RESEARCH ARTICLE

Predictors of presumptive treatment of uncomplicated malaria among children in private retail outlets in Kenya: mixed effects logistic regression modelling [version 1; peer review: 2 approved with reservations]

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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 the disease. Presumptive treatment remains a major challenge in Kenya, especially in the private sector, with major gaps in literature identified on predictors of this treatment. Mixed-effects regression modelling considers county clustering, is more accurate in prediction and is more efficient and flexible.

Methods: 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. 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).

Results: Out of the 333 health care providers who treated patients, 190 (57%) treated patients presumptively. From the mixed effects logistic regression model, 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)).

Conclusions: Presumptive treatment of uncomplicated malaria remains a challenge in the private retail sector. Malaria case management training and health care providers asking of signs and

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symptoms and results presented predicts presumptive treatment. To address the issue of presumptive treatment of Malaria, strengthening of malaria case management training is key for health care providers in the private sector.

Keywords

Presumptive Treatment, Uncomplicated Malaria among Children, Private Sector, Mixed Effects Models

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Introduction

Malaria is a health problem across the globe; the World Health Organization (WHO) estimates that nearly one-half (3.4 billion) of the population in the world is at risk of the disease¹. Africa continues to have a disproportionately large share of the global malaria burden. According to the 2018 WHO Malaria Report, in 2017 the region reported 92% and 93% of malaria morbidity and mortality, respectively². In 2010, Kenya adopted the Test and Treat case management policy by WHO, which is in line with the malaria treatment guidelines in Kenya³. 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 Division of National Malaria Programme 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 facilities⁴.

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 others⁴. 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 sector⁵. However, there were challenges in access in the private sector primarily due to price⁶.

The Affordable Medicine Facility for malaria (AMFm) project, 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 Artemisinin-based combined therapies (ACTs) availability, affordability and use⁷. 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 proved to be effective in the countries piloted⁷. Though ACTs and rapid diagnostic tests (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^{8–12}.

Logistic regression is a statistical method of analysis that is used when the dependent (outcome) variable is binary (dichotomous)¹³. 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 multi-level data¹⁴. 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 modeling to predict treatment of children with uncomplicated malaria presumptively in the retail outlets.

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 retail sector⁵. 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. 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.

Methods

Study design and setting

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 private retail outlets in Kenya.

Study population and eligibility of participants

The study populations included the health care providers who treated the patients in the retail outlets during the survey (September 2018), sampled randomly in both the rural and urban settings in Kenya.

The study included health care providers who treated patients in privately owned and predominantly dispensing retail outlets while health care providers from Public facilities, faith-based outlets and NGOs, non-functional outlets and pharmacies within a private facility were not included in this study.

Sample size determination

This study adopted the sample size in the primary study that was determined based on the Cochran's formula¹⁵:

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

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%¹⁶

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.

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 surveyed. Specifically, all the 47 counties were included in the survey, but the sampling was done in two categories. In the first category, the 43 counties with less than 10 sub-counties had two sub-counties randomly sampled while in the second category, four counties with more than 10 sub-counties (namely Nairobi, Kiambu, Kakamega and Nakuru) had four sub-counties randomly sampled.

In the first stage for the first category, two 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 two or fewer, all were selected; if more than two, the researcher randomly selected two.) Two unregistered retail outlets in the Sub-county were selected to a maximum of two. (If two or fewer, all were sampled; if more than two, the researcher randomly sampled two.) A total of eight outlets were sampled in each of the counties for this category.

In the first stage for the second category, four 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 two or fewer, all were sampled; if more than two, the researcher randomly sampled two.) 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

two, researcher randomly sampled two). A total of 16 retail outlets were sampled in each of the counties for this category.

The list of 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).

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 investigate 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 only 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 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 a 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, 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.

Study variables and methods of measurement

The potential predictor variables accessed comprised of: zone, malaria risk, availability of rapid diagnostic tests, availability of artemisinin-based combination therapies, artemisinin-based combination therapies (ACTs) price, health care provider cadre, client asked signs/symptoms, health care provider case management training, client presented results, any supervision and access to national malaria guidelines. The outcome variable was presumptive treatment of uncomplicated malaria among children. **Table 1** shows the measurement methods and study variables pertinent to this article assessed using the questionnaire, while **Figure 1** shows the relationship between the predictor and outcome variables.

Data management and statistical analysis

Data cleaning, coding and analysis was done using STATA version 15 and R version 3.5.3 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 about 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.

Multivariable logistic regression modelling was conducted to obtain the adjusted odds ratio, p-values, 95% CI and standard errors. The random effects were included to adjust for clustering

Table 1. Study variables and assessment methods.

Variable (type)	Method of measurement
Presumptive treatment of uncomplicated Malaria among children (nominal)	Binary form: Yes or No
Zone (nominal)	Accessed in two levels: Rural or Urban
Malaria risk (nominal)	Accessed in two levels: High or Low
Availability of Rapid Diagnostic Tests (nominal)	Binary form: Yes or No
Availability of Artemisinin-Based Combination Therapies (nominal)	Binary form: Yes or No
Artemisinin-Based Combination Therapies (ACTs) price (continuous)	Captured in Kenya Shillings
Health care provider cadre (nominal)	Accessed in 7 levels: Others, Nurse, Clinical officer, Laboratory Technologist, Pharmacy Assistant, Pharmaceutical Technologist & Pharmacist
Client asked signs/symptoms (nominal)	Binary form: Yes or No
Health care provider case management training (nominal)	Binary form: Yes or No
Client presented results (nominal)	Binary form: Yes or No
Any supervision (nominal)	Binary form: Yes or No
Access to national malaria guidelines (nominal)	Binary form: Yes or No

POTENTIAL PREDICTOR VARIABLES OUTCOME VARIABLE

Figure 1. Conceptual framework of potential predictors of presumptive treatment of uncomplicated Malaria in private retail outlets in Kenya.

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

Ethical considerations

Ethical approval for this study was obtained from the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UON/ ERC) – P457/06/2019. Permission to use the data for this study was obtained from the Division of National Malaria Programme (DNMP). During the primary study, an informed written consent was obtained from the respondents before they participated in the study.

Results

Descriptive statistics of the study data

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%) treated patients presumptively (Table 2). Less than one-third, 70 (21%) and 44 (13%) had access to malaria guidelines and attended case management training, respectively. A majority (163, 47%) of the health care providers were pharmaceutical technologists. During treatment, 170 (51%) of the health care providers asked the signs and symptoms of the patients while 112 (34%) 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%) had availability of ACTs. Only 77 (23%) of the retail outlets had availability of RDTs.

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

The de-identified raw dataset is available as *Underlying data*^{17,18}.

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, RDT availability, ACT 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.

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 associated 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; $P < 0.001$, 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; $P < 0.001$, 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 not 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. **Table 3** shows the results of the factors associated with presumptive treatment of uncomplicated malaria among children in the retail outlets.

Table 2. Frequency distribution of the retail outlet and health care provider characteristics in Kenya (n = 333).

Characteristic	Frequency (n = 333)	Percentage
Retail outlet	Zone	
	Rural	159
	Urban	174
	Availability of RDTs	
	No	256
	Yes	77
	Availability of ACTs	
	No	11
	Yes	322
Health care provider	Access to malaria case management guidelines	
	No	263
	Yes	70
	Asked signs/symptoms	
	No	163
	Yes	170
	Results presented	
	No	221
	Yes	112
	Any supervision	
	No	172
	Yes	161
	Presumptive treatment	
	No	143
	Yes	190
	Case management training	
	No	289
	Yes	44
	Cadre	
	Others	43
	Nurse	24
	Clinical officer	9
	Laboratory Technologist	3
	Pharmacy Assistant	57
	Pharmaceutical Technologist	162
	Pharmacist	35
Malaria Risk	Low	227
	High	106

Table 3. Bivariate analysis to test for factors associated with presumptive treatment of uncomplicated malaria in Kenya.

	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	
Health Care Provider	Yes	0.71 (0.14 - 3.63)	0.680
	Drug price	1.00 (0.99 - 1.01)	0.742
	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

*p<0.05.

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

A mixed effects logistic regression analyses was conducted and a liberal p-value of <0.2 was used to select the potential variables that were used to predict presumptive treatment of uncomplicated malaria¹⁹. 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% less likely to treat the patient presumptively to those who did not adjusting for the variability in the counties (AOR = 0.20; P<0.001, 95% CI = (0.10 - 0.39). In addition, health care providers who had results presented by the patient were 91% 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). **Table 4** shows the results for the mixed effects logistics regression analysis.

The model with the best fit based on the Akaike Information Criterion (AIC) was the one with health care provider who has

undergone a malaria case management training, who asked the patient for the signs and symptoms and for whom results were presented (**Table 5**). The built model will therefore be:

$$\text{Logit } [p_j] = 2.24 - 1.67 X_1 - 0.83 X_2 - 2.49 X_3 + u_j; \text{ where } u_j \sim N(0, \delta_g^2)$$

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

$$\text{Where } u_j = 1.96 \delta_g$$

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

Considering the different value of the predictor variables i.e. Yes = 1 or No = 0, **Table 6** below illustrates the different probabilities. The mixed effects logistic regression for the best-fitted model was conducted (**Table 6**).

Finally, the probability of a health care provider treating a patient presumptively if the patient presented results, were asked about signs and symptoms and the health care provider has been trained was 0.32. However, when the health care provider has

Table 4. Multivariable analysis to test for presumptive treatment of uncomplicated malaria.

Fixed effects	MELOGIT		
	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)	

*p<0.05.

Table 5. 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

*The smaller the AIC value, the better the model.

AIC, Akaike Information Criterion.

Table 6. 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

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 (Table 7).

Discussion

The proportion of health care providers who treat uncomplicated malaria presumptively was 57% out of the 333 health care providers. A study conducted in Tanzania found that 51% of the patients testing negative were treated presumptively for uncomplicated malaria²⁰. Another study conducted in the Coastal area of Kenya found that presumptive treatment of patients ranged from 0 to 13.9% in the private sectors²¹. In Nigeria a study conducted found that presumptive treatment among health care providers was higher in the private sector (95%) than the public sector (23%)²². 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%) to that in this study (57%).

The potential factors associated with presumptive treatment were as follows: zone, RDT availability, ACT 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 considering the county effect were zone, signs/symptoms asked, case management training, results presented and access to malaria case management guidelines. Several other studies have investigated the factors associated with presumptive treatment of uncomplicated malaria.

Table 7. 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	$P(1) = \text{logit}^{-1} (2.24 - 1.67(1) - 0.83(1) - 2.49(1) + 1.96(1.013))$	0.32
Asked signs/symptoms =0 Results presented = 1 Case management training = 1	$P(1) = \text{logit}^{-1} (2.24 - 1.67(0) - 0.83(1) - 2.49(1) + 1.96(1.013))$	0.71
Asked signs/symptoms =1 Results presented = 0 Case management training = 1	$P(1) = \text{logit}^{-1} (2.24 - 1.67(1) - 0.83(0) - 2.49(1) + 1.96(1.013))$	0.52
Asked signs/symptoms =1 Results presented = 1 Case management training = 0	$P(1) = \text{logit}^{-1} (2.24 - 1.67(1) - 0.83(1) - 2.49(0) + 1.96(1.013))$	0.85
Asked signs/symptoms = 0 Presented results = 0 Case management training = 0	$P(1) = \text{logit}^{-1} (2.24 - 1.67(0) - 0.83(0) - 2.49(0) + 1.96(1.013))$	0.99

A study that was conducted in Kenya assessed 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 treatment²³. 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 trial conducted in Ghana found that there was a significant association between availability of RDTs and presumptive treatment of uncomplicated malaria²⁴. The results contradict those of 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 Nigeria²². However, in this study, 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 models²⁵. This study applied the mixed effects logistic regression model with the best fitted model used as the 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 flexible²⁶.

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, who asked the patient for the signs and symptoms and for whom results were presented, the probability is 0.32. For one who has gone through a malaria case management training, for whom results were presented but did not ask for signs or symptoms of malaria the probability is 0.71. For a health care provider who had no results presented, the probability was 0.52. If 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.

Conclusion

Health seeking behavior in the private retail sector raises concerns in the provision of health care services in the private sector. Much has been done in the public sector but there is a 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 factors. 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, asking about signs/symptoms and having 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 an insight for policy makers to emphasize on testing and asking signs/symptoms when training health care providers on malaria case management.

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.
3. There is need to strengthen interventions in the private sector in realization of Universal Health Care in Kenya.

Data availability

Underlying data

Figshare: PPTUM_Kenya.xlsx. <https://doi.org/10.6084/m9.figshare.12783128.v2>¹⁷.

This file contains the de-identified dataset used in the present study.

Figshare: PPTUMK_DD. <https://doi.org/10.6084/m9.figshare.12783188.v2>¹⁸.

This file contains the data dictionary for the de-identified dataset.

Data are available under the terms of the [Creative Commons Attribution 4.0 International license \(CC-BY 4.0\)](#).

Acknowledgement

I would like to acknowledge the following people who have mentored and supported me throughout this project. I would also like to thank Dr. Marshal Mweu (University of Nairobi) for his continuous mentorship and advice. The University of Nairobi Institute of Tropical and Infectious Diseases (UNITID) for their support. The Division of National Malaria Programme (DNMP) in collaboration with the Global Fund for their support during this project.

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Luca Nelli

Institute of Biodiversity Animal Health and Comparative Medicine, University of Glasgow, Glasgow, UK

I've read the manuscript entitled "Predictors of presumptive treatment of uncomplicated malaria among children in private retail outlets in Kenya: mixed effects logistic regression modelling" with great interest. This is a very interesting and scientifically sound work, presenting an original investigation of the possible drivers of "inappropriate" malaria treatment in private health facilities in Kenya. The methods used are sound and the conclusion reflects the main findings.

I only have some minor comments with respect to the general presentation. In addition, most of the manuscript is well written, but there are some typos that should be checked for. Please also check punctuation errors.

Please see detailed comments:

ABSTRACT:

The summary is interesting and concise. However, instead of reporting only those 3 coefficients (and also, the first one is not significant, are you sure it's one of the main findings you want to put in the abstract?), I was wondering if you could provide some more results. If you don't have space, I guess you can easily reduce the method subsection (which I think contains too many details for an abstract).

INTRODUCTION:

I feel like some parts of the introduction could be removed (or at least reduced). For example, you have a whole paragraph with a general description of what a logistic regression is, how the response variable is distributed, and what a mixed-effect model is. I think all of this is irrelevant for the introduction, and you have already mentioned this in the methods section. I would suggest removing the paragraph.

On the contrary, I would recommend expanding a little bit on the (plausible) drivers of presumptive treatment. You only mention that “Inappropriate treatment practice [...] could be caused by several factors”, but it would be good to see some reference as to what these factors could be. In other words, how do you justify the choice of your variables in the model? If there’s no prior knowledge on this, that’s fine but you should flag this as an important knowledge gap (this would also strengthen your whole work).

I don’t agree with the final sentence: “This study focused on application of mixed effect model [...]”. While it is true that you used mixed-effect models to investigate, I think you have done much more than that (i.e. not “just” applying a method – which is well established and you haven’t established anything new from a methodological point of view – so I would put more emphasis on the main aim of the study (understanding which factors are influential on inappropriate practices). If, on the contrary, your main aim was to investigate if mixed-effect models can be applied to these data, I think the whole paper (including title, introduction, and discussion) should definitely have a different angle.

METHODS:

The whole method section is very long and full of unnecessary (just my opinion, of course) details and repetitions. For example:

- Unclear who/what the “mystery shopper” is. Please define this.
- I really enjoyed the description of the Data Collection Procedure. It’s like reading a novel :-)
- You have plenty of repetition in the description of your covariates (e.g. page 5 in the left column, page 5 in the right column, Table 1, Figure 1). Surely you can reduce this?
- You mention microscopy availability in the Data Collection, but you haven’t used that as a predictor in your models. Why?
- Akaike Information Criterion (first paragraph of page 6) doesn’t assess model accuracy. It’s a method to compare different models (as you rightly do in Table 5), but to validate the model I would suggest calculating the percentage of correct classification and values of area under the ROC curve.

RESULTS:

Again, plenty of repetitions here. For example, you don’t need to write again what response variable and predictors you used in the models. You already told us in the method.

I don’t think that the formulas on page 9 (and in Table 7) add anything to the interpretation of the results (you already report the coefficients). But at the same time, I like that you present the 4 different scenarios (Table 7) with all the possible combinations. Can you find a way to present this as a figure/plot instead? This would give a clearer picture of the five different scenarios (and it would make your manuscript more balanced – as it definitely has too many tables now).

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Quantitative Ecology and Epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 08 April 2021

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Moses Ocan

Department of Pharmacology & Therapeutics, Makerere University, Kampala, Uganda

I have enjoyed reading the work and here below are the summary of my comments:

1. Clearly define/provide the age range for the children considered in the study.
2. Provide key elements of the Kenya malaria treatment policy related to this study and how it is implemented in the country.
3. Abstract, last sentence of the background should be deleted. Add the aim of the study to the background.
  - The methods section; what provide retail outlets where included in this study, give details.

- Provide details of the healthcare cadres targeted for this study.
- Level of significance in the analysis of the data.
- How many retail outlets were visited or considered in this study.
- Include results for univariate and Bivariate analysis in the abstract

4. Introduction section

- Use the most recent world malaria report (WHO malaria report, 2020).
- Fourth sentence ...In 2010, Kenya adopted....., this sentence is not clear and should be re-written.
- Second paragraph sentence, ...Though medical care is....., is this referring to general healthcare or specifically malaria treatment?
- Third paragraph should include specific information on how AMFm has impacted malaria treatment in Kenya.
- Paragraph four should be removed from the introduction section of the manuscript and transferred to the methods section.
- The sentence, ...The health seeking behavior in Kenya....., is not clear, please clarify with some detail.

5. Methods section

- Clearly define what you mean by retail outlet.
- Provide the professions of the healthcare cadres targeted in this study.
- How many retail outlets were included in this study and how was the number arrived at?
- How was the data to be included in this study selected from the large dataset?
- Where is the dataset of the original study kept? Provide details and when the data was accessed by the study team.
- How was confidentiality of the study participants ensured while accessing the dataset?
- Revise the description of the sampling procedure. Focus on how you selected the data that you included in your analysis from the large dataset of the primary study.
- Provide details of ethical approval of the primary study as well.
- Describe how you collected data for your study. Please describe how the data points you analyzed were extracted from study units obtained from the original study.

Rewrite the section on data collection.

- What is the study unit for your study?
- How was quality control ensured in this study?

6. Results

- What patients are you referring to, please be specific.
- Stratify the results by the type of healthcare cadre and retail outlet type.
- What were the high malaria risk areas and how many study participants were obtained from this areas.
- Provide details of the ACTs used in the retail outlets (type, formulation etc).
- How was malaria diagnosed among the study participants?
- Who were your study participants, healthcare cadres or children?
- Please clarify what you mean by healthcare providers who were presented with results by the patients. Your target population for this study children, please clarify.
- When was the malaria case management training conducted for the healthcare cadres?

7. Discussion

- What is the prevalence of malaria in children in Kenya and what proportion of these is treated presumptively from previous studies?
- Is the extent of presumptive treatment of malaria among children similar to that in adults?
- Why would asking for signs and symptoms of disease as found in your study reduce the risk of presumptive treatment. Please explain.
- The meaning of the key results of the study has not been clearly described in the discussion section.

8. Conclusion and recommendations

- Summarize the conclusion and should come from the main finding of the study.
- Summarize the recommendation, who should take action and what action should they take.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Community medicine use, Antimicrobial resistance

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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