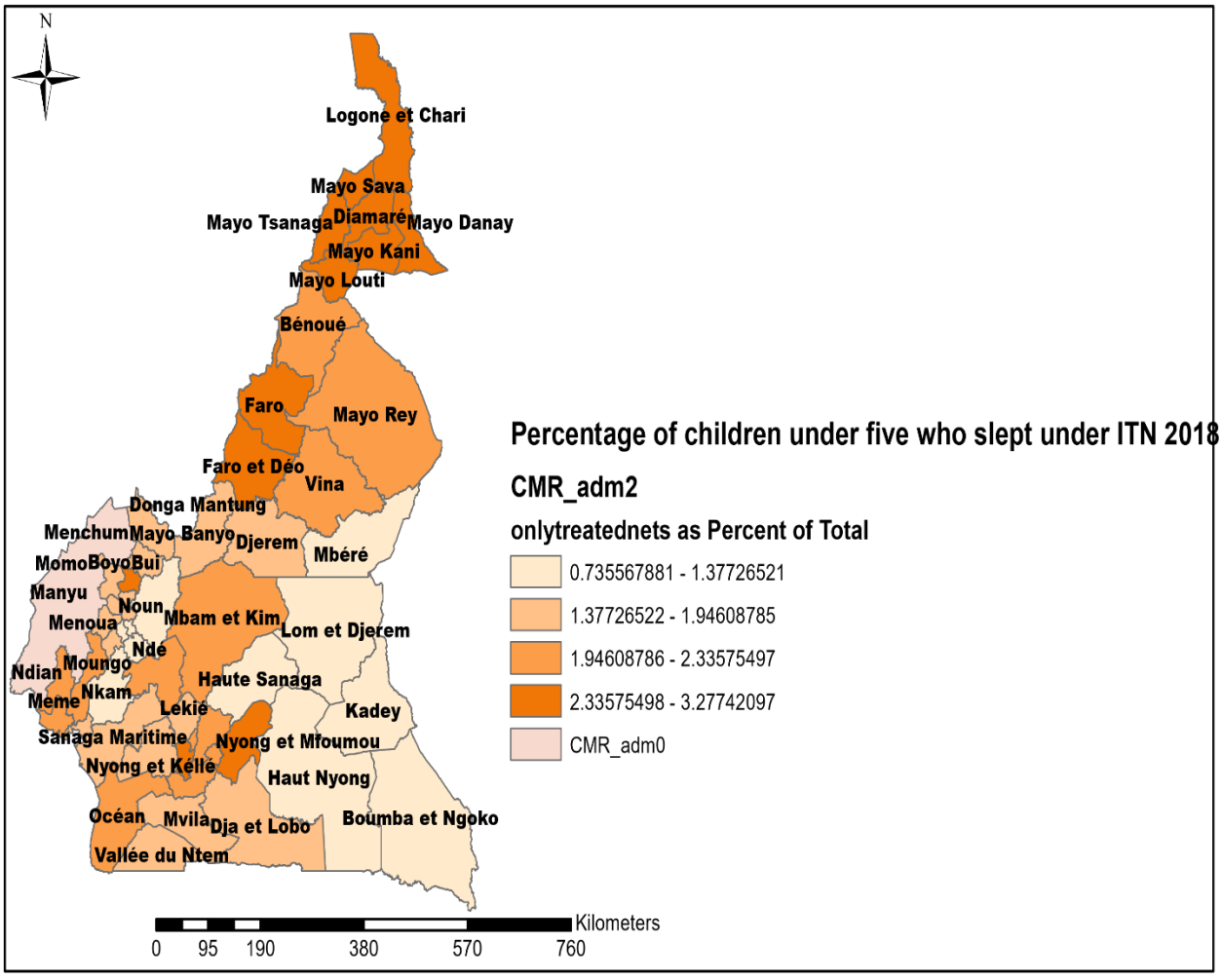


Key: CMR_adm2=second-level administrative divisions; CMR_adm0=country area not surveyed

Figure 3.3 Hotspot analysis for malaria prevalence.

3.6 ITN usage among children under five years in 2018

The proportion of children who slept under ITNs was mapped and the results are shown below (Figure 3.4). Divisions of the two northern regions had the highest percentages of ITN usage among children under five years. In contrast, divisions of the East and part of the Center regions had the least percentages of ITN usage.



Key: CMR_adm2= second-level administrative divisions; CMR_adm0=Cameroon boundary showing the unsurvey areas

Figure 3.4 Percentage of children who slept under ITN the night before survey

3.6.1 Univariable analysis of explanatory variables in the ITN and malaria model (N=4733)

The association between malaria and each independent variable was examined to determine which control variables to include in the multivariable analysis. The cut off p value was <0.1 for selection of variables. If the variable or one category of the variable was significant, that variable was selected.

The results presented (Table 3.3) showed almost all variables were included into the final model except for child's sex and mean temperature as they were not significant. The odds of contracting malaria among the studied children increased with increasing age. The odds were highest in the oldest age group (48-59months) compared to their younger counterparts (OR 2.59, 95%CI 1.89, 3.54). Compared to mothers with no education, children whose mothers attained higher education were less prone to have malaria (OR 0.19, 95%CI 0.09, 0.35). Likewise, children from more affluent households were less likely to contract malaria compared to those from poorest households (OR 0.21, 95%CI 0.15, 0.29).

Compared to children in the Adamawa region, children living in the Center region had the most odds of malaria (OR 1.93, 95%CI 1.40, 2.65) followed by the East (OR 1.19, 95%CI 0.86, 1.64) and South (OR 1.06, 95%CI 0.75, 1.48) regions respectively. Children living in rural areas were more likely to have malaria than those in urban areas (OR 2.70, 95%CI 2.28, 3.20).

The odds of contracting malaria were slightly increased for some children who slept under a mosquito net compared to none (OR1.36, 95%CI 1.09, 1.68). Children who slept under ITNs were less likely to have malaria than those who slept under untreated nets (OR0.86, 95%CI 0.73, 0.99).

Children with fever two weeks before the survey had higher odds of malaria than those without fever (OR 2.42, 95%CI 1.98, 2.95).

The children living in clusters 1,000 meters above sea level had a decreased odds of malaria compared to those in lower altitude (OR 0.32, 95%CI 0.25, 0.40). By contrast, the odds of malaria were increased in areas with higher vegetation coverage compared to areas with least vegetation (OR 2.13, 95%CI 1.31, 3.47). Children in areas with moderate rainfall had increased malaria odds than children in areas with low rainfall (OR 1.22, 95%CI 1.01, 1.48).

Table 3.3 Univariable analyses of the explanatory variables from survey weights adjustment (N=4733)

Variables and categories	**Unadjusted OR (95% CI)**	**p-value**	**global p-value**
Sex			0.4415
Male	Ref		
Female	0.94(0.81, 1.09)	0.434	
Child's age (months)			
6-11	Ref		<0.0001
12-23	1.94(1.40, 2.68)	<0.001	
24-35	1.92(1.39, 2.65)	<0.001	
36-47	2.57(1.87, 3.53)	0.001	
48-59	2.59(1.89, 3.54)	<0.001	
Mother's educational level			
No education	Ref		<0.0001
Primary	0.84(0.68, 1.03)	0.098	
Secondary	0.59(0.48, 0.74)	< 0.001	
Higher	0.19(0.09, 0.35)	<0.001	
Wealth Index			
Poorest	Ref		<0.0001
Poorer	1.04(0.84, 1.29)	0.692	
Middle	0.76(0.61, 0.95)	0.016	
Richer	0.43(0.33, 0.56)	<0.001	
Richest	0.21(0.15, 0.29)	<0.001	
Region			
Adamawa	Ref		<0.0001
Centre (excluding Yaoundé)	1.93(1.40, 2.65)	<0.001	
Douala	0.21(0.12, 0.39)	<0.001	
East	1.19(0.86, 1.64)	0.294	
Far-north	0.61(0.44, 0.85)	0.004	
Littoral (excluding Douala)	0.56(0.37, 0.87)	0.009	
North	0.77(0.55, 1.08)	0.128	
North-west	0.23(0.13, 0.41)	<0.001	
West	0.41(0.28, 0.59)	<0.001	
South	1.06(0.75, 1.48)	0.746	
South-west	0.24(0.11, 0.50)	<0.001	
Yaoundé	0.38(0.24, 0.59)	<0.001	
Place of residence			
Urban	Ref		<0.0001

Rural	2.70(2.28, 3.20)	<0.001	
Children < 5 that slept under mosquito net last night			
No	Ref		0.009
All children	0.91(0.76, 1.09)	0.307	
Some children	1.36(1.09, 1.68)	0.005	
Type of net child slept under			
No net or untreated	Ref		0.1119
Only treated (ITN)	0.86(0.73, 0.99)	0.047	
Child had fever 2 weeks before survey			
No	Ref		<0.0001
Yes	2.42 (1.98, 2.95)	<0.001	
Cluster altitude (meters)			
Less than 1000m above sea level	Ref		<0.0001
Greater than 1000m above sea level	0.32(0.25, 0.40)	<0.001	
Enhanced vegetation index			
Least vegetation	Ref		0.0001
Much vegetation	1.05(0.64, 1.72)	0.854	
Abundant vegetation	1.01(0.61, 1.66)	0.976	
Most vegetation	2.13(1.31, 3.47)	0.002	
Mean temperature (degrees Celsius)			
Below room temperature(<25◦c)	Ref		0.6959
Above room temperature(>25◦c)	1.05(0.90, 1.23)	0.499	
Rainfall			
Low rainfall	Ref		0.0013
Moderate rainfall	1.22(1.01, 1.48)	0.038	
Abundant rainfall	0.51(0.37, 0.71)	0.000	

Key: OR (OddsRatio), CI (ConfidenceIntervals)

3.6.2 Multilevel analysis of the association of ITN and malaria adjusting for other variables

Multivariable analysis was done with variables significant in the univariable analysis to examine the association between the primary predictors and malaria while adjusting for socio-demographic and environmental factors. Malaria status (positive or negative) was the outcome variable. Child's age, mother's educational level, wealth index, region, place of residence, cluster altitude, enhanced vegetation index, rainfall were control variables. Children that slept under a mosquito net last night, type of net child slept under and fever two weeks before were the primary predictors. A Non-random effects model was fitted as well as a random effects model. The result from the random effects model were considered (Table 3.4).

Results of the random effects model showed that The odds of malaria increased with increasing age and rural residence. Older children from 36 months had higher malaria odds compared to younger children (AOR 2.51, 95%CI 1.94, 3.25**)**. Children living in rural areas had increased malaria odds than their urban counterparts (AOR 1.46, 95%CI 1.03, 2.05).

Conversely, Children whose mothers attained higher education had lower odds of acquiring malaria than those whose mothers had no education (AOR 0.50, 95%CI 0.29, 0.87)**.** Those from middle income, richer and richest homes were also less likely to have malaria than children from poorest homes (AOR 0.62, 95%CI 0.39,0.97; AOR 0.36, 95%CI 0.20, 0.65 and AOR 0.27, 95%CI 0.13, 0.53 respectively). Children from the northwest and southwest regions had lower odds of malaria than other regions (AOR 0.12, 95%CI 0.03, 0.63 and AOR 0.15, 95%CI 0.08, 0.28 respectively). Those who live at higher cluster altitude had decreased odds of malaria than children in lower altitude (AOR 0.24, 95%CI 0.13, 0.42).

The odds of malaria were slightly increased for some children who slept under a mosquito net compared to none (AOR 1.35, 95%CI 1.03, 1.77). The odds of malaria were marginally decreased for children who used ITN compared to those who did not (AOR 0.76, 95%CI 0.57, 1.03). On the other hand, the odds of malaria increased for children with fever two weeks before survey than those without fever (AOR 2.51, 95%CI 1.94, 3.25).

Table 3.4 Analysis of factors associated with malaria with ITN use as the determinate explanatory variable (N=4733)

Variables and categories	**Multilevel (Nonrandom effects)** AOR (95% CI) p-value	**Multilevel (random-effects)** AOR (95%CI) p-value
Child's age (months)		
6-11	Ref	ref
12-23	2.01(1.39,2.89)<0.001	2.01(1.38, 2.93)<0.001
24-35	1.86(1.29, 2.68)0.001	1.88(1.23, 2.88) 0.003
36-47	2.71(1.88,3.90)<0.001	2.51(1.94, 3.25)<0.001

48-59	2.59(1.81,3.71)<0.001	2.65(1.84, 3.81)<0.001
Mother's educational level		
No education	Ref	ref
Primary	0.78(0.59, 1.02) 0.066	0.79(0.55, 1.14) 0.205
Secondary	0.73(0.54, 0.99) 0.042	0.74(0.51, 1.06) 0.098
Higher	0.50(0.25, 1.03) 0.060	0.50(0.29, 0.87) 0.014
Wealth Index		
Poorest	Ref	ref
Poorer	0.85(0.63, 1.14) 0.272	0.85(0.54, 1.33) 0.471
Middle	0.65(0.47,0.92) 0.013	0.62(0.39,0.97) 0.035
Richer	0.41(0.27,0.62)<0.001	0.36(0.20, 0.65) 0.001
Richest	0.32(0.18,0.55)<0.001	0.27(0.13, 0.53)<0.001
Region		
Adamawa	Ref	Ref
Centre (excluding Yaoundé)	0.75(0.45, 1.25) 0.270	0.75(0.38, 1.52) 0.429
Douala	0.14(0.04,0.470)0.001	0.21(0.08, 0.52) 0.001
East	0.43(0.25, 0.72) 0.002	0.41(0.21, 0.82) 0.012
Far-north	0.30(0.16, 0.59)0.001	0.26(0.08, 0.77) 0.016
Littoral (excluding Douala)	0.27(0.13,0.54)<0.001	0.35(0.14, 0.81) 0.014
North	0.39(0.21, 0.73) 0.003	0.32(0.15, 0.67) 0.003
North-west	0.21(0.11,0.41)<0.001	0.12(0.03, 0.63) 0.012
West	0.52(0.32, 0.85) 0.010	0.44(0.21, 0.94) 0.034
South	0.60(0.35, 1.03) 0.066	0.62(0.33, 1.17) 0.139
South-west	0.15(0.05, 0.48) 0.001	0.15(0.08, 0.28)<0.001
Yaoundé	0.43(0.23, 0.82)0.010	0.47(0.25, 0.90) 0.022
Place of residence		
Urban	Ref	ref
Rural	1.61(1.25,2.07)<0.001	1.46(1.03, 2.05) 0.033
Cluster altitude (meters)		
Less than 1000m above sea level	Ref	ref
Greater than 1000m above sea level	0.20(0.13,0.32)<0.001	0.24(0.13, 0.42)<0.001
Rainfall		
Low rainfall	Ref	ref
Moderate rainfall	1.13(0.71, 1.79) 0.606	0.58(0.21, 1.60) 0.293
Abundant rainfall	1.60(0.75, 3.42) 0.221	0.73(0.24, 2.27) 0.589
Enhanced vegetation index		
Least vegetation	Ref	ref
Much vegetation	0.91(0.51, 1.61) 0.742	0.60(0.29, 1.26) 0.177
Abundant vegetation	1.57(0.79, 3.13) 0.198	1.71(0.74, 3.99) 0.210
Most vegetation	1.69(0.82, 3.52) 0.157	1.84(0.79, 4.29) 0.156
Children < 5 that slept under mosquito net last night		
No	Ref	ref
All children	1.33(0.87, 2.04) 0.192	1.42(0.92, 2.20) 0.113
Some children	1.35(0.97, 1.88) 0.071	1.35(1.03, 1.77) 0.032
Type of net child slept under		
No net or untreated	Ref	Ref
Only treated (ITN)	0.79(0.55, 1.15) 0.219	0.76(0.57, 1.03) 0.082
Child had fever 2 weeks before survey		
No	Ref	ref
Yes	2.38(1.89,2.98)<0.001	2.51(1.94, 3.25)<0.001

AOR (Adjusted Odds Ratio), ref (Reference), CI (Confidence Interval)

3.7. ACT usage among children under five years

The percentage of children who took ACT for fever two weeks before the survey is illustrated in figure 3.5. Results indicate that ACT use varied nationally though predominant in the Center and

West regions. The Mayo-Sava, Mayo-Rey, Mbam-et-Kim, Haute-Sanaga, Lekkie, Nyong-et-Kelle, Haute-Nyong, Noun, Mifi, Nde, Menoua, Nkam, and Fako divisions had the highest ACT usage.

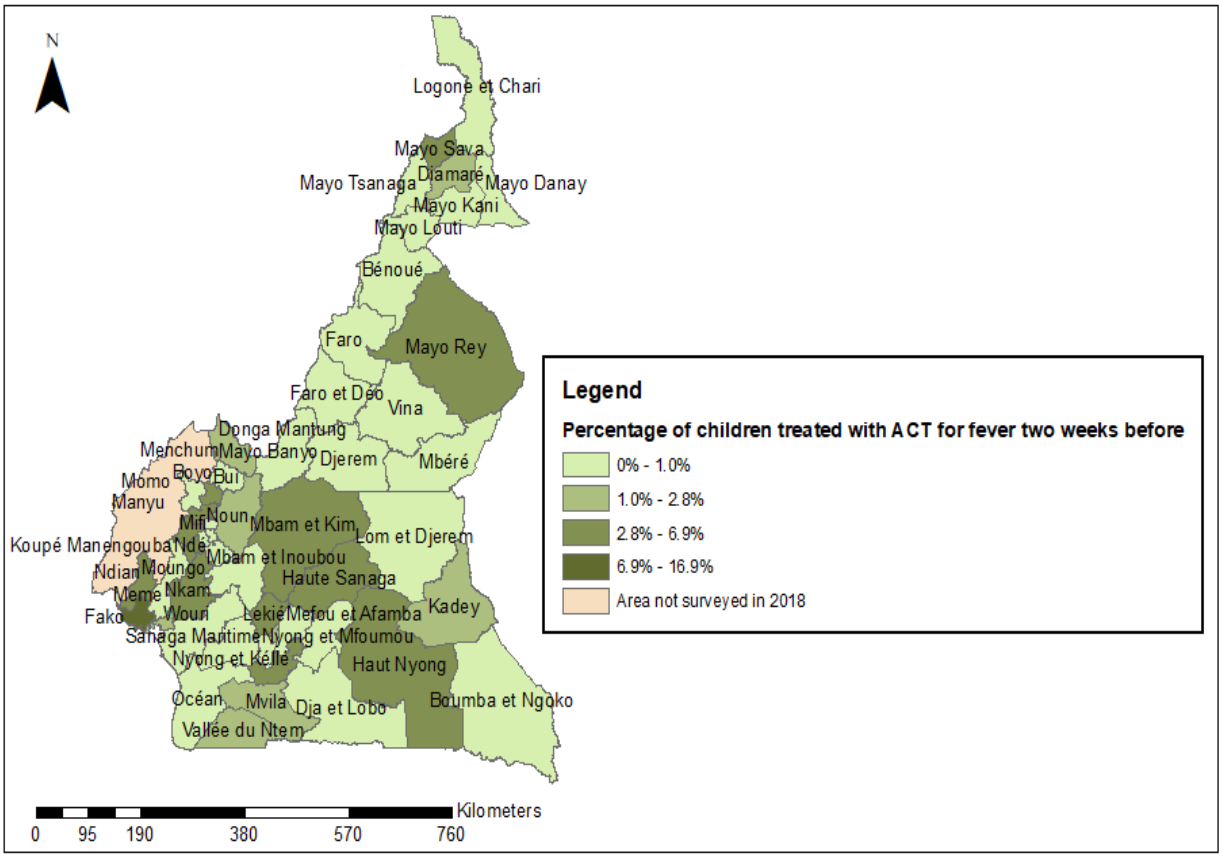


Figure 3.5 Percentage of children treated with ACT

3.7.1 Univariable analysis of explanatory variables in the ACT and malaria model (N=845)

Table 3.5 presents the results of univariable analysis of the subsample of children with fever two weeks before survey who were treated with ACT or not. The primary explanatory variables were child had fever two weeks before survey and child received ACT. The other variables were control

variables. Only significant control variables were included in multivariable analysis based on a cutoff p-value of <0.1.

The odds of malaria increased with increasing age as older children aged 36 to 59 months had the highest odds than younger children aged six to 11 months (OR 3.56, 95%CI 1.83, 6.93). On the contrary, children whose mothers had higher education had the least odds of malaria compared to children whose mothers had no education (OR 0.19, 95%CI 0.06, 0.69). Also, children from richer and richest households had lower odds of malaria (OR 0.4195%CI 0.23, 0.71 and OR 0.33,95%CI 0.16, 0.67 respectively) than those from poorest households. Compared to Adamawa region, children in the South and Centre regions had increased malaria odds (OR 1.69, 95%CI 0.32, 1.51) and (OR 1.41, 95%CI 0.69, 2.88) respectively. Children in rural areas were more likely to have malaria than those in urban areas (OR 2.81, 95%CI 1.99, 3.95).

Children with fever two weeks before had four times the likelihood of malaria than those without fever (OR 4.43, 95%CI 2.48, 7.94). There was no significant change in malaria odds for children treated with ACT compared to children not treated with ACT (OR 0.85, 95%CI 0.40, 1.80).

Living at higher cluster altitude decreased the odds of malaria than lower altitude (OR 0.37, 95%CI 0.23, 0.58). Enhanced vegetation index, mean temperature and rainfall were not significant.

Table 3.5 Univariable analysis of the explanatory variables from survey weights adjustment (N=845)

Variables and categories	Unadjusted OR (95% CI)	p-value	Global p-value
DEMOGRAPHIC AND SOCIOECONOMIC VARIABLES			
Sex			0.5235
Male	ref		
Female	0.91(0.65, 1.26)	0.554	
Child's age (months)			
6-11	ref		0.0030
12-23	2.15(1.13, 4.11)	0.020	
24-35	3.06(1.59, 5.87)	0.001	
36-47	3.56(1.83, 6.93)	<0.001	
48-59	3.32(1.69, 6.50)	<0.001	
Mother's educational level			

No education	ref		0.0117
Primary	0.82(0.52, 1.28)	0.384	
Secondary	0.56(0.36, 0.87)	0.011	
Higher	0.19(0.06, 0.69)	0.012	
Wealth Index			
Poorest	ref		0.0004
Poorer	1.14(0.69, 1.86)	0.603	
Middle	0.82(0.49, 1.34)	0.425	
Richer	0.41(0.23, 0.71)	0.002	
Richest	0.33(0.16, 0.67)	0.002	
Region			
Adamawa	ref		<0.0001
Centre (excluding Yaoundé)	1.41(0.69, 2.88)	0.344	
Douala	0.09(0.02, 0.38)	0.001	
East	0.54(0.26, 1.10)	0.091	
Far-north	0.65(0.31, 1.36)	0.251	
Littoral (excluding Douala)	0.35(0.14, 0.89)	0.029	
North	0.36(0.15, 0.87)	0.024	
North-west	0.24(0.08, 0.70)	0.009	
West	0.30(0.14, 0.66)	0.002	
South	1.69(0.32, 1.51)	0.353	
South-west	0.55(0.15, 2.10)	0.386	
Yaoundé	0.27(0.10, 0.69)	0.006	
Place of residence			
Urban	ref		<0.0001
Rural	2.81(1.99, 3.95)	<0.001	
MALARIA VARIABLES			
Child had fever 2 weeks before survey			
No	ref		<0.0001
Yes	4.43 (2.48, 7.94)	<0.001	
Child received ACT			
No	ref		0.6576
Yes	0.85 (0.40, 1.80)	0.672	
ENVIRONMENTAL/CLIMATIC VARIABLES			
Cluster altitude (meters)			
Less than 1000m above sea level	ref		0.0009
Greater than 1000m above sea level	0.37(0.23, 0.58)	<0.001	
Enhanced vegetation index			
Least vegetation	ref		0.1299
Much vegetation	0.75(0.31, 1.81)	0.522	
Abundant vegetation	0.82(0.34, 1.97)	0.660	
Most vegetation	1.42(0.61, 3.32)	0.414	
Mean temperature (degrees Celsius)			
Below room temperature(<25◦c)	ref		0.4824
Above room temperature(>25◦c)	1.17(0.84, 1.63)	0.348	
Rainfall			
Low rainfall	ref		0.1524
Moderate rainfall	1.04(0.58, 1.84)	0.901	
Abundant rainfall	0.47(0.19, 1.12)	0.089	

Key: OR (OddsRatio), CI (ConfidenceIntervals)

3.7.2 Multilevel analysis of the association of ACT and malaria adjusting for other variables

The nonrandom and random effects of the association between ACT and malaria adjusting for other variables are shown below (table 3.6). Malaria is the dependent variable, factors associated with malaria are control variables while fever and ACT use are primary independent variables. The results of the random effects were discussed.

The odds of malaria were highest from 36 months old than younger ages (AOR 3.35, 95%CI 1.66, 6.77). Children in rural areas were twice more likely to have malaria than their counterparts in urban areas (AOR 2.08, 95%CI 1.35, 3.20). Conversely, children living in Douala, those whose mother's attained higher education, and those living in higher clusters were less likely to have malaria (AOR 0.17, 95%CI 0.06, 0.49, AOR 0.23, 95%CI 0.07, 0.76 and AOR 0.33, 95%CI 0.12, 0.90 respectively)

Children with fever two weeks before the survey had increased odd of malaria compared to children without fever (AOR 3.83, 95%CI 2.49, 5.90). Among these children who had fever, the odds of malaria were similar for those who took ACT and those who did not (AOR 0.76, 95%CI 0.30, 1.89).

Table 3.6 Analysis of factors associated with malaria with ACT use as the determinate explanatory variable (N=845)

Categories and variables	**Multilevel (Nonrandom effects)** AOR (95% CI) p-value	**Multilevel (random-effects)** AOR (95%CI) p-value
Child's age (months)		
6-11	ref	ref
12-23	2.03(1.03, 4.03) 0.042	1.94(1.06, 3.55) 0.031
24-35	2.74(1.38, 5.45) 0.004	2.73(1.54, 4.82) 0.001
36-47	3.43(1.68, 7.02) 0.001	3.35(1.66, 6.77) 0.001
48-59	3.20(1.54, 6.65) 0.002	3.12(1.45, 6.71) 0.004
Mother's educational level		
No education	ref	ref
Primary	0.68(0.38, 1.23) 0.203	0.68(0.36, 1.30) 0.240
Secondary	0.63(0.34, 1.17) 0.145	0.62(0.33, 1.16) 0.136
Higher	0.25(0.06, 1.03) 0.054	0.23(0.07, 0.76) 0.016
Wealth Index		
Poorest	ref	ref
Poorer	1.01(0.54, 1.88) 0.968	1.07(0.53, 2.19) 0.844

Middle	1.04(0.53, 2.04) 0.900	1.07(0.53, 2.16) 0.853
Richer	0.71(0.32, 1.57) 0.397	0.72(0.28, 1.86) 0.504
Richest	0.78(0.30, 2.06) 0.623	0.79(0.28, 2.24) 0.661
Region		
Adamawa	ref	ref
Centre (without Yaoundé)	1.10(0.41, 2.97) 0.847	1.13(0.37, 3.45) 0.830
Douala	0.17(0.03, 0.86) 0.032	0.17(0.06, 0.49)0.001
East	0.44(0.16, 1.16) 0.098	0.43(0.17, 1.10) 0.080
Far-north	0.29(0.11, 0.78) 0.015	0.30(0.11, 0.87) 0.027
Littoral (without Douala)	0.36(0.12, 1.19) 0.094	0.37(0.12, 1.12) 0.078
North	0.15(0.05, 0.44) 0.001	0.15(0.049, 0.46) 0.001
North-west	0.39(0.15, 1.07) 0.067	0.35(0.06, 1.93) 0.229
West	0.55(0.22, 1.36) 0.197	0.49(0.20, 1.22) 0.128
South	0.55(0.19, 1.55) 0.259	0.55(0.17, 1.73) 0.305
South-west	0.79(0.15, 4.17) 0.782	0.82(0.28, 2.37) 0.716
Yaoundé	0.42(0.12,1.45) 0.171	0.43(0.16, 1.18) 0.101
Place of residence		
Urban	ref	ref
Rural	2.07(1.30, 3.29) 0.002	2.08(1.35, 3.20) 0.001
Cluster altitude (meters)		
Less than 1000m above sea level	ref	ref
Greater than 1000m above sea level	0.31(0.14, 0.70) 0.005	0.33(0.12, 0.90) 0.031
Child had fever 2 weeks before survey		
No	ref	ref
Yes	3.82(2.13, 6.85) 0.000	3.83(2.49, 5.90)<0.001
Child took ACT for fever two week before		
No	ref	ref
Yes	0.77(0.31, 1.91) 0.578	0.76(0.30, 1.89) 0.548

AOR (Adjusted Odds Ratio), ref (Reference), CI (Confidence Interval).

3.8 Multilevel analysis of the association of the combined ITN and ACT usage and malaria adjusting for other variables

The net variables (use of net and type of net used) and ACT use were combined to generate a composite variable. This was analyzed in multilevel and spatial models to demonstrate the association between the combined ITN and ACT usage and malaria. Control variables that showed significance in univariate analysis of the subsample were adjusted for in the models. Again in the multilevel analysis, nonrandom and random effects models were fitted (table 3.7). The results of the random effects will be considered.

Findings of the combined ITN and ACT showed that older children from 36 months of age were more likely to have malaria than younger children (AOR 3.61, 95%CI 1.73, 7.52). The odds of

malaria were lower for children whose mothers had higher education compared to those with no maternal education (AOR 0.28, 95%CI 0.09, 0.90). children living in rural areas had increased odds of malaria than those in urban areas (AOR 2.09, 95%CI 1.34, 3.29). In contrast, children living in higher altitude had lower malaria odds than those in lower altitude (AOR 0.29, 95%CI 0.09, 0.85).

The odds of malaria were higher among some children who slept under a net that was untreated and who did not use ACT compared to those who used none (AOR 2.42, 95%CI 1.15, 5.10). Also, children with fever two weeks before had increased malaria odds than those without fever (AOR 3.93, 95%CI 2.45, 6.28).

Table 3.7 Multilevel analysis of combined ITN and ACT usage associated with malaria adjusting for sociodemographic and environmental factors (N=845)

Categories and variables	**Multilevel (Nonrandom effects)** AOR (95% CI) p-value	**Multilevel (random-effects)** AOR (95%CI) p-value
Child's age (months)		
6-11	ref	ref
12-23	2.07(1.02, 4.19)0.043	1.98(1.07, 3.66) 0.029
24-35	2.71(1.34, 5.49) 0.006	2.68(1.48, 4.89) 0.001
36-47	3.68(1.74, 7.79) 0.001	3.61(1.73, 7.52) 0.001
48-59	3.41(1.60, 7.29) 0.002	3.34(1.57, 7.14) 0.002
Mother's educational level		
No education	ref	Ref
Primary	0.71(0.39, 1.28)0.260	0.71(0.39, 1.30) 0.272
Secondary	0.69(0.37, 1.28) 0.234	0.67(0.36, 1.27) 0.224
Higher	0.31(0.08, 1.22) 0.093	0.28(0.09, 0.90) 0.032
Wealth Index		
Poorest	ref	ref
Poorer	1.09(0.58, 2.05)0.780	1.15(0.54, 2.45) 0.721
Middle	1.02(0.52, 2.00) 0.961	1.03(0.51, 2.12) 0.927
Richer	0.81(0.37, 1.78) 0.602	0.82(0.30, 2.24) 0.701
Richest	0.80(0.31, 2.08) 0.645	0.80(0.25, 2.53) 0.700
Region		
Adamawa	ref	ref
Centre (without Yaoundé)	1.04(0.39, 2.78) 0.942	1.06(0.33, 3.34) 0.927
Douala	0.18(0.04, 0.89) 0.036	0.18(0.06, 0.53) 0.002
East	0.39(0.14, 1.06) 0.066	0.38(0.14, 1.04) 0.059
Far-north	0.30(0.11, 0.79) 0.015	0.31(0.11, 0.87) 0.027
Littoral (without Douala)	0.35(0.11, 1.14) 0.081	0.35(0.12, 1.06) 0.063
North	0.13(0.04, 0.39) 0.001	0.13(0.04, 0.43) 0.001
North-west	0.42(0.16, 1.14) 0.088	0.38(0.07, 2.08) 0.267
West	0.53(0.21, 1.34) 0.181	0.49(0.20, 1.18) 0.111
South	0.46(0.16, 1.29) 0.139	0.45(0.14, 1.47) 0.188
South-west	0.99(0.19, 5.19) 0.987	1.01(0.29, 3.54) 0.994
Yaoundé	0.35(0.11, 1.17) 0.088	0.35(0.13, 0.99) 0.050
Place of residence		

Urban	ref	ref
Rural	2.10(1.31, 3.37) 0.002	2.09(1.34, 3.29) 0.001
Cluster altitude (meters)		
Less than 1000m above sea level	ref	ref
Greater than 1000m above sea level	0.27(0.12, 0.62) 0.002	0.29(0.09, 0.85) 0.025
Combined variable of ITN and ACT usage		
None	ref	ref
no & untreated & ACT	0.39(0.08, 1.80) 0.226	0.39(0.05, 2.81) 0.353
All children & untreated & no ACT	0.57(0.09, 3.32) 0.530	0.61(0.07, 5.16) 0.654
All children & ITN & no ACT	0.86(0.55, 1.35) 0.510	0.86(0.65, 1.15) 0.306
All children & ITN & ACT	0.750.23, 2.46) 0.633	0.72(0.20, 2.53) 0.604
Some children & untreated & no ACT	2.47(1.22, 5.01) 0.012	2.42(1.15, 5.10) 0.020
Some children & untreated & ACT	5.51(0.51, 58.98) 0.156	5.63(0.41, 77.80) 0.197
Some children & ITN & no ACT	1.36(0.72, 2.56) 0.339	1.37(0.64, 2.93) 0.412
Child had fever 2 weeks before survey		
No	ref	ref
Yes	3.92(2.14, 7.20)<0.001	3.93(2.45, 6.28) <0.001

AOR (Adjusted Odds Ratio), ref (Reference), CI (Confidence Interval).

3.9 Conditional autoregressive (CAR) modelling

CAR models were fitted to examine the correlation of malaria in space due to common exposures affecting neighbouring areas (spatial random effects). CAR modelling uses priors to analyze data providing more reliable estimates. The variables included in the multilevel analysis to fit the three different multilevel models were also included in the CAR models.

3.9.1 Spatial analysis of ITN usage and malaria adjusting for socio-demographic, climatic and environmental variables.

Table 3.8 summarizes the estimates of spatial effects of variables in the ITN model predicting malaria risk. The analysis excluded the region variable as this would be accounted for in the spatial modelling The results were similar to the random effects multilevel model though with minor differences.

As their age increases, older children from 36 months had higher malaria odds compared to younger children (AOR 2.74, 95%BCI 2.00, 3.78). Children in rural areas had increase malaria odds compared to those in urban areas (A0R 1.33, 95%BCI 1.05, 1.68). The odds of malaria were increased among children living in areas with higher vegetation coverage (AOR 2.15, 95%BCI

1.11, 4.26 and AOR 2.10, 95%BCI 1.08, 4.19 respectively) compared to children in areas with least vegetation. In contrast, children from middle income, richer and richest homes had lower malaria odds (AOR 0.58, 95%BCI 0.43, 0.78; AOR 0.27, 95%BCI 0.19, 0.40 and AOR 0.22, 95%BCI 0.14, 0.36 respectively) compared to children from poorest homes. Finally, children living in households at higher altitude also had lesser malaria odds than those in lower altitude (AOR 0.25, 95%BCI 0.18, 0.36).

The use of mosquito nets and ITN in particular had no effect on malaria odds. Children with fever two weeks before survey had a higher malaria odds compared to children without fever (AOR 2.44, 95%BCI 2.01, 2.97).

Table 3.8 CAR model analysis of ITN usage adjusting for spatial random effects

Variables and categories	Bayesian adjusted odds ratios (Bayesian credible intervals BCI)
Child's age (months)	
6-11	Ref
12-23	1.90 (1.39, 2.62)
24-35	1.89 (1.38, 2.61)
36-47	2.74 (2.00, 3.78)
48-59	2.71 (1.98, 3.73)
Mother's educational level	
No education	Ref
Primary	0.78 (0.61, 1.00)
Secondary	0.84 (0.64, 1.10)
Higher	0.59 (0.31, 1.10)
Wealth Index	
Poorest	Ref
Poorer	0.81 (0.63, 1.04)
Middle	0.58 (0.43, 0.78)
Richer	0.27 (0.19, 0.40)
Richest	0.22 (0.14, 0.36)
Place of residence	
Urban	ref
Rural	1.33 (1.05, 1.68)
Cluster altitude (meters)	
Less than 1000m above sea level	ref
Greater than 1000m above sea level	0.25 (0.18, 0.36)
Rainfall	
Low rainfall	ref
Moderate rainfall	0.85 (0.50, 1.44)
Abundant rainfall	0.56 (0.29, 1.09)
Enhanced vegetation index	
Least vegetation	ref
Much vegetation	0.81(0.45, 1.47)
Abundant vegetation	2.15 (1.11, 4.26)
Most vegetation	2.10 (1.08, 4.19)
Children < 5 that slept under mosquito net last night	

No	Ref
All children	1.18 (0.82, 1.71)
Some children	1.18 (0.89, 1.57)
Type of net slept under	
No net or untreated	Ref
Only treated (ITN)	0.86 (0.63, 1.19)
Child had fever 2 weeks before survey	
No	Ref
Yes	2.44 (2.01, 2.97)

Figure 3.6 depicts the predicted malaria risk from estimates of the significant variables of the CAR model analysis. The spatial random effects for the malaria data was summarized as high and low values clustered together resulting in darker and lighter red color shades respectively. The grey areas on the predicted map represent polygons without data as some areas were not surveyed. The predicted map was similar to the observed map but fewer divisions were predicted to be at highest risk than the unadjusted map. The highest malaria risk was predicted in Mayo-Louti, Faro-et-Deo, Djerem, Haute-Sanaga, Lekie and Nyong-et-Mfoumou divisions. These divisions are in the North, Adamawa and Center regions. Fever two weeks before survey, rural residence and increased age were general predictors of high malaria in all these divisions. In contrast, higher cluster altitude predicted lower malaria risk for some divisions in the Far-north, North, Northwest and West regions meanwhile higher socioeconomic status predicted lower malaria risk in the Littoral region.

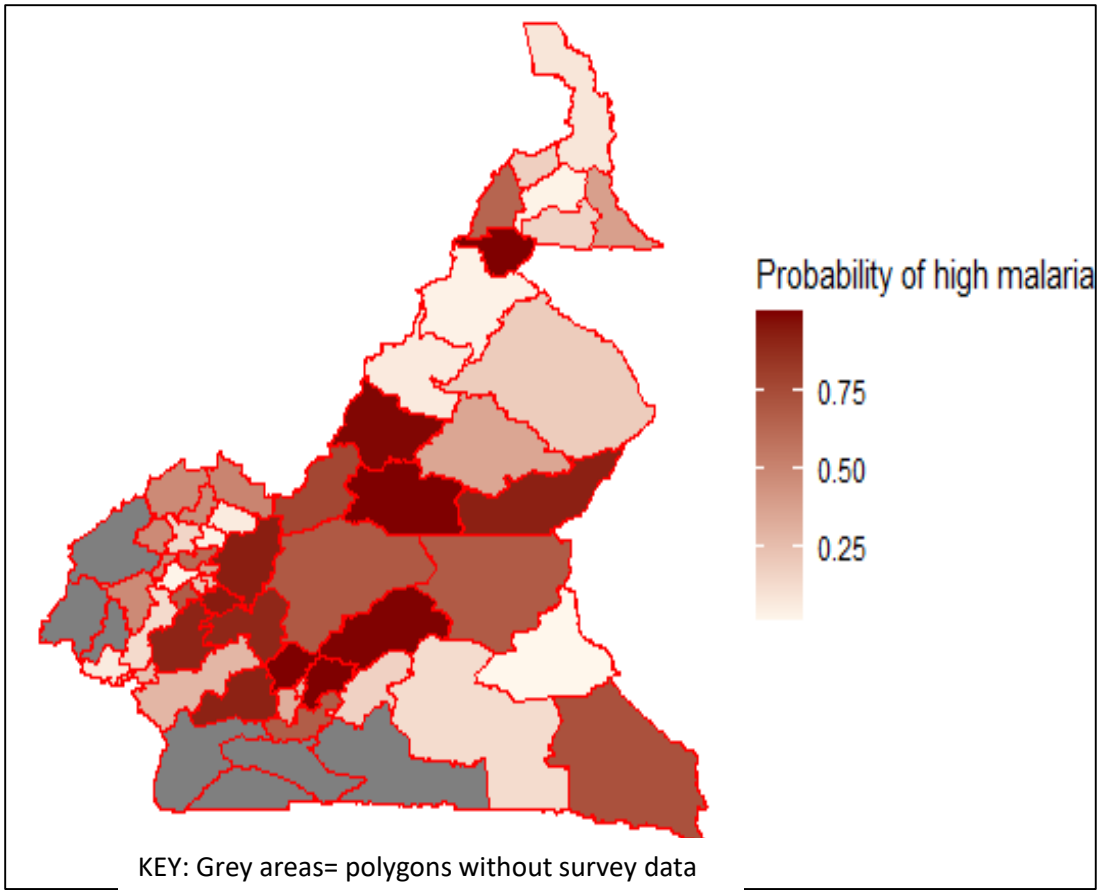


Figure 3.6 Predicted malaria risk with ITN model

3.9.2 Spatial analysis of ACT usage and malaria adjusting for socio-demographic, climatic/environmental variables.

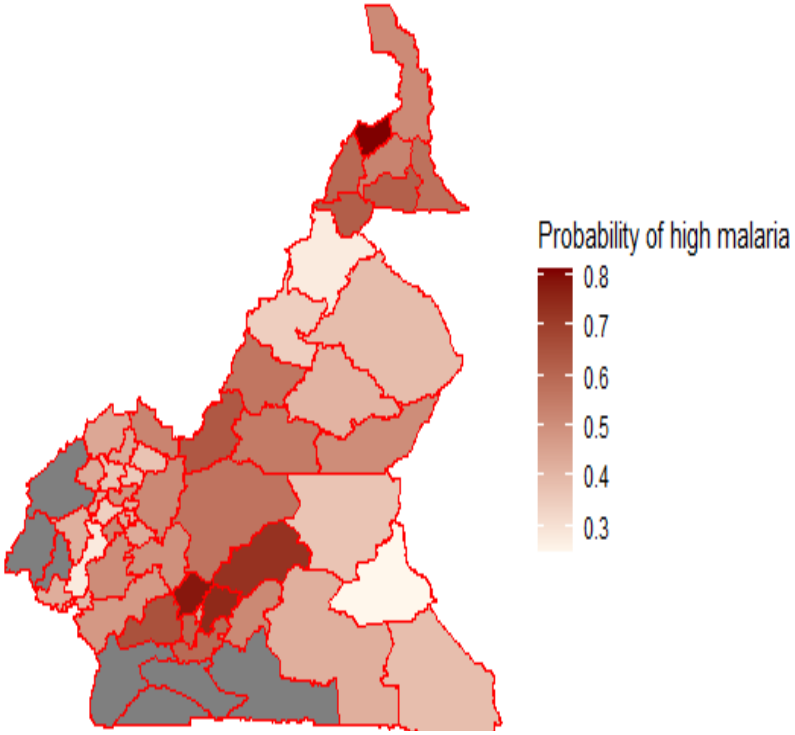
The results of the spatial ACT model (table 3.9) showed that children in the 36 to 47 months' age category had high malaria odds than children in other age groups (AOR 3.97, 95%BCI 2.18, 7.46). Those of rural residence were associated with increased malaria odds than those of urban residence (AOR 1.81, 95%BCI 1.20, 2.75). Whereas, higher maternal education and altitude were associated with lower malaria odds (AOR,0.27, 95%BCI 0.08, 0.83 and AOR 0.29, 95%BCI 0.16, 0.53 respectively).

ACT use had no effect on the odds of malaria. However, children who had fever two weeks before had increased malaria odds than those without fever (AOR 3.52, 95%BCI 2.06, 6.22).

Table 3.9 CAR model analysis of ACT usage associated with malaria adjusting for spatial random effects.

Variables and categories	Bayesian adjusted odds ratios (credible intervals)
Child's age (months)	
6-11	ref
12-23	2.08 (1.16, 3.85)
24-35	2.56 (1.43, 4.72)
36-47	3.97 (2.18, 7.46)
48-59	3.53 (1.91, 6.70)
Mother's educational level	
No education	ref
Primary	0.63 (0.38, 1.02)
Secondary	0.60 (0.36, 1.01)
Higher	0.27 (0.08, 0.83)
Wealth Index	
Poorest	ref
Poorer	1.19 (0.72, 1.99)
Middle	1.10 (0.62, 1.95)
Richer	0.70 (0.34, 1.41)
Richest	0.56 (0.24, 1.28)
Place of residence	
Urban	ref
Rural	1.81 (1.20, 2.75)
Cluster altitude (meters)	
Less than 1000m above sea level	ref
Greater than 1000m above sea level	0.29 (0.16, 0.53)
Child took ACT for fever two week before	
No	ref
Yes	0.76 (0.37, 1.49)
Child had fever 2 weeks before survey	
No	ref
Yes	3.52 (2.06, 6.22)

The posterior marginal probability estimates of significant predictors following spatial adjustments are summarized in figure 3.7. The map showed that fever two weeks before survey, increased aged and rural residence predicted the highest malaria risk in Mayo-Sava division in the Far-north region. Meanwhile, higher cluster altitude and maternal education predicted low malaria risk in Benoue, Kadey, Bui, Mifi, Nde, Noun and Mungo divisions of the North, East, Northwest, West and Littoral regions. The Blue areas depicts the unsurvey polygons.



KEY: Grey areas= polygons without survey data

Figure 3.7 Predicted probability of malaria risk with ACT model

3.9.3 Spatial analysis of the combined ITN and ACT usage

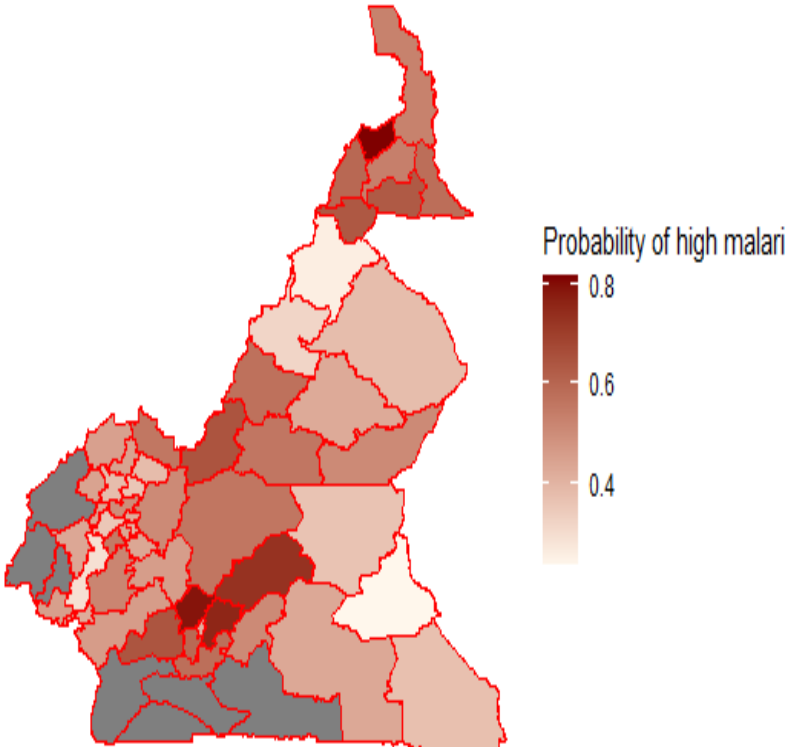
Results of the spatial fixed effects on the combined ITN and ACT usage are presented below (table 3.10). Older children from 36 months old and rural residence increased the odds of malaria (AOR 4.29, 95%BCI 2.32, 8.16 and AOR 1.79, 95%BCI 1.17, 2.73 respectively). By contrast, higher mother's educational level and altitude lowered the odds of malaria (AOR 0.30, 95%BCI 0.09, 0.94 and AOR 0.28, 95% BCI 0.16, 0.51) respectively. The combined usage was not associated with a change in malaria odds meanwhile fever two weeks before survey increased the odds of malaria (AOR 3.54, 95% BCI 2.07, 6.27)

Table 3.10 CAR model for combined ITN and ACT usage

Variables and categories	Bayesian adjusted odds ratios (credible intervals)

Child's age (months)	
6-11	ref
12-23	2.11 (1.16, 3.94)
24-35	2.65 (1.47, 4.92)
36-47	4.29 (2.32, 8.16)
48-59	3.74 (1.99, 7.18)
Mother's educational level	
No education	ref
Primary	0.66 (0.40, 1.09)
Secondary	0.64 (0.37, 1.08)
Higher	0.30 (0.09, 0.94)
Wealth Index	
Poorest	ref
Poorer	1.23 (0.74, 2.06)
Middle	1.07 (0.60, 1.91)
Richer	0.75 (0.37, 1.53)
Richest	0.57 (0.24, 1.32)
Place of residence	
Urban	ref
Rural	1.79 (1.17, 2.73)
Cluster altitude (meters)	
Less than 1000m above sea level	ref
Greater than 1000m above sea level	0.28 (0.16, 0.51)
Combined variable of ITN and ACT usage	
None	ref
no & untreated & ACT	0.64 (0.17, 2.04)
All children & untreated & no ACT	0.73 (0.11, 3.79)
All children & ITN & no ACT	0.91 (0.62, 1.34)
All children & ITN & ACT	0.75 (0.26, 2.01)
Some children & untreated & no ACT	1.79 (0.96. 3.36)
Some children & untreated & ACT	2.32 (0.30, 17.98)
Some children & ITN & no ACT	1.60 (0.91, 2.82)
Child had fever 2 weeks before survey	
No	ref
Yes	3.54 (2.07, 6.27)

A summary of the spatial random effects of significant predictors are depicted in the map of predicted malaria risk (figure 3.8). The combined effects showed that fever two weeks before, increased age and rural residence predicted highest malaria risk in Mayo-Sava division. On the contrary, higher cluster altitude and higher maternal education predicted lower risk predominantly in divisions of the Northwest, West and Littoral regions.



KEY: Grey areas= polygons without survey data

Figure 3.8 Predicted malaria probability on combined ITN and ACT usage

All three predicted maps are demonstrated in figure 3.9. Fever two weeks before survey, increased age and rural residence were drivers of high malaria clusters in all models. Cluster altitude was the driver of low predicted malaria risk in all three models. Higher socioeconomic status was a driver of low malaria risk in the ITN model. Meanwhile higher maternal education was a driver of low malaria risk in both ACT and Combined models.

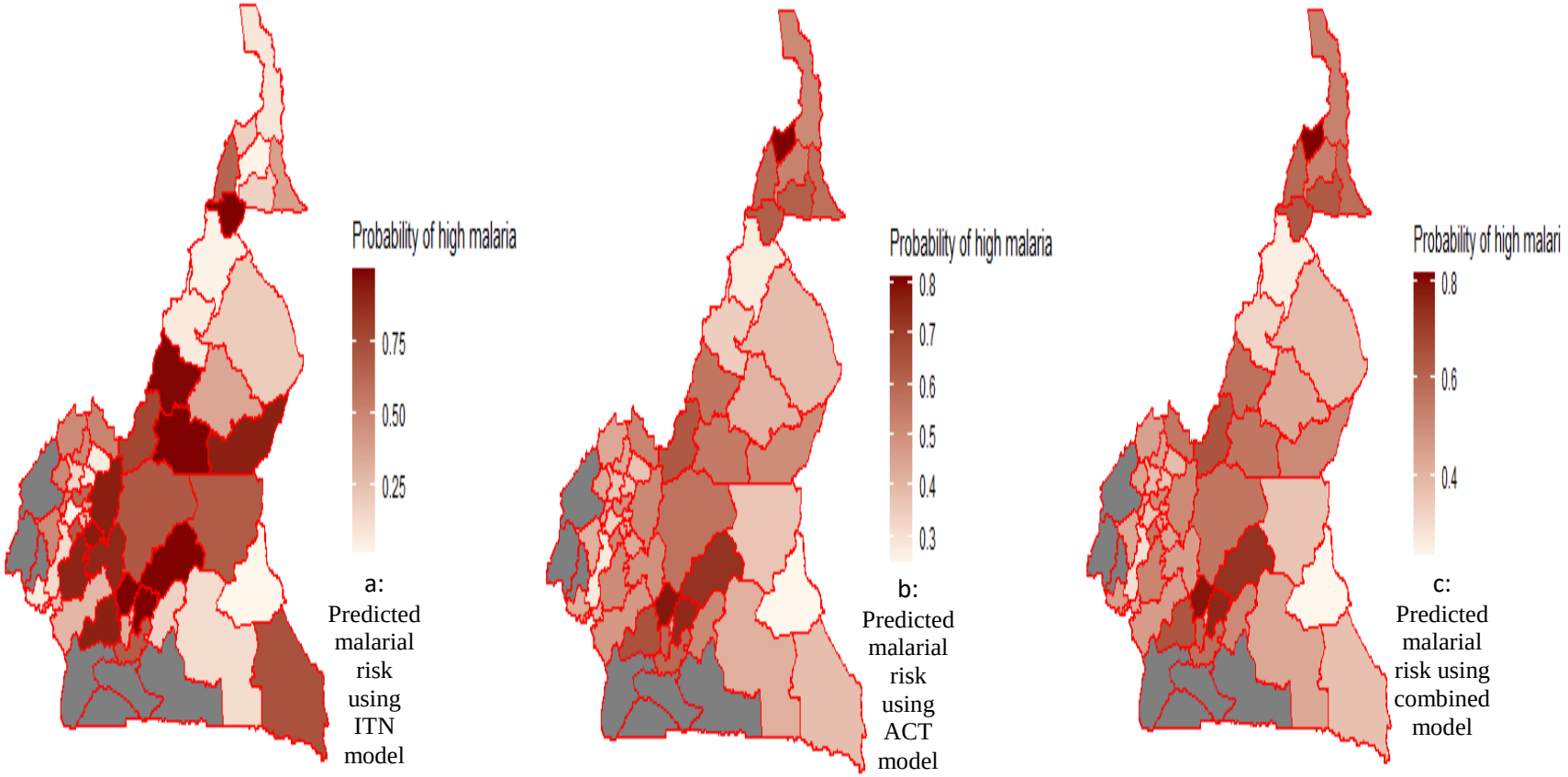


Figure 3.9 Maps of the predicted probability of malaria.

CHAPTER FOUR

DISCUSSION

4. Introduction

This chapter discusses the study's major findings, the meaning of the findings, and their relation to other similar studies. Next is the strengths and limitations of the study, leading to the study conclusion and recommendations.

Malaria is highly endemic in Cameroon with children under five years being the most vulnerable despite widespread provision of preventative and curative interventions (ITN and ACT) (9). This study examined the spatial distribution of malaria, ITN and ACT use among children under five years in Cameroon in 2018. Overall, the prevalence of malaria among children under five years was high (24%). Malaria hotspots were identified in the Adamawa, East, Centre and South regions while malaria cold spots were found in the the Northwest, West, Littoral and Southwest regions. History of Recent fever, rural residence and increased age (>36 months) contributed immensely in the high malaria prevalence. Low prevalence was associated with higher altitude, higher socioeconomic status and, in some divisions, higher maternal education. ITN usage was 58% and was highest in the Far-north and North regions. ACT use was low (5.5%) and highest in the Center region. ITN and ACT use were not significantly associated with change in malaria risk nationally. However, the combined ITN and ACT use demonstrated an increased malaria risk among some children who neither used ITN nor ACT.

4.1.1 Observed malaria prevalence

The observed prevalence of malaria varied across the divisions in Cameroon. This can be explained by the variability in malaria endemicity given the geographic diversity of Cameroon, and also the uneven distribution and use of interventions (7–9). Highest prevalence was observed in the Adamawa, Center and East regions due to low ITN usage in these regions. Also these regions are characterized by the large equatorial forest and two rainy seasons which are predisposing factors of malaria. The lowest prevalence in the West, Northwest and Southwest regions is as a result of hypo and holo-endemic transmissions respectively (7,8). These findings are similar to that obtained in a study which found low parasite risk in the West, Northwest and coastal regions, and high risk in the East (50). Contrarily they identified high malaria in the North and Far north region using the MIS data because the MIS is usually done during the raining season when transmission peaks especially in the North and Far-North regions. Also ITN coverage in 2011 was still very low and it was prior to the commencement of seasonal malaria chemoprevention in these two regions which only began in 2016.

4.1.2 Spatial autocorrelation

The finding of a statistically significant clustering pattern for malaria meant the children with malaria were closely related in terms of their geographical location and shared other common characteristics. This was similar to a longitudinal study in Cameroon which used the 2011 DHS geospatial covariate data in five-year intervals (2000-2015) (25). They found a clustering pattern for the 2000 and 2015 malaria years. However, no spatial correlation was observed for the 2005 and 2010 malaria years. Equally, a study by Ouédraogo et al found that malaria in children under five years in 24 districts in Burkina-Faso were spatially correlated (47).

4.1.3 Hot and cold spots

Malaria hotspots were located in the divisions of the Center, East, Adamawa and South regions. These areas are largely dominated by the equatorial evergreen forest and characterized by long rainy season which favors breeding of vectors. The Northwest, West and coastal areas (Southwest, Littoral) were identified as malaria cold spots. Tewara et al identified hotspots in the urban-rural clusters of the Center, East, West, Southwest, Yaoundé, Littoral, Douala and South regions (25). By contrast, they studied the general population in a longitudinal study whereas this study focused on children under five years in 2018. Studies elsewhere also identified significant clusters of malaria in inland and highland areas in Equatorial Guinea, Kenya and Nigeria (22,46,63)

4.1.4 Predicted malaria risk

Fever two weeks before survey, child's age, higher maternal education, higher altitude and rural residence were important predictors of malaria risk. Studies done in other settings had similar findings (43,49,64). Contrarily, some studies also found climatic and environmental factors as important drivers of malaria (43,45,49). Low malaria risk was predicted in the Northern and coastal regions whereas high risk was predicted in the Center region. Massoda Tonye et al also found low malaria risk in the north and coastal areas in their study using DHS data (50). The Mayo Sava division in the Far-North region was predicted to be a high risk in the ACT and combined model. This is probably due to epidemic seasonal malaria transmission usually during the rainy season in the Far-North region. Imelda et al also found high clusters in the northern region to be associated with the rainy season (26).

4.1.5 ITN usage

The proportion of children under five years that slept under an ITN the night before survey was 58%. This is similar to that reported by the national institute of statistics in the DHS report (10). However, ITN use is still below the 80% target of the national malaria control program by 2023(6). The divisions in North and Far north regions had the highest proportion of ITN usage. This could be attributed to the activities of the U.S president's malaria initiative which distributes and promotes the use of ITN in these two regions (6). The divisions in the East region and part of the center region had the lowest proportion of ITN usage.

This study surprisingly found that malaria odds were slightly increased for some children who slept under any type of mosquito net (either treated of not). This intriguing finding could be as a result of the in proper use of nets or insecticide resistance in case of ITNs. A study in Ghana reported similar findings which was attributed to the fact that children were more like put to sleep under nets only after they developed symptoms or tested positive for malaria (32). Another study in Rwanda demonstrated that the use of ITNs among children was not only influenced by a high coverage of intervention but an interaction of individual, household and community factors (65).

The fact that ITN usage in this study was not protective against malaria was contrary to local studies done in Cameroon involving rural and semi-urban communities. These studies found that regular use of ITN decreased susceptibility to malaria (20,34,35,66). In the same manner, a study in the Southwest region did not find a significant evidence that ITN reduced malaria prevalence (13). These studies were however limited to local levels with varied populations. Moreover, they did not use spatial statistical methods and did not adjust for clustering, random and spatial random

effects. Studies in different settings using spatial methods found varying results. For instance studies in Uganda, Burkina Faso and a study involving six Sub-Saharan African countries found ITN to be protective (31,43,45). But others found that ITN use was not associated with malaria nationally (32,52).

4.1.6 ACT usage

The proportion of children with fever two weeks before survey that were treated with ACT was 5.5%. Massode Tonye et al had similar findings in their study which showed the proportion of children treated with ACT to be 6% (50). The use of ACT was not significant given the low number of children with fever treated with ACT. This low use of ACT was also demonstrated in a study in Benin due to cost and unavailability (38). The low use of ACT in this study could possibly be due to supply chain problems and poor decentralization of services. Another reason could be due to health providers prescription preference of other antimalarials than ACTs and the unregulated private sector which dispense other types of antimalarials (9). Similar results were obtained in other countries among children with fever treated with ACT (43,52). However, a study in Uganda, found a strong association of ACTs with parasite risk reduction. This was attributed to a three-fold increase in ACT coverage (41). It has been proven in a randomized trial that parasite clearance was faster when ACT was used among febrile under-five Nigerian children (36). Also in Burkina Faso, the malaria case fatality rate was significantly reduced when ACT was used (67).

4.1.7 Combined ITN and ACT usage

The combined use of ITN and ACT in this study demonstrated that some children who slept under untreated nets and who did not use ACT had an increased risk of malaria. The untreated nets lacked insecticides to kill mosquitoes thus were not protective. Also the none use of ACT among those infected would allow progression to severe disease thus increasing the malaria prevalence in the population (39,41). Therefore, it is important to combine interventions to achieve a synergetic effect and effective control of malaria at different stages of disease lifecycle. The beneficial effect of combining ACT and ITN was also demonstrated in a study in Zanzibar to decrease *P. falciparum* prevalence, morbidity and mortality (40). Bhatt et al also showed that the combined use of ITN and ACT was most impactful in reducing malaria in Africa from 2000 to 2015 (39).

4.1.8 Sociodemographic, climatic and environmental risk factors of malaria

This study also showed that the likelihood of malaria was higher among the older children (>36 months) than their younger counterpart. This can be attributed to the fact that younger children acquire functional immunity from their mothers during pregnancy and breastfeeding which last only some months (14). Again, younger children are less active, mostly staying indoors and sleeping regularly for longer hours and can be easily confined to sleep under bed nets. As such they are less exposed to mosquito bites. In contrast, older children tend to be active and play especially outdoor with higher chances of being bitten by mosquitoes. The result was consistent with other studies which also found that older children were more likely to have malaria (43,49,68).

Children residing in rural areas were also more likely to have malaria. The increased risk was associated with low educational levels including poor knowledge of malaria control in the population living in these rural areas (50). In addition, the low coverage and usage of ITN in rural

areas increased the susceptibility to malaria (20). Similar studies showed that malaria prevalence increased in rural areas compared to urban areas (43,68). In the same vein, fever two weeks before was demonstrated to be strongly associated with increased malaria risk. Fever is a main symptom of the malaria. This was in line with findings from another study that showed malaria prevalence was higher in febrile subjects (24).

This study revealed that malaria risk decreased with increased wealth index as children from wealthier households were less prone. Socio-economic status has been said to influence access to healthcare services, better housing conditions, and knowledge of malaria prevention (41). Malaria risk was also lower among children whose mothers attained secondary and higher education. These findings were complemented by other studies which showed decreased risk with higher socioeconomic status and higher educational levels of mothers (43,49,68).

The likelihood of malaria was less with higher cluster altitude which could be as a result of effective drainage and low temperatures at higher elevation. These have been shown not to favor the survival of mosquitoes (23). Similar findings were obtained in Cameroon (24,50) and elsewhere (26,46).

Climatic factor (rainfall and temperature) were not significantly associated with malaria. This finding is unexpected since these climatic conditions favor the transmission of malaria (21,22,61). Temperatures ranging from 16°C to 30°C influences the development of malaria parasites within mosquitoes (15,18). Rainfall causes stagnant pools of water in inundated areas with poor drainage and these serve as breeding sites for some mosquito species with consequent increase in parasite

transmission (23). Similar findings were obtained in Tanzania were none of the climatic proxies was significantly associated with malaria risk (68). In contrast, studies done locally and elsewhere showed these predictors were positively associated with malaria risk (43,49,50,63,66). Varied results were obtained for environmental estimates of malaria risk in six countries in sub-Saharan Africa (Angola, Liberia, Mozambique, Senegal, Rwanda, and Tanzania) (45).

4.2 Strengths and Limitations

The strengths are discussed in the following categories; robustness of analytic methods and relevance of results. On the other hand, the limitations are discussed based on the study design, bias and confounding in the data.

4.2.1 Strengths

The study used robust Bayesian spatial statistical methods to give reliable estimates. It also accounted for cluster random effects and correlation of malaria in space due to common exposures affecting neighboring areas. To the best of the author's knowledge, this study was the first to examine the spatial malaria distribution and use of interventions at the divisional level in Cameroon. This was important to assess the decentralization of malaria services. In addition, it was able to assess the usage of two malaria control interventions on a national scale

4.2.2 Limitations

Being a cross-sectional study, causality cannot be established since the exposure and outcome variables were collected at the same period. The data was prone to recall bias as some variables were reported requiring the interviewee to remember past events. The data for the two English speaking regions of Cameroon (North West and South West regions) was underestimated because

of socio-political unrest during the time of the survey rendering it impossible to reach some areas in these regions. The GPS data was displaced up to 2km and 5km in urban and rural clusters respectively for confidentiality and this introduces random error in the results of the analysis. The RDT testkit used (SD BIOLINE Malaria Ag Pf/Pan) was shown have 99% and 92% sensitivity for *P falciparum* and other *Plasmodium* species respectively hence not all malaria cases could have been confirmed (69). In addition, the persistence of the residual histidine-rich protein 2 antigens for 42days after being treated and cleared of malaria can results in false positives when using RDT.

4.3 Conclusion

The study shows a high prevalence of malaria in children under five years in 2018 despite preventive and treatment efforts made towards control. The prevalence varied across the country suggesting more area-specific targeted actions against malaria. Recent fever, rural residence and increased age (>36 months) contributed significantly to high malaria prevalence in the Adamawa, Centre, East and South regions. Malaria prevalence was lowest in the Northwest, West, Littoral and Southwest regions. Low prevalence was associated with higher altitude, higher socioeconomic status and, in some divisions, higher maternal education.

Overall, the two interventions (ITN and ACT) were not significantly associated with change in malaria risk nationally as a sizeable percentage of children under five years did not use them. On average 58% of children slept under ITN the night before survey and this is still far below achieving the 80% target of the national malaria control program by 2023 (6). ITN usage was generally higher in the northern parts of the country due to donor support from PMI funding ITN

distribution in these regions (6,53). ITN usage was lowest in the East and Center regions which explains the high malaria prevalence in these regions.

Children who recently had fever and were given ACT was low (5.5%) probably due to supply chain problems and low ACT prescriptions compared to other antimalarial drugs. The findings suggest the need for increased use of ACT as another way of reducing malaria mortality in children under five years. The combined use of ITN and ACT was important as some children who neither used ITN nor ACT had heightened risk of malaria. High usage of different interventions is therefore required especially in combination to achieve a strong and synergistic effect on parasite risk reduction

The mapping of malaria prevalence and interventions provides useful information to the NMCP for planning, identifying places where prevalence is high and providing focused interventions. In addition, looking at spatial trends over time, will enable the effect of interventions to be assessed.

4.4 Recommendations

- Based on findings of this study, the malaria prevalence among children under five years can be drastically reduced if the coverage and utilization of ITN and ACT are optimized in order to achieved a “mass effect”. The type of insecticidal nets should be based on their sensitivity to specific entomologic vector species predominant in a given area for effective reduction of the mosquito population in the community. ITN Coverage can be increased by using distribution channels such as the Expanded Program for Immunization, antenatal clinics and the sale of subsidized ITNs in the private sector. The NMCP should address supply chain problems limiting ACTs scale-up and encouraging all healthcare providers to

prescribe ACT. Also private health facilities and drug stores should be regulated to prescribe the recommended ACT than other types of antimalarial for uncomplicated malaria.

- An integrated approach should be adopted and additional vector interventions such as IRS, larval control, repellants, outdoor vector management being implemented targeting those areas with little entomological resistance. Although resistance to ACTs have not yet been widely observed, while increasing its used, there is a need for molecular and epidemiological surveillance activities to monitor the emergence of artemisinin resistance.
- Information, education and communication of malaria prevention and treatment services should be intensified by the National Malaria Control Programme especially in rural areas where malaria burden is high. Community health workers should be involved in sensitizing and educating rural communities on the use of control measures. In the same vein maternal education should be promoted as increased maternal education is a driver of lower malaria risk.
- Advocacy should be made to funders like the U.S. President's Malaria Initiative to also sponsor ITN distribution in the hotspot areas like the East, South and Center regions.
- The NMCP should ensure even access of malaria control interventions between rural and urban areas.
- Finally, more studies should be carried out with a larger sample size to explore the gains in combining both preventive and therapeutic intervention strategies in order to curb the spread of malaria.

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Appendix A

A.1 Plagiarism Declaration



PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I **Sylvie Ngum Njong** (Student number: **2213554**) am a student registered for the degree of **Master of Science in Epidemiology in the field of Implementation Science** in the academic year **2020**.

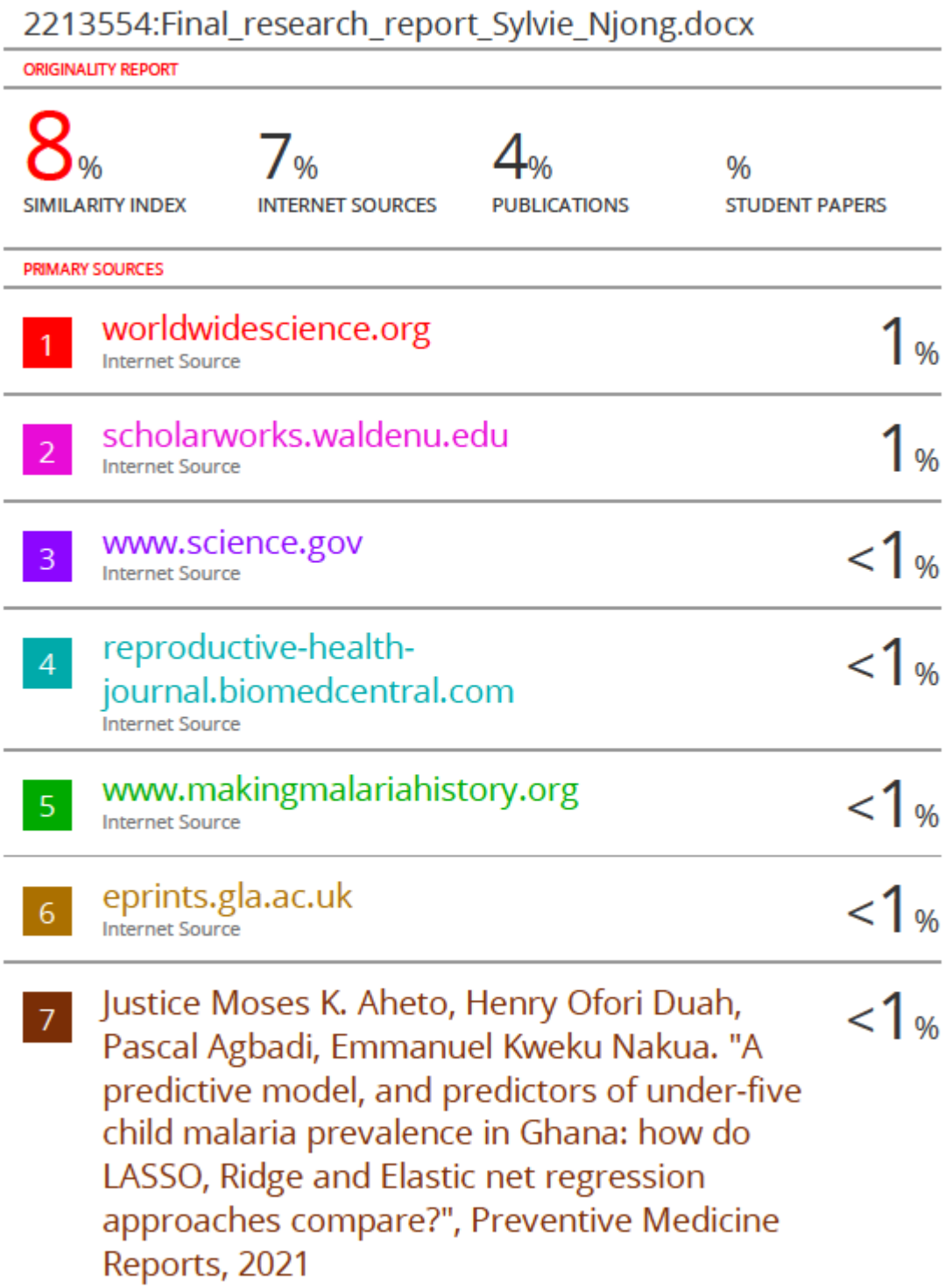
I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: 

Date: July 29th 2021

A.2 Turnitin report



2213554:Final_research_report_Sylvie_Njong.docx

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6	eprints.gla.ac.uk Internet Source	<1%
7	Justice Moses K. Aheto, Henry Ofori Duah, Pascal Agbadi, Emmanuel Kweku Nakua. "A predictive model, and predictors of under-five child malaria prevalence in Ghana: how do LASSO, Ridge and Elastic net regression approaches compare?", Preventive Medicine Reports, 2021	<1%

A.3 Ethics clearance certificate

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

R 14/49 Dr Sylvie Njong

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M210276

NAME: (Principal Investigator)	Dr Sylvie Njong
DEPARTMENT:	School of Public Health - Epidemiology and Biostatistics
PROJECT TITLE:	Spatial malaria distribution and, insecticide-treated bed nets and artemisinin combination therapy usage among children under-five years in Cameroon, 2018
DATE CONSIDERED:	26/02/2021
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Ntombizodwa Ndlovu and Prof Eustasius Musenge

APPROVED BY: Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 06/04/2021

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and ONE COPY returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. I agree to submit a yearly progress report. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in February and will therefore be due in the month of February each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature — Date: 07/04/2021

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

A.4 Demographic and health survey authorisation letter

Dec 07, 2020

NJONG SYLVIA
University of the Witwatersrand
South Africa
Phone: (+27) 615276370
Email: njongsylvia@gmail.com
Request Date: 12/05/2020

Dear NJONG SYLVIA:

This is to confirm that you are approved to use the following Survey Datasets for your registered research paper titled: "SPATIAL DISTRIBUTION OF MALARIA AND THE USE OF BED-NETS AND ARTEMISININ COMBINATION THERAPY AMONG CHILDREN UNDER-FIVE YEARS IN CAMEROON, 2018":

Cameroon

To access the datasets, please login at: https://www.dhsprogram.com/data/dataset_admin/login_main.cfm. The user name is the registered email address, and the password is the one selected during registration.

The IRB-approved procedures for DHS public-use datasets do not in any way allow respondents, households, or sample communities to be identified. There are no names of individuals or household addresses in the data files. The geographic identifiers only go down to the regional level (where regions are typically very large geographical areas encompassing several states/provinces). Each enumeration area (Primary Sampling Unit) has a PSU number in the data file, but the PSU numbers do not have any labels to indicate their names or locations. In surveys that collect GIS coordinates in the field, the coordinates are only for the enumeration area (EA) as a whole, and not for individual households, and the measured coordinates are randomly displaced within a large geographic area so that specific enumeration areas cannot be identified.

The DHS Data may be used only for the purpose of statistical reporting and analysis, and only for your registered research. To use the data for another purpose, a new research project must be registered. All DHS data should be treated as confidential, and no effort should be made to identify any household or individual respondent interviewed in the survey. Please reference the complete terms of use at: https://dhsprogram.com/Data/terms-of-use.cfm.

The data must not be passed on to other researchers without the written consent of DHS. However, if you have coresearchers registered in your account for this research paper, you are authorized to share the data with them. All data users are required to submit an electronic copy (pdf) of any reports/publications resulting from using the DHS data files to: references@dhsprogram.com.

Sincerely,

Bridgette Wellington

Bridgette Wellington
Data Archivist
The Demographic and Health Surveys (DHS) Program

530 Gaither Road, Suite 500, Rockville, MD 20850 USA +1.301.407.6500 +1.301.407.6501 fax icf.com

APPENDIX B

B.1 Longitudes and Latitudes of Cameroon



Figure 2: Map of Cameroon showing the longitudes and latitude

Source: Encyclopaedia Britannica.com

B.2 Power computation

The formula for power computation is given below

$$Z_\beta = \sqrt{\frac{k-1}{(p_a-p_0)(Bcv_{sizes}+1)\rho}} - Z\propto_{/2}$$ Where power = 1- $\boldsymbol{\beta}$

A previous malaria prevalence among children under five years using the 2011 DHS was 33% (p_o). The prevalence from the 2018 dataset was 24% (p_a). The intra-cluster correlation was 0.02 (ρ), from a total of 428 clusters, with an average cluster size of 11 (m) and a coefficient of variation of cluster size of 5.97 (Bcv_{sizes}). The power was calculated to be at least 90% at 0.05 significance.

Stata synthax for power.

clustersampsi, binomial power p1(0.33) p2(0.24) m(11) k(428) rho(0.02) size_cv(5.97) base_correl(0)