PREDICTORS OF PRESUMPTIVE TREATMENT OF UNCOMPLICATED MALARIA AMONG CHILDREN IN PRIVATE RETAIL OUTLETS IN KENYA: MIXED EFFECTS LOGISTIC REGRESSION MODELLING

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

Name:…….. **Registration No:……**

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SUPERVISOR'S APPROVAL

This thesis has been submitted for examination with our approval as university supervisors in partial fulfilment for the award of the Master of Science degree in Medical Statistics at the University of Nairobi.

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DEDICATION

I would like to dedicate this thesis to my family, friends, and the University of Nairobi staff for their encouragement and support.

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LIST OF ABBREVIATIONS

ACTs	Artemisinin-based Combination Therapies
AMFm	Affordable Medicines facility – malaria
FBO	Faith-Based Organization
LLIN	Long Lasting Insecticide Treated Net
MOH	Ministry of Health
DNMP	National Malaria Control Program
PPB	Pharmacy and Poisons Board of Kenya
QAACTs	Quality-Assured Artemisinin Combination Therapies
DHAPPQ	Dihydroartemisinin - Piperaquine
RDTs	Rapid Diagnostic Tests
SOPs	Standard Operating Procedures
SP	Sulfadoxine-Pyrimethamine

DEFINITION OF TERMS

Presumptive treatment: A one – time treatment for an infection that is presumed (based on probability) in an individual or group of individuals based on the risk of infection or the signs and symptoms.

Health care provider: An individual who provides health related services to a patient/patient in a health seeking setting.

Retail outlet: A store that sells services or products in smaller quantities to the general public.

Logistic regression: A statistical method/approach of analyzing data where the outcome variable is binary (dichotomous).

Mixed effects models: A model where the predictor variables has both the fixed and random effects to account for cluster correlations.

Rapid Diagnostic Test (RDTs): This is a medical diagnostic test for malaria to detect presence of malaria parasites in human blood.

Artemisinin-based Combination Therapies (ACTs) – Antimalarial drugs with a combination of therapies e.g. Dihydroartemisinin – Piperaquine (DHAPPQ), Sulfadoxine-Pyrimethamine (SP).

ABSTRACT

Background: The health seeking behavior in Kenya raises concerns in malaria case management at the private sector. Adherence to the national guidelines for the diagnosis, treatment and prevention of malaria is key in management of malaria. Presumptive treatment remains to be a major challenge in Kenya especially in the private sector with major gaps in literature identified on predictors of this treatment. Taking into account county clustering is key in modelling the predictors of presumptive treatment to strengthen interventions. Mixed-effects regression modelling takes into account county clustering, is more accurate in prediction and more efficient and flexible.

Objective: The study modeled predictors of presumptive treatment of uncomplicated malaria among children in the private retail outlets in Kenya using the mixed effects logistic regression model.

Methodology: The study design was a cross-sectional, nationally representative, retail outlet survey secondary data analysis. The study populations included the health care providers in the retail outlets sampled randomly in both the rural and urban settings in Kenya. The primary outcome of interest was the proportion of health care providers who treated patients presumptively. Descriptive statistics formed the basis of analysis for the selected indicators through frequencies and percentages. Bivariate analysis taking onto account county clustering was conducted to measure the factors associated with presumptive treatment of uncomplicated malaria. Finally, multivariable analysis was conducted for the significant variables adjusting for clustering at the county level to determine the predictors of presumptive treatment. The best fitting model was examined using the Akaike Information Criterion (AIC). Analysis was conducted using STATA and R software.

Findings: Out of the 333 health care providers who treated the patient's 190 (57 percent) treated patients presumptively. The factors that were significantly associated with presumptive treatment adjusting for county clustering at 95% CI were health care providers who asked signs or symptoms, presented with results and access to national guidelines for malaria treatment. All these predictors were negatively associated at (OR=0.24; P-value=<0.001; 95% CI= (0.13 - 0.45), (OR=0.08; P-value = <0.001; 95% CI = (0.03 - 0.20) and (OR = 0.49; P-value = 0.038; 95% CI = (0.25 - 0.96) respectively. Finally, the predictors of presumptive treatment of uncomplicated malaria were case management training (AOR = 0.44; 95% CI = (0.18 – 1.09)), asked signs or symptoms (AOR = 0.19; 95% CI = (0.10 - 0.37)) and results presented (AOR = 0.08 95% CI = (0.03 - 0.19)).

Conclusion: Presumptive treatment of uncomplicated malaria remains to be a challenge in the private retail sector. However, case management training and health care providers asking of signs and symptoms and results presented predicts presumptive treatment. Specifically a health care provider who has gone through all the three factors has a lower probability of treating a patient presumptively compared to the other case scenarios.

CHAPTER 1: INTRODUCTION

1.1 Background

Malaria is a health problem across the globe and the World Health Organization (WHO) estimates that nearly a half (3.4 billion) of the population in the world is at risk of the disease [1]. WHO African region continues to have a disproportionately global malaria burden. According to the 2018 WHO malaria report, in 2017 the region reported 92% and 93% of malaria morbidity and mortality respectively [2]. In 2010, Kenya adopted the Test and Treat case management policy by WHO which is in line with the malaria treatment guidelines in Kenya [3].

Although the burden is high in Sub-Saharan Africa, Kenya has made major efforts to reduce and eliminate malaria. The Ministry of Health through the National Malaria Control Program has implemented comprehensive evidence-based strategies and policies to fight this disease. The key interventions used include the provision of mosquito nets and indoor residual spraying of households for vector control, case-management interventions & surveillance and monitoring and evaluation. Case management focuses on prompt diagnosis, effective treatment, capacity building among health workers and provision of quality diagnostics and effective medicines in all health facilities [4].

To ensure universal health coverage of these interventions, recognition of the private sector's role in malaria is clearly stated as one of the strategies of case management for the Division of National Malaria Programme. This includes ensuring access to affordable malaria medicines, training of health workers among others [4]. Though medical care is majorly sought in the public sector by the population, up to 25% of the population medical care is sought from the private sector [5]. However, there were challenges in access in the private sector primarily due to price [6] .

The Affordable Medicine Facility for malaria (AMFm), was implemented in nine countries as a pilot activity including Kenya between mid-2010 and 2012. The four major objectives of the AMFm was to increase ACTs availability, affordability and use. [7]. The AMFm went through a transition

of two years finally adapting to the private sector co-pay where grant funds were dedicated at initio to procure subsidized medicines and implement supporting interventions. The AMFm strategy has been proved to be effective in the countries piloted [8].

Though ACTs and RDTs have been made available in the private sector in Kenya, adherence to the national guidelines for malaria treatment is key by the health care providers. Several studies have shown that children are treated presumptively especially when they have fever cases [9]–[13]. This study sought to understand the predictors of uncomplicated malaria presumptive treatment among children in the private retail sector in Kenya.

Logistic regression is a statistical method of analysis that is used when the dependent (outcome) variable is binary (dichotomous) [14]. In this study, the outcome variable is presumptive treatment (Yes/No) which is a binary outcome variable. Mixed effects models on the other hand means that the predictor variables includes both the fixed and random effects whereby the random effects adjust for cluster correlations with multilevel data [15]. The health care providers in this study are nested in the retail outlets which are nested in the counties. The predictor variables included the county as the random effect to adjust for inter-county correlations. This study used the application of mixed effects logistic regression model to predict treatment of children with uncomplicated malaria presumptively in the retail outlets.

1.2 Problem statement

Malaria remains a major cause of mortality and morbidity and more than 70% of the population in Kenya is at risk. Monitoring has been done to assess the quality of care of both inpatients and outpatients in the public sector through surveys. However, medical care is sought by about 25% of the population in the private sector in Kenya. Health workers undergo case management trainings to build their capacity on management of Malaria. WHO recommends that all suspected cases should be tested using microscopy or Rapid Diagnostic Tests (RDTs) before being treated with an antimalarial drug.

Despite Kenya adopting the Test and Treat policy in 2010, several studies have reported presumptive treatment of malaria specifically in children [9]–[13], [16]. In the primary study, 53.2% and 78.6% of the patients who tested negative for malaria and those without a test respectively were prescribed with an AL. Presumptive treatment of malaria causes irrational use of ACTs as well as lack of treatment of other febrile illnesses that may have symptoms almost similar to malaria. However, gaps identified in literature include determining predictors of presumptive treatment of children with uncomplicated malaria in the retail outlets.

1.3 Research objectives

1.3.1 Broad objective

To apply mixed effects logistic regression modelling in determining the predictors of presumptive treatment of children with uncomplicated malaria in the private retail outlets in Kenya.

1.3.2 Specific objectives

1. To determine the proportion of health care providers who treat uncomplicated malaria presumptively among children in the retail outlets.
2. Todetermine the factors associated with presumptive treatment of uncomplicated malaria among children in the retail outlets.
3. To model predictors of presumptive treatment of uncomplicated malaria among children in the retail outlets using mixed effects logistic regression.

1.4 Research questions

1. What is the proportion of health care providers who treat malaria presumptively among children in the retail outlets?
2. What is the best fitting mixed effects logistic regression model for prediction of presumptive treatment of uncomplicated malaria among children in the retail outlets?

1.5 Hypotheses

Null hypotheses

There is no association between presumptive treatment of uncomplicated malaria among children and the predictor variables.

Alternative hypotheses

There is an association between presumptive treatment of uncomplicated malaria among children and the predictor variables.

NB: The predictor variables that were tested were: Zone, RDTs availability, ACTs availability, Drug price, Cadre, asked any signs/symptoms, case management trading, results presented, any supervision, access to national malaria case management guidelines.

1.6 Justification for the study

The health seeking behavior in Kenya raises concerns in improvement in provision of health services in the private retail sector. About 25% of the population in Kenya seek medical care from the private retails sector [5]. The AMFm has made ACTs available in the private retail sector through co-payment done at the manufacturer level to enable public and private buyers in approved countries purchase high-quality ACTs at a fraction of the market price. Though there is access to medicines at affordable prices as well as health worker capacity building on management of malaria, adherence to the national guidelines for the treatment of malaria is a key factor to be considered by the health care providers.

“Inappropriate” treatment practices (presumptive treatment) of uncomplicated malaria among children could be caused several factors. This study examined these factors using a mixed effects logistic regression model. This study will inform strengthening of interventions in malaria management in the private sector. The study will also give insight for further research on malaria in the private retail sector.

1.7 Scope of the study

This study focused on application of mixed effects logistic regression modelling in establishing the predictors of treatment of children with uncomplicated malaria presumptively in the private retail sector in Kenya.

CHAPTER 2: LITERATURE REVIEW

Preamble

An overview of uncomplicated malaria treatment has been given in this section, the private retail sector behavior, presumptive uncomplicated malaria treatment, and potential predictors of presumptive treatment of uncomplicated malaria among children. This literature review examined peer-reviewed, journal articles and published resources relevant globally, in the sub-Saharan Africa and finally in Kenya. Finally, the methodological review has expounded on the modelling touching on the overview of mixed effects logistic regression modelling.

Overview of treatment of uncomplicated malaria among children

The World Health Organization (WHO) recommends that all malaria cases suspected should be tested through microscopy or rapid diagnostic tests (RDTs) before treatment. All uncomplicated plasmodium falciparum confirmed malaria cases for children need to be treated with artemisinin-based combination therapy (ACTs) e.g. Arthemether lumefantrine (AL) [17]. The United Kingdom malaria treatment guidelines also have recommended testing of all suspected malaria cases prior to treatment. Though there is almost no use of the ACTs in the non-endemic paediatric population, they are recommended as the first-line treatment of uncomplicated malaria for children in the endemic regions[18].

A study was conducted in the Sub-saharan Africa region to compare treatment of uncomplicated malaria using ACTs for children. The study found ACTs being most effective in uncomplicated malaria treatment. The major challenges however are high cost, availability, poor delivery and weak health care systems. The study further recommended improved supply chain management and reduction of ACTs prices in the private sector [19]. In a clinical trial conducted in Ghana to study the efficacy of antimalarial drugs, 168 children under 5 years were evaluated clinically and there was 100% cure rates on the 28^{th} day for amodiaquine + artesunate; AL (coartem) – 97.5%,

Sulphadoxine Pyrimethamine (SP) – 60% and chloroquine – 25%. The study found out that ACTs should be used in treatment of children with uncomplicated malaria [20].

In 2010, Kenya adopted the test and treat strategy and the rapid diagnostic tests (RDTs) were launched officially as one of the milestones in reducing malaria in Kenya. This translates to testing a patient either through microscopy or RDTs before treatment [4]. A randomized clinical trial (RCT) was conducted in Kenya to compare AL and DHAPPQ in the treatment of children with uncomplicated malaria. Log rank test was employed to compare the survival curves for the two ACTs where parasitological and clinical response rate was 83% at the DHAPPQ arm and 61% in the AL arm (p-value = 0.001). The study then concluded that DHAPPQ is effective for children with uncomplicated malaria in western Kenya [21]. Several other studies have shown that ACTs are the best drugs for treatment of uncomplicated malaria [22]–[26].

Treatment seeking behavior in the private retail sector

In 2018, the World Health Organization (WHO) convened a technical consultation on universal access to core malaria interventions in high malaria burden countries. The private sector is often the closest place to seek health care for patients in most of the cases. It recommended that training, supervision and other interventions would be useful in improving the quality of care of malaria patients in the private retail sector. The consultation concluded that the private drug retail sector is important in delivering quality of care for malaria patients in high burden countries in both rural and urban areas [27].

A study was conducted in five Sub-Saharan Africa countries (Kenya, Ghana, Nigeria, Tanzania & Uganda) on malaria treatment seeking patterns in retail outlets. The study concluded that the private sector plays a crucial role in management of fever cases in the Sub-Saharan Africa. The study further recommended that there is a need to understand retail outlet needs so as to provide a design of effective malaria interventions [28].

In Kenya, about 25% of the population seek treatment fromm the Retail outlet[5]. In a study that was conducted in Kenya, social economic factors influenced treatment seeking behavior with a majority of the patients seeking treatment from the private retail sector [29]. In another study that was conducted in Kenya to access prompt and effective malaria treatment barriers among the Kenya poorest population. about 40 percent of the participants preferred self-treatment by purchasing drugs from the retail outlets [30].

Presumptive treatment of uncomplicated malaria

A systematic review was conducted to review the performance of different health care providers in order to scale up malaria treatment. The review found out that over-prescription of medicine leads to a high risk in term of treatment in the private retail sector. The risk was identified as the inability to test and treat non-malarial fevers. The study recommended investing in the private retail providers to improve the quality of case management of malaria. [31].

Another systematic review was conducted in countries within the Sub-Saharan Africa to evaluate the necessity of "test and treat" strategy in the high malaria endemic zones. The review concluded that there is relevance of a diagnostic test if the region is of low parasite prevalence. However, if the prevalence is high, the test does not provide information of any clinical usefulness amongst children[32].

In 2015, a cluster randomized trial was conducted in Ghana whereby out of 4603 patients, the test negatives for malaria by RDT were 74%. RDTs were provided in the treatment arm where 32% and 88% in the treatment and control arm respectively received an antimalarial drug. The study recommended provision of RDTs in the private retail sector for the purpose of reducing presumptive treatment of uncomplicated malaria [33]. Another study was conducted in Nigeria where presumptive treatment of malaria remains widespread even with the recommendation of the teat treat strategy by WHO [34].

In Kenya, a survey was conducted where 47% out of 11,505 children with fever were treated with an antimalarial drug even before testing but during this period presumptive treatment was recommended [35]. In another survey conducted in the coastal area of Kenya, antimalarial provision to test-negatives ranged between 0 to 13.9% in retail outlets [36].

Potential predictors of presumptive treatment of uncomplicated malaria

Recent studies have shown that there is limited knowledge by health care providers in the private retail sector through a systematic review conducted for developing countries [37]. However, though there is improved knowledge there are still levels of presumptive treatment of malaria in the private sector amongst children [38].

In Tanzania, a randomized trial was conducted in the pharmacies where out 1204 of children 1,005 (85%) tested negative for malaria by RDTs. However, 54% of the patients test-negatives were treated for malaria (OR = 1.13; 95% CI = (0.95 - 1.34; p-value = 0.18). The study concluded that there is over-treatment of malaria even with the negative test results and recommended interventions to improve health care providers management of fever patients in the private retail sector [39].

A cluster randomized control trial that was conducted in Kenya with the intervention arm having patients who had gone for at least one training on case management. The study using a binary logistic regression model found out that providers in the intervention arm significantly increased antimalarial prescription presumptively by 23.6% (95% CI = (18.7 - 28.6); p-value=0.0001) [40].

A cluster randomized trial that was conducted in Ghana to examine the RDTs provision impact on management of fever in the retail outlets. The study found a significant association between RDT availability and presumptive treatment of malaria (RR= 0.41;95% CI = (0.29 - 0.58); p-value<0.0001)) [33].

In a study that was conducted in Nigeria, though there was RDTs availability in the retail sector, the perception of health care workers on unreliability of RDTs increases presumptive treatment of malaria (p-value<0.0001). The study also found out that availability of antimalarial drugs in the retail outlets increased presumptive treatment of malaria ($p = 0.027$). The study concluded that interventions to improve the private retail sector should be priority [41].

A study was conducted in rural Tanzania, where the price of ACTs was significantly less for children than adults ($p<0.001$). The study concluded that the AMFm subsidy in the private retail sector can significantly increase the use of ACTs which might lead to presumptive treatment. However, adherence to the treatment guidelines should be key in treatment of malaria [42].

Application of mixed effects logistic regression modelling

Generalized linear mixed models (GLMMs) are an extension of the class of generalized linear models (GLMs) in which both fixed and random effects as predictor variables. The generalized mixed models (GLMs) models are used when the outcome variables not continuous but follows other types of probability distributions [43]. GLMMs allows the modeling of correlated, perhaps data which is not normally distributed with flexible room of covariates [44]. Fixed effects are predictors that describe the effect of a factor in ordinary linear models. A random effect on the other hand are predictors that describe predictor variable representing a cluster e.g. if retail outlets are located within counties then the county is the cluster which is the random effect [45].

Binary logistic regression modelling is used when the outcome variable is binary i.e. has two categories [46]. Suppose we have health workers nested within health facilities which are nested within counties. If we have an outcome of interest for health workers, fixed effects and random effects an illustration of a two-level model with random effects with a binary outcome is given below [59]:

$$\text{Logit}(p_i) = \beta_0 + \beta_1 X_{1i} + \ldots\ldots + \beta_k X_{ki} + u_{group(i)}\ ; \text{where } u_{group(i)} \sim N(0,\delta_g^2)$$

Where:

$\mathbf{p_i}$ is the probability of the outcome of interest happening

i is the individual in a given group

β's are the regression coefficients

$\mathbf{X_i s}$ are the predictor values for the i^{th} individual

$\boldsymbol{u}_{group(i)}$ is the random effect for the group containing individual *i*

K is the number of predictor variable

The determinants of the accuracy of a model are based on the likelihood of the model to predict the future. The measure of likelihood determines the best fitting accurate model to be considered for prediction [47]. The Akaike Information Criterion (AIC) is used to measure the best fitting model for prediction [48]. The mixed effects models typically produces optimally low standard errors hence this method is more accurate compared to a generalized linear model [49].

Mixed effects models are recommended for repeated measures and hierarchical data, which provides flexibility for studying data with both fixed and random effects. Since the mixed effects models provides shrinkage in estimates for the associated units sampled with a random effect factor, the model provides enhanced prediction accuracy [49]. The mixed effects models has been illustrated to be more efficient and flexible, and can handle missing data more effectively[50].

Several studies have been conducted in the health sector using the mixed effects logistic regression model for prediction. In Australia a study was conducted to determine the use of cannabis in adolescence predisposes higher rates of anxiety and depression in younger adulthood. A mixed effect regression model was used to adjust for correlation of participants over time. The study concluded that teenage girls who frequently use cannabis predicts anxiety and depression with girl who use the drug daily being at the highest risk. The study recommended interventions to reduce

cannabis use among girls in adolescence [51]. Another study was conducted in Kenya to compare insecticide-treated bed net use to Malaria infection among schoolchildren. Five thousand one hundred and eighty eight children in 54 schools were randomly sampled and a mixed effect logistic regression was used to account for the hierarchical nature of the data to adjust for clustering in the different schools. After adjusting for schools, there was a significant odds reduction by 14 percent [52]. Several other health studies have been conducted using the mixed effects regression models approach to adjust for clustering [53]–[56].

In this study, mixed effects logistic regression was applied to predict presumptive treatment of malaria among children. Health care providers have been nested within retail outlets and retail outlets nested within counties. The outcome variable was binary and the predictor variables were have both fixed and random effects. The model was:

$$\text{Logit}\,(p_i) = \beta_0 + \beta_1 X_{1i} + \ldots\ldots + \beta_k X_{ki} + u_{county\ (i)}\ ;\ \text{where}\ u_{county\ (i)} \sim N(0,\delta_c^2)$$

Where:

$\mathbf{p_i}$ is the probability of the outcome of interest happening

i is the individual in a given group

β's are the regression coefficients

$\mathbf{X_i s}$ are the predictor values for the i^{th} individual

$u_{county\ (i)}$ is the random effect for the county containing individual *i*

K is the number of predictor variable

CHAPTER 3: METHODOLOGY

Preamble

This chapter describes the study area, the research design, and the study population. It also includes the sampling procedure and sample size determination. It details the data collection procedure, the study variables clearly showing the dependent and independent variables.

3.1 Study design

This study design was a secondary data analysis from a cross-sectional, nationally representative, retail outlet survey that was measuring levels in key indicators on availability of ACTs and RDTs, and dispensing practices of ACTs in accordance with the diagnosis, treatment and prevention national treatment guidelines for malaria in Kenya.

This secondary analysis proposed in this study explored the predictors of 'inappropriate 'treatment practices (presumptive treatment) of health care providers in the retail outlets in Kenya.

3.2 Study area

The study adopted the study area for the primary study that was conducted in the retail outlets sampled randomly from all the counties in Kenya.

3.3 Study populations

The study populations included the health care providers who treated the patients in the retail outlets sampled randomly in both the rural and urban settings in Kenya.

The inclusion and exclusion criteria was as follows:

3.3.1 Inclusion criteria

Inclusion criteria are:

- Privately owned retail outlets

- Predominantly dispensing retail outlets
- Health care providers who treated patients

3.3.2 Exclusion criteria

Exclusion criteria are:

- Public facilities, faith-based outlets and NGOs
- Non-functional outlets
- Pharmacies within a private facility
- Health care providers who did not treat patients

3.4 Sample size determination and sampling procedure

3.4.1 Sample size determination

This study adopted the sample size in the primary study that was determined based on the Cochran's formula [47]:

$$n = \frac{Z^2 * p * q}{d^2}$$

Where:

n = the desired sample size

Z = standard normal deviate at required 95% confidence level =1.96

p = Variability in the proportion of patients treated in the private sector assumed to be 50% [57]

q = 1-p

d = margin of error = 0.05

To cater for non-response the sample was raised by 5%, hence the sample size was 405.

3.4.2 Sampling procedure

This study used the data for the health care providers who treated the patients during the primary study. In the primary study, a multistage random sampling method was used to obtain data in the retail outlets with each outlet having one health care provider interviewed. Specifically, all the 47 counties were included in the survey but the sampling was done in two categories. In the first category, 43 counties with less than 10 sub-counties with 2 sub-counties randomly sampled while in the second category, 4 counties namely; Nairobi, Kiambu, Kakamega and Nakuru with more than 10 sub-counties with 4 sub-counties were randomly sampled.

In the first stage for the first category, 2 sub-counties were randomly sampled. In the second stage, a rural and an urban area were randomly sampled from each sub-county. In the third stage, each of the rural/urban setting with two retail outlets was sampled; one registered and one unregistered. However, two registered retail outlets in the sub-county were selected. (If 2 or less, all were selected, if more than 2, the researcher randomly selected 2) and two unregistered retail outlets in the Sub-county were selected to a maximum of 2 (If 2 or less, all were sampled, if more than 2, researcher randomly sampled 2). A total of 8 outlets were sampled in each of the counties for this category.

In the first stage for the second category, 4 sub-counties were randomly sampled. In the second stage, a rural and an urban area were randomly sampled from each sub-county (with the exception of Nairobi where researchers went to one that is a relatively formal settlement and one that is a relatively informal settlement (slum). In the third stage, each of the rural/urban setting had two retail outlets sampled; one registered and one unregistered. However, two registered retail outlets in the sub-county were selected. (If 2 or less, all were sampled, if more than 2, researcher randomly sampled 2) and two unregistered retail outlets in the Sub-county were selected to a maximum of 2 (If 2 or less, all were sampled, if more than 2, researcher randomly sampled 2). A total of 16 retail outlets were sampled in each of the counties for this category.

The list of the unregistered retail outlets was obtained from the county pharmacist, the drug inspectors or the public health officer. Registered retail outlets were more likely to be around the municipal areas unlike the unregistered ones. The registered retail outlets were selected from a list from the pharmacy and Poisons Board (PPB). A total of 405 outlets were assessed.

3.5 Data collection procedure

This study drew the data from the primary study that was conducted in September 2018 in the sampled private retail outlets in Kenya. The primary study accessed the availability of ACTs and RDTs and the dispensing practices of the health care providers in the private retail outlets. The data was valuable in this study since presumptive treatment was identified from the primary study report and the variables to look into the predictors of this treatment were available for this study. The data was requested from the Division of National Malaria Programme (DNMP) for secondary data analysis in this study. The variables not of interest from the primary data were dropped leaving the variables of interest to be used in this study. After the study conclusions for the primary study, the primary researcher had planned to store the data for a period of 5 years.

During the primary study, each survey team consisting of two persons visited a number of facilities as assigned. For the mystery shopper to yield positive results, only one of the data collectors obtained consent and administered the survey questionnaire while the other posed as the mystery shopper. One member of the team introduced him/herself to the outlet staff and seek audience with the superintendent. The superintendent of the retail outlets was told that the DNMP was monitoring national availability of case management for malaria commodities and malaria case management practices as part of the DNMP's Monitoring and Evaluation activities. He/she was advised on the confidentiality of the results. The data collectors were given a letter from the MoH specifying the nature and purpose of the survey.

One method was through administration of a standardized retail outlets questionnaire (Appendix 3) where each retail outlet was assessed to determine the availability of non-expired, recommended

and non-recommended ACTs and other anti-malarial drugs on the day of the survey. The presence of functional malaria microscopy service and availability of RDTs was assessed on the day of the survey and retrospectively over the last three months. Finally, the availability of weighing scales, ACT guidelines, and health workers' exposure to malaria case-management training was also established. The retail outlets assessment data was collected using combination of methods including direct observations of antimalarials in stock and interviewing superintendent of the retail outlets.

Secondly, the mystery shopper presented themselves to the retail outlets and requested for medicine based on a case scenario. After the encounter the information was recorded on a standardized tool (Appendix 3) designed to answer key counseling and dispensing of drugs tasks performed during this retail outlets visit.

Thirdly, the retail outlets superintendent and assistants who attended to the patients were interviewed on key aspects of in-service training, guidelines accessibility, supervision and practice at the retail outlets. The team thanked the outlet staff and departed.

3.6 Study variables

Dependent variable

The outcome variable was presumptive treatment of uncomplicated Malaria among children (Yes/No).

Potential predictor variables

- Zone (Rural/Urban)
- Malaria risk (High/Low)
- RDTs availability (Yes/No)
- ACTs availability (Yes/No)
- Price

- Cadre (Retail outlets Assistant/tech/pharmacist/other)
- Asked any signs/symptoms (Yes/No)
- Case management training (Yes/No)
- Presented results (Yes/No)
- Any supervision (Yes/No)
- Case management supervision (Yes/No)
- Access to national malaria guidelines (Yes/No)

3.7 Data management and statistical analysis

Data cleaning, coding and analysis was done using STATA and R software. Exploratory data analysis was done to detect missing data, check for assumptions, and determine relationships between explanatory and outcome variables.

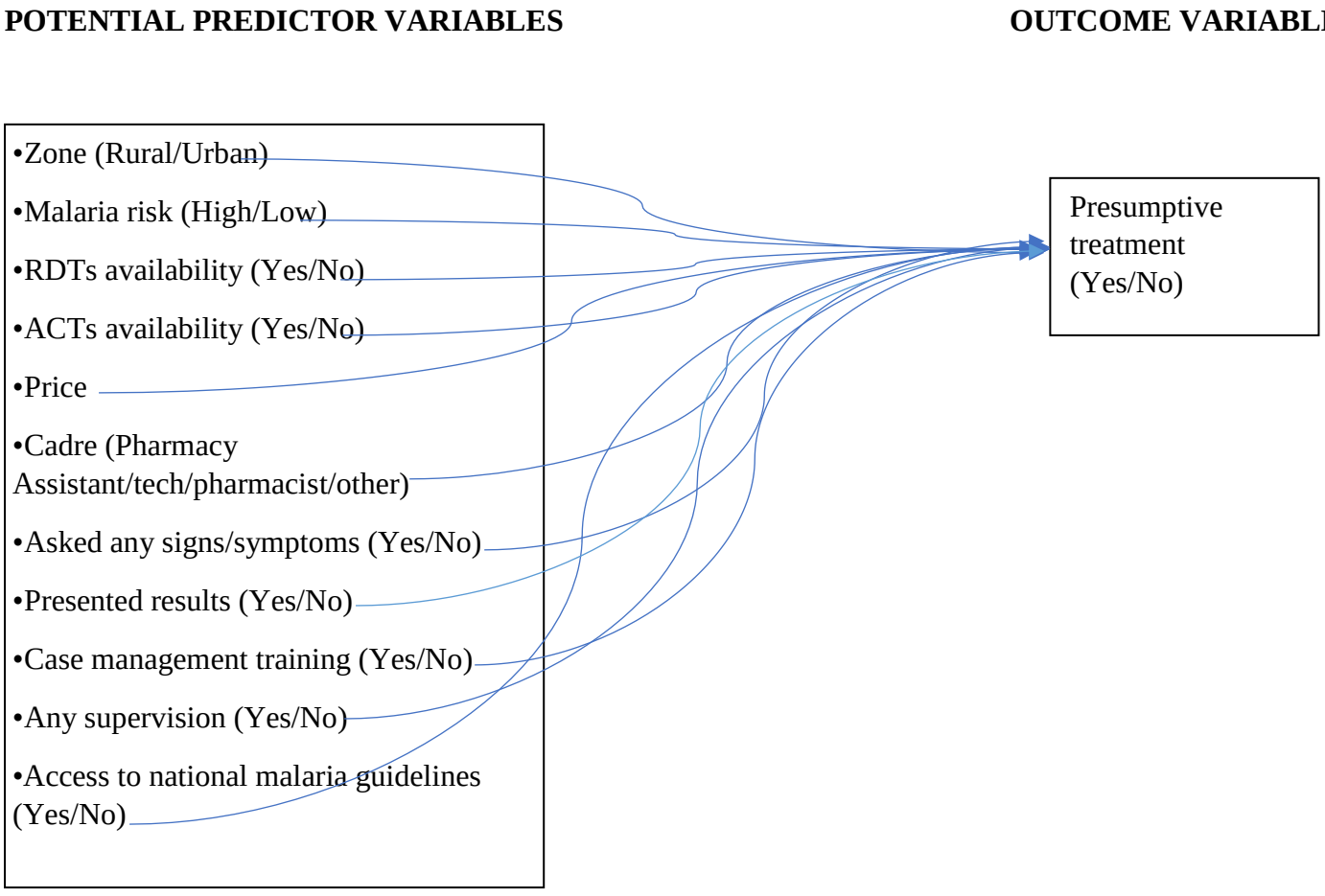
Descriptive statistics formed the basis of analysis for the variables of interest using frequencies. Specifically, the descriptive statistics determined were proportion of health care providers who treat patients presumptively, cadre, asked any signs/symptoms, had gone through the case management training, had any supervision, had a case management supervision and had access to the national malaria guidelines. In addition, the proportion of the private retail outlets with RDTs and ACTs available was determined as well as the zone and the malaria risk. Finally, the median for the price of ACTs was since the data was skewed.

Bivariate analysis was performed using a mixed effects logistic regression at 95% CI to examine the association between the outcome and predictor variables which are categorical (zone, malaria risk, RDTs availability, ACTs availability, cadre, signs/symptoms asked, case management training, results presented, any supervision, case management supervision and access to national malaria guidelines) adjusting for county effects. Bivariate analysis is the analysis of two variables or an analysis that attributes to a two-way classification [48].

Multivariable logistic regression modelling was conducted to obtain the adjusted odds ratio, p-values, 95% CI and standard errors. First, the ordinal logistic regression was conducted without the random effect (County). Secondly, the random effects was included to adjust for clustering at the county level to obtain adjusted odds ratios. The accuracy of the model was examined using the Akaike Information Criterion and the predictor variables for the best fitting model was used to predict the outcome of interest.

Data was presented in tables clearly indicating the odds ratios, p-values, confidence intervals and standard errors.

Conceptual framework



Source: Author

3.9 Study limitations

Since this study is dependent on the primary data available, there was a limitation on investigation of other areas that might be of interest. However, the results for this study will give an insight on strengthening interventions for Malaria Case Management at the private retail outlets in Kenya.

3.10 Ethical consideration

Ethical approval for this study was obtained from the Kenyatta National Hospital/University of Nairobi- Ethics and Research Committee (KNH/UON/ ERC). Permission to use the data for this study was obtained from the National Malaria Control Program (DNMP). During the primary study, an informed written consent (appendix 3) was obtained from the respondents before they participated in the study.

3.11 Study results dissemination plan

The results from this study will be disseminated to the University of Nairobi Institute of Tropical and Infectious Diseases (UNITID), publications, conferences and journal clubs.

CHAPTER 4: RESULTS

Preamble

This chapter gives the results of the study based on the research questions to be answered. The results are presented in tables giving the appropriate measures e.g. frequencies, percentages, odds ratios, p-values etc.

4.1 Study sample

A total of 405 health care providers were interviewed during the primary study. However, this study focused on the health care providers who treated the patient on the day of the survey. Out of the 405 health care providers interviewed, 333 (82 percent) treated patients on the day of the survey.

4.2 Proportion of health care providers who treat uncomplicated malaria presumptively among children in retail outlets

The proportion of health care providers who treated patients presumptively was the first objective of this study. Out of the 333 health care providers who were interviewed, slightly more than a half, 190 (57 percent) treated patients presumptively as shown in table 1 below. Less than a third, 70 (21 percent) and 44 (13 percent) had access to malaria guidelines and gone for the case management training respectively. A majority of the health care providers were pharmaceutical technologists, 163 (47 percent). During treatment, 170 (51 percent) of the health care providers asked the signs and symptoms of the patients while 112 (34 percent) of the patients presented results.

In terms of the retail outlet characteristics, out of the 333 outlets where the health care providers were interviewed, almost all, 322 (97 percent) had availability of ACTs. Only 77 (23 percent) of the retail outlets had availability of RDTs.

The distribution of the retail outlet zone was almost equal whereby 159 (48 percent) and 174 (52 percent) were located in the rural and urban areas respectively. Finally, slightly more than a third, 106 (32 percent) of the health workers accessed were from the high malaria risk area.

Table 1: Frequency distribution of the retail outlet and health care provider characteristics

	Characteristic	Frequency *(n = 333)*	Percentage
Retail outlet	***Zone***		
	Rural	159	48%
	Urban	174	52%
	Availability of RDTs		
	No	256	77%
	Yes	77	23%
	Availability of ACTs		
	No	11	3%
	Yes	322	97%
Health care provider	***Access to malaria case management guidelines***		
	No	263	79%
	Yes	70	21%
	Asked signs/symptoms		
	No	163	49%
	Yes	170	51%
	Results presented		
	No	221	66%
	Yes	112	34%
	Any supervision		
	No	172	52%
	Yes	161	48%
	Presumptive treatment		
	No	143	43%
	Yes	190	**57%**
	Case management training		
	No	289	87%
	Yes	44	13%
	Cadre		
	Others	43	13%
	Nurse	24	7%
	Clinical officer	9	3%
	Laboratory Technologist	3	1%
	Pharmacy Assistant	57	17%
	Pharmaceutical Technologist	162	47%
	Pharmacist	35	12%
Malaria Risk	Low	227	68%
	High	106	32%

4.3 Factors associated with presumptive treatment of uncomplicated malaria among children in the retail outlets

The outcome variable of interest was presumptive treatment (Yes/No). The potential predictor variables were zone, RDTs availability, ACTs availability, drug price, cadre, health care provider asked signs or symptoms, case management training, results presented, any supervision, access to national malaria guidelines and malaria risk. Table 2 below shows the results for the factors associated with presumptive treatment of uncomplicated malaria adjusting for county effects.

Table 2: Bivariate analysis to test for factors associated with presumptive treatment of uncomplicated malaria

	Independent variable	Odds ratio (95% CI)	P-value
Retail outlet	***Zone***		
	Urban (Ref)	1	
	Rural	1.46 (0.87 - 2.45)	0.151
	RDTs available		
	No (Ref)	1	
	Yes	1.02 (0.53 - 1.98)	0.943
	ACTs available		
	No (Ref)	1	
	Yes	0.71 (0.14 – 3.63)	0.680
	Drug price	1.00 (0.99 - 1.01)	0.742
Health Care Provider	***Cadre***		
	Others (Ref)	1	
	Nurse	0.88 (0.20 - 3.90)	0.846
	Clinical officer	0.53 (0.07 - 4.22)	
	Laboratory Technologist	1.70 0.06 - 48.99)	
	Pharmacy Assistant	1.17 (0.32 - 4.24)	
	Pharmaceutical Technologist	0.90 (0.42 - 1.92)	
	Pharmacist	1.77 (0.72 - 4.36)	
	Asked any signs or symptoms		
	No (Ref)	1	
	Yes	0.24 (0.13 - 0.45)	<0.001*
	Case management training		
	No (Ref)	1	
	Yes	0.55 (0.23 – 1.27)	0.159
	Results presented		
	No (Ref)	1	
	Yes	0.08 (0.03 - 0.20)	<0.001*
	Any supervision		
	No (Ref)	1	
	Yes	0.99 (0.58 - 1.71)	0.979
	Access to national malaria case management guidelines		
	No (Ref)	1	

	Yes	0.49 (0.25 - 0.96)	0.038*
Malaria risk	Low (Ref)	1	
	High	0.84 (0.30 – 2.33)	0.734

** Significant at level p<0.05*

Out of the 10 variables, a health care provider who asked signs or symptoms, results were presented and had access to the national malaria case management guidelines were significantly association with presumptive treatment of malaria at 95% CI adjusting for county effects.

Specifically, health care providers who asked signs or symptoms from the patient were negatively associated with presumptive treatment compared to those who did not (OR = 0.24; P-value = <0.001, 95% CI = (0.13 - 0.45). In addition, health care providers who were presented with results from the patients were negatively associated with presumptive treatment compared to those who were not presented with results (OR = 0.08; P-value = <0.001, 95% CI = (0.03 - 0.20). Finally, health care providers who had access to national malaria case management guidelines were negatively associated with presumptive treatment compared to those who have not (OR = 0.49; P-value = 0.038, 95% CI = (0.25 - 0.96).

There was no sufficient statistical evidence to indicate that there was a significant association between the other potential predictor variable and presumptive treatment of uncomplicated malaria among the health care providers.

4.4 Predictors of presumptive treatment of uncomplicated malaria among children in the retail outlets using mixed effects logistic regression

As shown in table 3 below, both the ordinary and the mixed effects logistic regression analyses were conducted. A liberal p-value of <0.2 was used to select the potential variables that were used to predict presumptive treatment of uncomplicated malaria [59]. The variables were zone (P-value = 0.151), health care provider asked any signs or symptoms (P-value = <0.001), case management training (P-value = 0.159), results presented (P-value = <0.001) and access to national malaria case management guidelines (P-value = 0.038).

Table 3: Multivariable analysis to test for presumptive treatment of uncomplicated malaria

		MELOGIT	
Fixed effects	**AOR (95% CI)**	**Coeff (SE)**	**P-value**
Zone			
Urban (Ref)	1		
Rural	1.39 (0.79 - 2.44)	0.33 (0.29)	0.255
Asked any signs or symptoms			
No (Ref)	1		
Yes	0.20 (0.10 - 0.39)	-1.63 (0.35)	<0.001*
Case management training			
No (Ref)	1		
Yes	0.44 (0.17 - 1.12)	-0.82 (0.47)	0.084
Results presented			
No (Ref)	1		
Yes	0.09 (0.04 - 0.20)	-2.46 (0.43)	<0.001*
Access to national malaria case management guidelines			
No (Ref)	1		
Yes	0.75 (0.37 - 1.54)	-0.29 (0.37)	0.434
Random effect			
County		(0.9991)	

** Significant at p<0.05*

The mixed effects logistic regression found that a health care provider who asked patients signs or symptoms and results were presented were predictors that were statistically significant at 95% CI. The county variance was 0.99, which indicated that there was evidence for variance of the different counties. A health care provider who asked the patient any signs or symptoms was 80 percent less

likely to treat the patient presumptively to those who did not adjusting for the variability in the counties (AOR = 0.20; P-value = <0.001, 95% CI = (0.10 - 0.39). In addition, health care providers who had results presented by the patient were 91 percent less likely to treat a patient presumptively compared to one the one whom he results were not presented adjusting for county effects (AOR = 0.09; P-value = <0.001, 95% CI = (0.04 - 0.20).

As shown in table 4 below, the model with the best fit was the one with health care providers asked signs or symptoms, results were presented and they had gone through a case management training.

Table 4: Candidate models to test for the best model fit

Predictor variables included	**MELOGIT AIC value**
Zone; access to guidelines; asked signs or symptoms; presented results; case management training	356.9
Access to guidelines; asked signs or symptoms; presented results; case management training	356.3
Zone; asked signs or symptoms; presented results; case management training	355.6
Zone; access to guidelines; asked signs or symptoms; presented results	358.0
Asked signs or symptoms; presented results; case management training	354.9*
Asked signs or symptoms; presented results	356.1

AIC – Akaike Information Criterion
**The smaller the AIC value, the better the model*

The mixed effects logistic regression for the best-fitted model was done and the results are as presented in table 5 below.

Table 5: Mixed effects logistic regression for the best model fit

	AOR (95% CI)	Coeff (SE)	P-value
Intercept	9.44 (4.69 – 19.02)	2.24 (0.34)	<0.001
Fixed effects			
Asked any signs or symptoms **(X_1)**			
No (Ref)	1		
Yes	0.19 (0.10 - 0.37)	-1.67 (0.34)	<0.001
Case management training **(X_2)**			
No (Ref)	1		
Yes	0.44 (0.18 – 1.09)	-0.83 (0.46)	0.073
Results presented **(X_3)**			
No (Ref)	1		
Yes	0.08 (0.03 - 0.19)	-2.49 (0.43)	<0.001
Random effect			
County		Variance = 1.027	Standard deviation= 1.013

The built model will therefore be:

Logit $[pj] = 2.24 - 1.67\,X_1 - 0.83X_2 - 2.49X_3 + u_{j;}$ where $u_{j} \sim_N (0, \delta_g^2)$

The probability of treating a patient presumptively = $\text{logit}^{-1} (\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + u_j)$

Where $u_j = 1.96 * \delta_g$

Therefore, the probability (Treating a patient presumptively) of any hypothetical county = logit^{-1} $(2.24 - 1.67X_1 - 0.83\,X_2 - 2.49\,X_3 + 1.96\,(1.013)$

Considering the different value of the predictor variables i.e. Yes = 1 or No = 0, table 6 below illustrates the different probabilities:

Table 6: Probabilities of the predicted model for presumptive treatment of uncomplicated malaria

Predictor variable	Equation	Probability
Asked signs/symptoms =1 Results presented = 1 Case management training = 1	P (1) = logit $^{-1}$ (2.24 - 1.67(1)- 0.83 (1) - 2.49 (1) + 1.96 (1.013)	0.32
Asked signs/symptoms =0 Results presented = 1 Case management training = 1	P (1) = logit $^{-1}$ (2.24 - 1.67(0)- 0.83 (1) - 2.49 (1) + 1.96 (1.013)	0.71
Asked signs/symptoms =1 Results presented = 0 Case management training = 1	P (1) = logit $^{-1}$ (2.24 - 1.67(1)- 0.83 (0) - 2.49 (1) + 1.96 (1.013)	0.52
Asked signs/symptoms =1 Results presented = 1 Case management training = 0	P (1) = logit $^{-1}$ (2.24 - 1.67(1)- 0.83 (1) - 2.49 (0) + 1.96 (1.013)	0.85
Asked signs/symptoms = 0 Presented results = 0 Case management training = 0	P (1) = logit $^{-1}$ (2.24 - 1.67(0)- 0.83 (0) - 2.49 (0) + 1.96 (1.013)	0.99

As shown in table 6 above, the probability of a health care provider to treat a patient presumptively if the patient presented results, signs and symptoms were asked and the health care provider has been trained was 0.32. However, when the health care provider has not gone for a case management training but the results were presented and the health care provider asked for the signs and symptoms the probability of treating a patient presumptively is 0.85.

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

This chapter gives a discussion of the study objectives with a view of what other studies related to the objectives found, conclusions and recommendations drawn. The objectives of this study were to determine the proportion of health care providers who treat uncomplicated malaria presumptively, examine the factors associated with presumptive treatment of uncomplicated malaria and model predictors of presumptive treatment of uncomplicated malaria among children in the retail outlets. The discussion has been done for the three specific objectives.

The proportion of health care providers who treat uncomplicated malaria presumptively was 57 percent out of the 333 health care providers. A study conducted in Tanzania found that 51 percent of the test negative patients were treated presumptively for uncomplicated malaria [39]. Another study conducted in the Coastal area of Kenya found that presumptive treatment of patients ranged from 0 percent to 13.9 percent in the private sectors [36]. In Nigeria a study conducted found that presumptive treatment among health care providers was higher in the private sector (95 percent) compared to the public sector (23 percent) [41]. These studies have shown that presumptive treatment in the private sector is being practiced. The study conducted in Tanzania had a percentage of health care providers who treat patients presumptively almost equal (51 percent) to that in this study (57 percent).

The potential factors associated with presumptive treatment were: zone, RDTs availability, ACTs availability, drug price, cadre, health care provider asked signs or symptoms, case management training, results presented, any supervision, access to national malaria guidelines and malaria risk. However, the factors that were associated with presumptive treatment of uncomplicated malaria taking into account of the county effect were zone, signs/symptoms asked, case management training, results presented and access to malaria case management guidelines. Several other studies have looked into the factors associated with presumptive treatment of uncomplicated malaria.

In a study that was conducted in Kenya accessed the association between presumptive treatment and case management training among health care providers in the private retail sector. The study showed that malaria case management training was significantly associated with presumptive treatment [58]. These results are in line with that of this study as malaria case management training was significantly associated with presumptive treatment taking into account the county effects. A cluster randomized trail conducted in Ghana found that there was a significant association between availability of RDTs and presumptive treatment of uncomplicated malaria [33]. The results contradicts with that in this study since the data did not provide enough evidence to indicate the association between availability of RDTs and presumptive treatment of uncomplicated malaria taking into account the county effect.

Availability of antimalarial drugs was significantly associated with presumptive treatment of uncomplicated malaria in a study that was conducted in Nigeria [41]. However, in this study there is a contradiction since the data did not provide sufficient evidence to indicate that there was an association.

Both the test for association and model building for this study was done using the mixed effects logistic regression models. The random effect which was the county was taken into account due to the county clustering. This method has been proved to be more accurate for prediction compared to the ordinary logistic regression models [49]. This study applied the mixed effects logistic regression model with the best fitted model used as the Akaike Information Critetion (AIC). Generally, comparing the AIC value, the mixed effects logistic regression model had a better fit compared to the ordinary logistic regression model. The mixed effects models have also been proven to be more efficient and flexible [50].

Based on the AIC values for the different candidate models to predict presumptive treatment of uncomplicated malaria among children in the private retail outlets, if the test was presented, if the health care provider asked the signs and symptoms and had undergone case management training

were the predictor variables that fitted the best model. The model further predicted the probability of a health care provider to treat a patient presumptively based on the three factors. For a health care provider who has undergone a malaria case management training, asked the patient for the signs and symptoms and results were presented, the probability is 0.32. For one who has gone through a malaria case management training, results were presented but did not ask for signs or symptoms the probability is 0.71. For a health care provider who had no results presented, the probability was 0.52. Though the test results were presented, and the health care provider asked for the signs and symptoms but had not undergone a case management training the probability of treating a patient presumptively was 0.85. These results show that all the three predictors are crucial for a health care provider. However, malaria case management training plays a key role in treatment of malaria at the private retail sector.

In conclusion, the health care providers practices and knowledge in case management of malaria is key in diagnosis, treatment and prevention of malaria in Kenya. Presumptive treatment is due to misdiagnosis of a patient which may lead to drug resistance.

5.2 Conclusion

The health seeking behavior in the private retail sector raises concern in provision of health care services in the private sector. Much has been done in the public sector but there is need to also strengthen interventions in the private sector in realization of Universal Health Care in Kenya to reach the Sustainable Development Goals (SDGs). Presumptive treatment of uncomplicated malaria among children in Kenya has been an issue which depends on the health care providers as well as the retail outlet facotrs. Adherence to the national malaria case management guidelines in key in ensuring quality of treatment to the malaria patients. Interventions in place to curb presumptive treatment include provision of malaria case management guidelines, case management training, supervision and availability of RDTs to ensure testing before treatment. On the other hand availability of ACTs due to the AMFM subsidies could possibly influence presumptive treatment of uncomplicated malaria.

The results from this study show that case management training, signs/symptoms asked and results presented predict presumptive treatment of uncomplicated malaria. A mixed effects logistic regression model was used to adjust for the county clustering effect. This model provides more accurate prediction compared to an ordinary logistic regression model measured by the AIC values. Apart from asking the signs and symptoms or results presented , case management training for the health care providers play a key role in management of malaria by health care providers in the private retail outlets.

Malaria case management training touches on testing and asking of patients for signs/symptoms before diagnosis and treatment of a patient, However, this study gives and insight for policy makers to emphasize on testing and asking signs/symptoms when training health care providers on malaria case management.

5.3 Recommendations

Based on the discussion and conclusion drawn, this study recommends:

1. The Division of National Malaria Programme (DNMP) and other partners should focus on malaria case management in the private sector to improve the quality of treatment.
2. Further research to look into the factors that may predict presumptive treatment since the data in this study did not provide evidence to indicate the other potential factors predictability.

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