Original Research Article

Influence of vector control and chemotherapy interventions on treatment outcomes and parasite incidence in Artemether combined therapies treated populations of Kisii County, Kenya

Abstract

Introduction:

Malaria remains the major vector borne disease in the world. Currently Kenya the ministry of health has scaled up interventions with chemotherapy and vector control standing out as a major strategy. Therefore, this study examined the influence of vector control and chemotherapy interventions on the treatment outcomes in Kisii County.

Methods:

Multi-stage random sampling was used for this study. The study was conducted from February 2021 to June 2021. Malaria-positive 275 participants were recruited into the study, treated with ACTs and followed for a period of 28 days at specified follow up days for parasite diagnosis. Occurrence of malaria clinical symptoms on the patients was also conducted. Molecular analysis was done by characterizing Merozoite proteins (MSP2) on the samples showing parasite recurrence. A Questionnaire was administered to determine the utilization of drugs for malaria treatment prior to this study and the usage of vector control after patient treatment with ACTs. Meanwhile, emphasis was laid on intervention strategies such as the use the usage of insecticide-treated nets (ITNs), Indoor residual spraying and chemotherapeutic practices as recommended by the World Health Organization (WHO).

Results:

Early treatment failure was reported among 27(12%) respondents, late clinical failures 20(8%), late parasitological failures 11(5%), and adequate clinical and parasitological outcomes 173(75%).Chemotherapeutic practices influencing treatment outcomes included; previous self-

medication (OR=0.417; 95% CI: 0.153-1.385; p=0.035), ability of previously finishing doses (OR=0.328; 95% CI: 0.168-0.941; p=0.003,) and Frequency of previous antimalarial usage (OR=3.259; 95% CI: 1.054-4.721; p=0.004). While vector control interventions influencing treatment outcomes included; usage of indoor residual spraying (OR=0.408; 95% CI: 0.132-0.682; p=0.002), sleeping under the mosquito net (OR=0.218; 95% CI: 0.119-0.909; p=0.025,) and mosquito net treatment (OR=0.262; 95% CI: 0.092-0.823; p=0.003).With the molecular analysis detecting 10 samples with parasite recrudescence.

Conclusions:

Based on these findings, Antimalarial usage practices prior to current usage of ACTs and vector control after treatment remain important predictor factors for treatment outcomes.

.**Keywords:** interventions, ACTs, treatment outcomes, Kisii County**.**

Introduction

Malaria infection remains one of the major killer diseases. According to the latest report, there were an estimated 229 000 cases and 409 000 deaths globally in 2019 (1). Malaria remains the leading vector borne disease in Kenya, recording approximately 3.5 clinical cases annually, leading to 10,700 deaths. The majority of cases are recorded in Lake Basin and western parts of the country. Kisii County has not been spared either by malaria menace. However, the malaria prevalence in Kenya has dropped from 8 percent in 2015 to 6 percent in 2019 (2). To combat mortality, the Kenya ministry of health in collaboration with the National malaria control program has initiated several intervention programs, which includes, but not limited to vector control, proper diagnosis and chemotherapy. Globally, malaria interventions have been scaled up, but their malaria reduction potential is not clearly documented.

In Kenya, there is confirmation of general reduction in malaria cases among the general population for the last few years. Kenya has embraced a robust national malaria control program (NMCP) grounded on strengthened management. The NMCP with coordination from the ministry of health have implemented integrated intervention strategies including universal coverage with long-lasting insecticide-impregnated bed nets since 2008 (LLINs), artemisinin-based combination therapy (ACT) in 2006 and effective diagnosis using rapid diagnostic tests (RDTs) and microscopy in 2007 (3).

Previous reports have indicated that the best method of malaria elimination is through the integration of the interventions (4, 5). Currently Artemether-Lumefantrine (AL) is used in Kenya as a drug of choice for the treatment of complicated and uncomplicated malaria caused by *Plasmodium falciparum*. However, past studies have recorded different treatment outcomes, with some studies reporting poor efficacy profiles. The use of the intervention methods before and after treatment with ACTs may be influencing different treatment outcomes witnessed.

There is inadequate data on regard to the clinical outcome of the antimalarial drugs thus calling for more effectiveness studies. Since the bulk of the world's malaria occurs in Africa, where countries are increasingly switching to combination treatments, there is a need to document how well the drug is being used by both adults and children in the community and how effectively specific interventions can improve drug use and therapeutic outcome in these settings. This includes, but not limited to the pre- and post-treatment intervention practices employed by patients. Presently, there is insufficient information on the influence of the malaria intervention on ACTs treatment outcome in Kisii County.

Currently, Kenya has not developed a standard health operating procedure to be followed by malaria patients after undergoing treatment. This can be achieved by first evaluating the influence of previous and post patient malaria treatment practices before ACTs treatment, which may be influencing the recurrence of parasitemia after treatment with recommended drug of choice. Hence calling for studies to address the problem. The findings from this study are significant to a proposal by the Ministry of Health of Kenya in eliminating malaria infection by 2030. Moreover, the findings from this geographic specific trial embedded within the routine Kenyan national malaria intervention campaign will make an important contribution to malaria control policy in Kenya and throughout Africa, where malaria infection has increased dramatically.

MATERIALS AND METHODS

Study area

This study was conducted in Kisii County, Kenya. Epidemiologically, the county is located in the western region of Kenya. Kisii County is situated around 306 kilometers from Nairobi, Kenyan central administrative city. It is located on latitude: (0.41°) South, longitude: (34.46°) East. The main economic activity is agriculture. As per the last 2019 census, there were 1,266,860 persons in the county (6). The county has one teaching and referral hospital (KTRH), which serves as a regional reference hospital and a teaching hospital for Kisii University Medical School, however diagnosis and treatment services of malaria are available in all government health facilities and some few private facilities. The county records three rain seasons namely; April-May, August-September, and November-December. The main malaria intervention approaches used to combat malaria in this region includes proper case management with antimalarial drugs such as ACTs, intermittent prophylaxis during pregnancy (IPTp) and vector control. The drug of choice for treatment of uncomplicated malaria is Artemether-Lumefantrine. The current study was conducted in hospitals selected from 4 sub-counties of Kisii County (Figure 1).

Research design and participants

The current study utilized cross-sectional healthy point study design. All malaria out-patient participants diagnosed with uncomplicated malaria clinically were recruited to this study.

PARTICIPANT RECRUITMENT, TREATMENT AND FOLLOW UP

275 participants were recruited into this study. Only participants who consented to participate in the study were recruited. Further, participants who had resided in Kisii County for at least six months prior to the commencement of the study and those without severe malnutrition were recruited into the study. Those who didn't consent, those who were on transit, those who were

unable to tolerate oral treatment, and those who had hypersensitivity or allergy to ACTs and clinical danger or severe malaria were excluded from the study. The participants were requested to fill in the questionnaires pertaining the treatment and vector control practices carried out before initiation of current ACTs treatment. Consequently observations were carried out during the study period on the different methods used for malaria control.

Malaria positive participants were followed-up for a period of 28 days by evaluating clinical and parasitological parameters on days 1, 3, 7, 14, and 28 respectively after ACTs (A-L) treatment initiation. During the follow up period measurement of axillary temperature was done, physical examinations and identification of *Plasmodium falciparum* parasites. Blood samples were obtained by using finger pricks during the entire period. For molecular typing, blood spots were collected on filter papers (Whatman No. 3) on day 0 before treatment on day 28 for those which showed failure (recurrent parasitemia and recurrent fever). A detailed description of the study protocol has been provided and published elsewhere (7). Briefly, Blood samples were collected before the initiation of treatment. Blood samples were collected by obtaining 1 ml of venous blood for the participants older than 2 years after cleaning the surface with 70% alcohol. In the case of children below 2 years of age, 2 drops of finger-pricked blood samples were collected. Microscopy was used for diagnosis. Clinical examination was performed by taking a complete medical history, demographic information and contact details of the participant. For body temperature, auxiliary temperature was measured with a thermometer which had a precision of 0.1°C.

MOLECULAR CHARACTERIZATION OF CLINICAL ISOLATES

To distinguish between recrudescence and re-infection, molecular analysis was conducted by following the previously described method (8), with slight modifications. Briefly blood spotted filter papers were soaked for 24 hours in 1 mL of 0.5% saponin-1 phosphate buffered saline. The mixture was washed two times in 1 mL of PBS and boiled for 8 min in 100 mL PCR grade water to release DNA from the cells. To elute the extracted DNA, 150 µL Buffer AE was added to each well using a multichannel pipette and incubated for 1 minute at room temperature. This set up was then centrifuged at 2608 rcf for 8 min. DNA was recovered and stored at -80 °C. Nested PCR was performed on the extracted DNA for subsequent genotyping of *P. falciparum* polymorphic gene loci encoding Merozoite surface protein 2 (MSP-2) by using the method described by (9). A master mix was prepared according to manufacturer instructions (New England BioLabs, Massachusetts, USA). 24 µL of Master Mix was added to the PCR 96 well plate and 25 µL of the master mix was also added to negative PCR control. The plates were sealed using a thermo seal plate sealer and placed in the PCR thermo cycler. Amplification was then done at the following conditions; denaturation (94°C), annealing (55°C), and extension (72°C). Amplification was confirmed by running the nested PCR product together with a DNA ladder on the QIAxcel capillary electrophoresis. Molecular outcomes were categorized as recrudescence in cases where any one matching MSP2 allele was reported for ACTs pre-treatment and ACTs post-treatment samples. In cases where MSP2 alleles did not match ACTs pre- and ACTs post-treatment, they were then categorized as new infections. Consequently, for samples which unsuccessful amplified, they were regarded as unclassified. Primers used in this protocol are shown in table 1.

TREATMENT OUTCOMES

Efficacy was assessed by clinical and parasitological outcomes using WHO definitions *viz.* early treatment failure (ETF) if there is a development of severe signs or symptoms, or insufficient parasitological response by day 3. Classified as late parasitological failure (LPF) if there was *P. falciparum* parasitemia occurring between 4 and 28 days without fever. Those having fever and parasites between day 4 and day 28 were classified as late clinical failure (LCF). Classified as an adequate clinical and parasitological response (ACPR) if no failure was recorded at all (10). ACPR treatment outcome was used as a standard reference cut-off for this study.

The Questionnaire and Direct Observation

Questionnaire was used as a data collection tool for examining the effect of interventions on malaria treatment outcomes. The study was conducted by using household questionnaire and biomarker questionnaire. The questionnaire was filled by adult participants only. For the case of children, parents or care-givers filled on their behalf. Household questionnaire was used to determine the demographic patterns. The questionnaires focused on the vector control and chemotherapy practices used in malaria control. The questionnaires were adopted from the Kenya malaria indicator survey (Kenya malaria Indicator Survey, 2020). They were then translated to Ekegusii and Kiswahili local languages. Before using the questionnaire, it was pre-tested by using 8 patients who were drawn equally from each facility. The details captured included the social demographic characteristics of the patient; previous malaria drugs usage patterns, drug dosage, previous malaria episodes. Consequently the source of drugs utilized for previous treatment was also examined. Additionally, direct observation of the current intervention practices was also done during the study.

Data management and Data analysis

All the data were incorporated into Visual FoxPro, version 6.0 databases (Microsoft Corp., Seattle, WA, USA) by double-entry. The data sets were then checked for discrepancies that were then resolved. All the analysis was conducted using Stata Statistical Software, version 7.0 (Stata Corp., College Station, TX, USA).To assess the relationship between treatment outcomes and intervention practices, Logistic regression analysis was done. Bivariate analysis was applied and all the variables with a *P* value of 0.2 or less were entered into a stepwise forward multiple logistic regression model to determine the ODDS ratio. Interaction and confounding were assessed and values of $P \leq 0.05$ were regarded as statistically significant relationships.

RESULTS

Treatment Outcomes

There were 27(12%) early treatment failures, 20 (8%) late clinical failures and 11 (5%) late parasitological failures and 173 (75%) adequate clinical and parasitological outcomes recorded across all sub-counties. However the treatment outcomes varied across each sub county (figure 2).

MOLECULAR OUTCOMES

After complete follow up of the participants, 13/231 (5.6%) had *Plasmodium falciparum* on day 28. Among the respondents with parasites on day 28 post-treatment, 10 samples had bands on both day 0 and day 28, hence classified as recrudescence, 3 samples had no bands on the respective days of parasite recurrence, hence classified as new infections (figure 3).

Previous chemotherapy practices associated with treatment outcomes

When the predicting chemotherapy practices associated with treatment outcomes, it was observed that those who had previously practiced self-medication had poor treatment outcomes compared to those who used drugs after health care workers recommendations (OR=0.417; 95%

CI: 0.153-1.385; p=0.035). Participants who had previously used self-medication had low ACPR of 14 (8%) compared to those who had used the drugs after proper recommendation from the health care workers, with those recommended previously by a nurse recording an ACPR of 132(76%) and those recommended by a doctor recording an ACPR of 27 (16%).Those participants who used antimalarial agents only after getting recommendations from the health workers such as a nurse and a doctor recorded an ACPR of 122 (71%), compared with an ACPR of 40 (23%) among the participant who usually utilized drugs after suspecting that they had malaria diagnosis without proper diagnosis. Consequently better treatment outcomes was observed for those who previously finished drug doses as recommended by health care workers such as a nurse and a doctor compared to those who never finished their previous drug doses (OR=0.328; 95% CI: 0.168-0.941).Those who previously finished their doses recorded an ACPR of 138 (80%) compared to those who never finished their doses previously who recorded an ACPR of 35 (20%). type of antimalarial drugs previously used and reasons for stopping the prescribed doses were found to be statistically insignificant in influencing the treatment outcomes after treatment with ACTs (Table 2)

Current vector control practices on treatment outcomes

When the predictor current vector control practices associated with treatment outcomes were subjected to bivariate analysis, it was observed that usage of indoor residual spraying (OR=0.408; 95% CI: 0.132-0.682; p=0.002,), sleeping under the mosquito net (OR=0.218; 95% CI: 0.119-0.909; $p = 0.025$) and mosquito net treatment (OR=0.262; 95% CI: 0.092-0.823; $p = 0.003$) were positively influencing the treatment outcomes after ACTs treatment. Those participants who were using IRS recorded an ACPR of 115 (66%) compared to an ACPR of 58 (34%) recorded among those who did not use IRS as a vector control method. Those who were

sleeping under the mosquito net recorded an ACPR of 149 (86%) compared with an ACPR of 24 (14%) recorded among participants who didn't utilize the mosquito net. Consequently an ACPR of 123 (71%) was observed among participants who utilized treated mosquito nets, in contrast to a low ACPR of 50 (29%) reported among those who did not sleep under treated mosquito nets. Other variables such as the last date when indoor residual spraying was conducted and source of the mosquito net were found to be statistically insignificant in influencing the treatment outcomes (Table 3).

Multivariate regression prediction of malaria control practices influencing treatment outcomes

When the bivariate significant malaria intervention measures were subjected to multiple regression analysis, it was observed that the predictor intervention practices which statistically influenced treatment outcomes were; source of antimalarial recommendations (OR=5.348; 95% CI: 0.170-13.735), Ability of finishing dose (OR=0.635; 95% CI: 0.077-10.307), Sleeping under mosquito net (OR=0.428; 95% CI: 0.035-1.550) and Use of indoor residual spraying (OR=0.171; 95% CI:0.047-0.582). Whereas Frequency of antimalarial drug use and mosquito net treatment were statistically insignificant in determining the outcomes (Table 4)

Discussions

The treatment of malaria suspected cases coupled with vector control and proper diagnosis of suspected cases remains a major pillar in the control and elimination of malaria globally (11). Currently, the Kenyan ministry of health with the help of different county governments has initiated a large-scale malaria intervention practices which includes proper diagnosis, proper treatment of malaria cases and vector control. Treatment by use of ACTs has been intensified too, with Kenya adopting the use of Artemether- Lumefantrine for uncomplicated malaria caused by *Plasmodium falciparum*. However, different clinical and parasitological outcomes have been reported previously in Kenya and other parts of the world, thus raising concerns (12, 13, 14, 15,

and 16). There is limited data on the influence of intervention practices on the reported outcomes. This scenario may be influenced by many factors which include but are not limited to community chemotherapeutic and vector control practices. Hence, calling for efforts directed at intensifying malaria control so that the risk of malaria infection in the community can be further reduced or eliminated. Thus, trying to identify where challenges lie in the malaria treatment pathway is crucial so that interventions to improve on the drug usage practices can be implemented.

The previous drug use patterns are one of the factors which might be influencing the treatment outcomes of treated patients. With the source of medication playing a major role in determining the treatment outcomes. The current study has established that patients who had obtained the drugs by using self-medication, without recommendation by a health care worker, had a low ACPR of 14(8%). This scenario may be contributed by the tendency of most of the patients with malaria not seeking treatment in the formal sector, and thus standing a chance of not receiving the correct regimen or sometimes purchasing counterfeit drugs, which might be substandard and expired. This is unsurprising as treatments are often purchased over the counter from untrained shop keepers where the choice of drug and amount purchased are limited by the cost of the drugs and their availability. This may be coupled with improper diagnosis since most of the patients conduct self-medication without diagnosis. This current study is in agreement with the previous study conducted in Ghana, which established that self-medication was a major predictor factor of poor treatment outcomes (17).

Ability of finishing previous drug doses has been indicated as an influencing factor in determining the treatment outcomes. This study reported an ACPR of 35 (20%) among those participants who usually didn't finish the previous doses, which was low compared to those who were capable of completing the dosage. Sometimes even if the correct regimen is obtained, some of the patients will not adhere to the

exact dosage of the drug regimen and this will not only end in treatment failure, but will also promote the development of antimalarial drug resistance. Poor adherence reduces the dose taken and therefore increases the chance of poor treatment outcomes. Previous reports have indicated that incomplete dosing would challenge the main logic underlying this new combination approach of ACTs in malaria treatment, which aims at increasing the cure rates (18). The findings from this study are supported by a recent study carried in Ghana, which has indicated poor treatment outcomes among patients who did not complete their dosage previously (19). Patient adherence to the appropriate drug during treatment characterizes the final step in a pathway from the first developing symptoms to receiving curative treatment (20), and the problem of patients not taking drugs as recommended maybe more a result of the patient not having access to affordable treatments and not receiving the correct instructions rather than only non-adherence, thus raising concern on the healthy organization systems in the malaria endemic countries (21, 22).

Previous studies have indicated that drug coverage is the primary determining factor of drug pressure and the driving force behind the evolution of drug resistance (23, 24, 25). The significance of understanding how anti-malarial drugs are used in the community, how their use might be improved, and the effect on the clinical outcome is crucial in giving the correct direction in the control of drug resistance in the community. Previous studies have reported that treatment and prevention of malaria deaths can be obtained by conducting proper diagnosis and appropriate case treatment. Moreover, a recent report by WHO has indicated lack of timely malaria treatment coupled with improper use of drugs is hampering malaria elimination goals in Africa (26). Treatment failure has been observed previously in Africa, Asia and South America continents and this scenario is as a result of evolution of resistance to drugs by parasites. However this is usually mediated by drug over use (27, 28).

In Kenya, a large percent of malaria cases are treated at home without seeking healthcare management. In some circumstances, treatment is sought by local chemists who don't conduct proper laboratory diagnosis. Thus majority of the patients seeking treatment at health care facilities might have utilized home-based treatment. Hence there is a high chance of such patients harboring drug resistant strains or sometimes presenting with severe malaria cases at health care facilities. This raises concern on the effectiveness and adequacy of household and community based malaria management. The efficacy of anti-malarial drugs could be increased through policy-mediated reductions in drug pressure.

Worldwide increase of malaria interventions, especially in malaria prevalent countries has led to tremendous reduction of malaria cases for the last 2 decades. Vector control has previously proved as the major intervention (29). The current study categorically evaluated two main intervention programs, viz; indoor residual spraying and use of mosquito nets.

Indoor Residual Spraying, which is regarded as the key malaria vector control strategy by WHO, is currently being embraced by 42 African countries' national malaria control programs (30). The findings from this study have indicated that indoor residual spraying was influencing the treatment outcomes. The study reported an ACPR of 115(66%) among participants who practiced IRS. Mosquito nets usage is vital in controlling clinical malaria. Insecticide-treated mosquito nets (ITNs) have emerged as one of the three primary interventions recommended by the World Health Organization Global Malaria Program (WHO/GMP) for robust malaria elimination. ITNs is used as a vector control intervention by reducing malaria transmission and other infections transmitted by insects. This study has reported that those who slept under the insecticide treated mosquito nets recorded a high ACPR of 123 (71%). This study was conducted during the time when there was a free distribution of nets by the ministry of health in conjunction with the county government, this might be the reason for the high usage of ITNs by the participants. The efficacy results reported here agreed with earlier observations in Africa (31, 32), which established that mosquito net usage substantially reduced the mortality in children. Furthermore, this study concurred with a previous study done in Kenyan coast, which revealed that mosquito net compacted malaria clinical episodes (33). This has been supported by a study conducted in western Kenya, which

reported an efficacy of 30% reduction malaria episodes in children aged between 1 and 59 months old (34). Moreover, a previous study conducted in Tanzania, an area having similar transmission intensity patterns to that in our study site in south western Kenya, detected a reduction of 27% in the mortality of 1–59-month-old children (35). Consequently, a study conducted in Ghana indicated that usage of ITN among children can reduce under-five mortality (36). This finding supports the study by (37), which reported a substantial risk reduction against parasitemia among individuals living in households with both ITNs and IRS in sub-Saharan Africa.

Limitation for the study

The study was limited due to the inadequate number of participants enrolled in the study. Moreover the study area may not be representative for other geographical locations of Kenya. Consequently the treatment outcomes might have also been influenced by immunological factors which were not evaluated in this study.

Conclusion and recommendations

The study hereby concludes that there exists a high prevalence of self-medication in the community without proper diagnosis. These drugs are used inappropriately in most circumstances, hence leading to subsequent poor ACTs treatment outcomes. Moreover Vector control by use of mosquito nets and indoor residual spraying before and after treatment with ACTs is a vital component of containing malaria episodes after treatment. Thus the study hereby recommends for embracement of practical and effective public health education in regard to safe utilization of anti-malaria drugs at the community level. Health education on the appropriate use of antimalarial drugs is highly recommended. Training and information actions must be reinforced for better care of malaria and to preserve efficacy and safety of ACTs in Kenya. Moreover, this study recommends the continuous use of indoor residual spraying and mosquito nets even after treatment initiation. Supplementary malaria control strategies to augment the current interventions are needed to control the residual transmission after and before ACTs treatment.

ETHICAL APPROVAL AND CONSENT

Ethical approval was sought from University of East Africa, Baraton Institutional Review Board (UEAB/REC/4/2/2021, research permit was issued by Kenya National Commission for Science, Technology and Innovation (NACOSTI) License No: NACOSTI/P/21/8974 and Kisii County government (DTR/4/27). Written informed consent was obtained from the adult participants. The consent of those below 18 years of age was provided by the parents or the care-givers. Permission was granted by different sub counties before commencing the study. All research procedures were conducted by adhering to the ethical standards of the committees on human experimentation laid down in the Helsinki declaration of 1975 and revised in 2000. Moreover, the study was conducted in accordance with the guidelines of WHO good clinical practices. Specify how pain was managed during the collection of blood samples from the participants.

Data Availability

Data in tables and figures used to support the findings of this study are included within the article. Raw materials used in this study can be produced from the authors in request.

DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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LIST OF TABLES AND FIGURES

Table 1: Primers used in the PCR for genotyping MSP

Primer name	Sequence (5'→3')	Purpose
MSP-2(1)	ATGAAGGTAATTAAAACATTGTCTATTATA	External forward primer
MSP-2(4)	ATATGGCAAAAGATAAAACAAGTGTTGCTG	External reverse primer
MSP-2(A1)	CAGAAAGTAAGCCTTCTACTGG	Internal forward primer (IC3D7)
MSP-2(A2)	GATTTGTTTCGGCATTATTATGA	Internal reverse primer (IC3D7)
MSP-2(B1)	CAAATGAAGGTTCTAATACTA	External forward

		primer (FC27)
MSP-2(B2)	GCTTTGGGTCCTTCTTCAGTTGATTC	Internal reverse primer (FC27)

Footnote: MSP= merozoite surface proteins, PCR= polymerase chain reaction

Table 2: Showing previous chemotherapy practices influencing with treatment outcomes

Variable	**Treatment outcomes n (%)**						
	Participants, N (%)	ACPR (n= 173)	LCF (n= 20)	LPF (n= 11)	ETF (n= 27)	cOR (95% CI)	*P*-value
Previous Antimalarial used							
ACTs (A-L)	192(83)	118(68)	9(45)	9(82)	16(59)	0.862 (0.047-7.824)	0.842
Quinine	7(3)	43(25)	3(15)	2(18)	7(26)	0.252 (0.038-6.242)	0.65
Fansider	32(14)	12(7)	8(40)	0(0)	4(15)	1.000	
Source of antimalarial recommendation							
Nurse	168 (73)	132(76)	1(5)	6(55)	12(44)	0.312 (0.101-0.904)	0.195
Self-medication	43(19)	14(8)	4(20)	3(27)	4(15)	0.417 (0.153-1.385)	0.035*
Doctor	20 (9)	27(16)	15(75)	2(18)	11(41)	1.000	
Ability to finish dose							
Yes	130(56)	138(80)	12(60)	4(36)	20(74)	0.328 (0.168-0.941)	0.003*
No	101(44)	35(20)	8(40)	7(64)	7(26)	1.000	
Causes for terminating the dose							
When I am treated	166(72)	156(90)	11(55)	2(18)	5(19)	2.984 (0.180-1.305)	0.325

When I complete dose	65(28)	17(10)	9 (45)	9(82)	22(81)	1.000	
Frequency of antimalarial drug use							
As recommended by health workers	91(39)	122(71)	16(80)	4(36)	9(33)	3.259 (1.054-4.721)	0.004*
Anytime I feel feverish	99(43)	40(23)	3(15)	5(45)	15(56)	1.000	

Footnote: ACT**s** =Artemisinin combined therapies, (A-L) = Artemether Lumefantrine, ACPR =Adequate clinical parasitological response, LCF= Late clinical failure, LPF= Late parasitological failure, ETF= Earlier treatment failure, CI =confidence interval, *P* = probability, OR = odds ratio, $P \leq 0.05$ value is statistically significant under logistic regression. *Statistically significant factors ($P< 0.05$) for ACPR treatment outcome were included in multivariate model

Table 3: Bivariate analysis of current vector control practices on treatment outcomes

Variable	Number of participants, n (%)	ACPR (n= 173)	LCF (n= 20)	LPF (n= 11)	ETF (n= 27)	cOR (95% CI)	*P*-value
Use of indoor residual spraying							
Yes	94(41)	115(66)	11(55)	3(27)	14(52)	0.408 (0.132-0.682)	0.002*
No	137(59)	58(34)	10 (45)	8(73)	13(48)	1.000	
Previous indoor residual spraying							
< 6 months	167(22.9)	59(10.5)	13(15.8)	3(15.8)	11(57.9)	0.705 (0.305-2.644)	0.925
≥ 6 months	64(77.1)	114(21.9)	7(10.9)	8(15.6)	16(51.6)	1.000	
Sleeping under mosquito net							

Yes	162(70)	149(86)	9(45)	9(82)	15(56)	0.218 (0.119-0.909)	0.025*
No	69(30)	24 (14)	11(55)	3(27)	12(44)	1.00	
Mosquito net treated							
Yes	173(75)	123(71)	7(35)	7(64)	17(63)	0.262 (0.092-0.823)	0.003*
No	58(25)	50(29)	13(65)	4(36)	10(37)	1.000	
Source of mosquito net							
Government facility	90(39)	130(75)	7(35)	1(9)	3(11)	0.184 (0.076-0.978)	0.34
Pharmacy shop/open market	83(36)	11(7)	11(55)	7(64)	14(52)	0.260 (0.083-1.428)	0.120
Malaria campaign	58(25)	32(18)	2(10)	3(27)	10(37)	0.605 (0.031-12.181)	0.812

Footnote: ACPR =Adequate clinical parasitological response, LCF= Late clinical failure, LPF= Late parasitological failure, ETF= Earlier treatment failure, CI=confidence interval, *P*=probability, OR=odds ratio, $P \leq 0.05$ value is statistically significant under logistic regression. *Statistically significant factors ($P < 0.05$) for ACPR treatment outcome were included in multivariate model

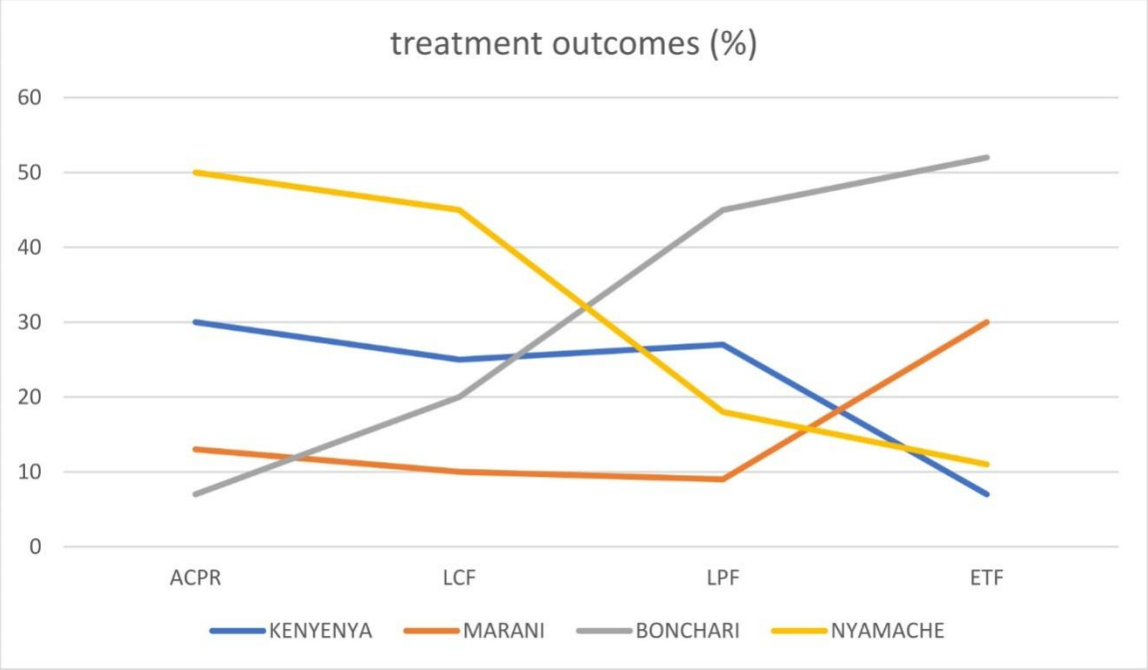
Table 4: Multivariate regression analysis of intervention factors associated with treatment outcomes

Predictor factor	**Adjusted Odds ratio**	**95% C I**	***P*-value**
Ability of finish dose			
Yes	0.635	0.077-10.307	0.004*
No	1.000		
Source of antimalarial recommendation			

Doctor	5.348	0.170-13.735	0.017*
Self-medication	1.000		
Use of indoor residual spraying			
Yes	0.171	0.047-0.582	0.021*
No	1.000		
Frequency of antimalarial drug use			
Anytime I feel feverish	0.229	0.072-2.524	0.151
As recommended in health care facility	1.00		
M**osquito net treatment**			
Yes	0.383	0.095-0.945	0.245
No	1.000		
Sleeping under mosquito net			
Yes	0.428	0.035-1.550	0.001*
No	1.000		

*Statistically significant intervention factors for ACPR treatment outcome at $p \leq 0.05$.

Figure 1: A map showing Kisii County *(Source: Google maps, 2019)*



Footnote: ACPR =Adequate clinical parasitological response, LCF= Late clinical failure, LPF= Late parasitological failure, ETF= Earlier treatment failure,

Figure 2: treatment outcomes in different sub counties

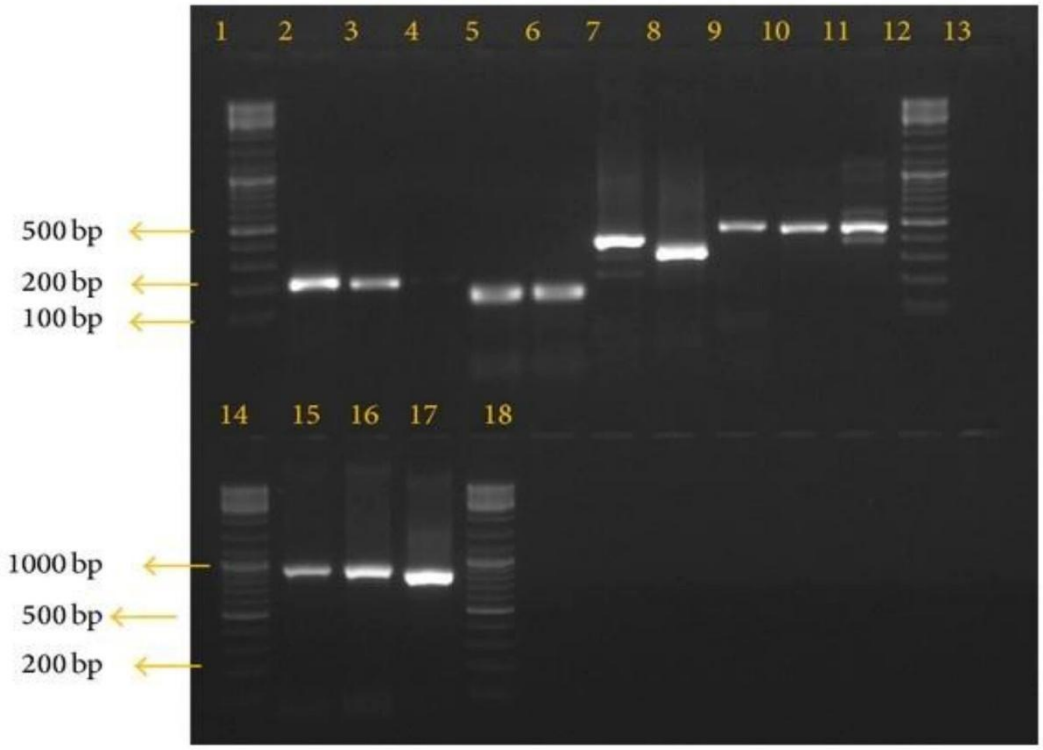


Figure 3: Gel image showing the amplification of *P. falciparum* msp2 of recurrent samples. Bands 2,3,4,5,6,7,8,9,10 and 11 shows positive msp2 allelic family. Band13 is the negative control, and lanes 1, 12, 14, and 18 shows 100 bp Molecular Weight DNA ladder (New England BioLabs, Massachusetts, USA).