USE OF ANTIBIOTICS AND ANTIMALARIALS IN THE MANAGEMENT OF FEBRILE ILLNESSES IN CHILDREN IN PUBLIC HEALTH FACILITIES IN WESTERN KENYA

BY:

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A THESIS SUBMITTED TOTHE SCHOOL OF PUBLIC HEALT DEPARTMENT OF EPIDEMIOLOGY AND NUTRITION, IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF PUBLIC HEALTH, (MPH)

MOI UNIVERSITY

JULY, 2015

DECLARATION

Declaration by the Candidate

This thesis is my original work and has not been presented for examination in any other university to the best of my knowledge. No part of this thesis may be reproduced without prior written permission of author and / or Moi University.

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To Mrs. E. Rono. You have moulded me into the person I have become and you have always stood by me. You always inspire me.

ABSTRACT

Title – Use of antibiotics and antimalarials in the management of febrile illnesses in children in public health facilities in Western Kenya

Background: Malaria is a global tropical disease associated with high morbidity and mortality, especially among the children. Over 90% of its distribution is in Africa with a high burden of the disease being felt in Kenya. Many diseases present clinically with fever and Integrated Management of Childhood Illnesses (IMCI) advocates for the use of antibiotics for other infections and antimalarials for malaria. With the signs and symptoms of malaria resembling those of other diseases, many febrile conditions are treated clinically as malaria. The current first line treatment for malaria is artemisinin-based combination therapy after resistance to earlier medications occurred with its unnecessary use caused by presumptive treatment practices that assume most febrile illnesses are caused by malaria. Without laboratory confirmation of malaria, continued use of artemisinin-based combination therapy on non-malaria cases may soon lead to resistance due to their unnecessary use. A randomized control study was put in place with the primary objective of testing whether financial incentives offered (to intervention group) at the facility level improve targeting of antimalarials to patients with parasitologically diagnosed malaria. This is a sub-study of the above describing the role of antibiotics and antimalarials in the management of febrile illnesses among children.

Objectives: The main objective of this study was to describe the prescription habits of both antimalarials and antibiotics in the management of febrile illnesses among children.

Methodology: This was a comparative, records-based cross-sectional study carried out in 17 public health facilities of high and low malaria endemicity in the western region of Kenya. Health facility records were reviewed by use of a checklist and data was analysed using STATA analysis package by use of descriptive statistics as well as logistic regressions. These were then presented in prose and in form of tables and graphs.

Results: A total of 6086 children under the age of 5 years were included in the study with a mean age of 2 years and 51.2% being female. Among the 2124 study subjects who received antibiotics and other treatment regimens including paracetamol, zinc sulphate, ORS and piriton, (37.5% of intervention and 31.8% of control) most of them received cotrimoxazole dispensed at 46%. Positive blood smear results for public health facilities in Western Province and Rift Valley Province were 26.5% and 11.6% respectively. Among those who received medication, 70% of those with a negative blood smear result were given antibiotics and 68% of those with a positive blood smear result got AL.

Conclusions: Antibiotics are used according to IMCI guidelines with healthcare workers in the intervention group using them more than healthcare workers in the control group. Twice as many children had positive malaria smears in the public health facilities in Western Province compared to the public health facilities in Rift Valley Province and patients with positive blood smear results receive AL while those with other diseases receive antibiotics.

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LIST OF ABBREVIATIONS

ACT	Artemisinin-based Combination Therapy
AIDS	Acquired Immunodeficiency Syndrome
AL	Artemeter Lumefantrine
AMPATH	Academic Model Providing Access To Healthcare
BBB	Blood Brain Barrier
CDC	Centres for Disease Control and Prevention
CI	Confidence Interval
DMOH	District Medical Officer of Health
DOMC	Division of Malaria Control
DALYs	Disability Adjusted Life Years
GDP	Gross Domestic Product
HIV	Human Immune Deficiency Virus
IMCI	Integrated Management of Childhood Illnesses
IPTp	Intermittent Presumptive Treatment for pregnant women
IREC	Institutional Review and Ethics Committee
IRS	Indoor Residual Spray
ITNs	Insecticide Treated Nets
KDHS	Kenya Demographic and Health Survey
KMIS	Kenya Malaria Indicator Survey
NHSSP	National Health Sector Strategic Plan
NMAUF	Non-malarial Acute Undifferentiated Fever
OPD	Out Patient Department

OR	Odds Ratio
P	P value
PMI	President's Malaria Initiative
PMOH	Provincial Medical Officer of Health
RDTs	Rapid Diagnostic Tests
SPs	Sulfadoxine-Pyrimethamine
USA	United States of America
USAID	United States Agency for International Development
USD	United States Dollar
WHO	World Health Organization

ACKNOWLEDGEMENT

It is indeed with great sense of fulfilment and humility that I acknowledge Prof. Wendy O'Meara and Dr. Samson K. Ndege for their commitment and constant dialogue. Their enormous support in achieving my objectives deserves credit and gratitude.

Sincere gratitude is given for the efforts made by the members of the School of Public Health for their tireless efforts to take me through the whole process of proposal development and write-up of this thesis throughout the academic years.

I salute and acknowledge Mable Jerop for her statistical support and advice and Rebecca Wafula for her technical support.

Special mention is made to the various authors whose writings inspired me to do this study and have been a constant reference point in my work.

Last but not least, I would like to thank my husband, Benard Rono, for his constant support technically, financially and emotionally. His role in the production of this thesis will forever be cherished.

It is your support, co-operation and constant dialogue that led to my success. I hope and trust that you all share with me the joy of the success of my masters.

CHAPTER ONE

INTRODUCTION

1.1 Background

Malaria is a global tropical disease causing more than 1 million deaths and 300 million clinical cases every year. It is a leading cause of morbidity and mortality for children in sub–Saharan Africa. This is a life threatening disease classically characterized by periodic chills, rigors, and high fever followed by profuse sweating, which may occur at regular intervals of 48 to 72 hours. It is caused by *Plasmodium* parasites that are transmitted through the bite of an infected female Anopheles mosquito [1]. There are four *Plasmodium* parasite species which cause the infection namely *P. falciparum, P. vivax, P. ovale* and *P. malariae. Plasmodium falciparum* is known to cause the most serious and wide spread cases of malaria.

The estimates of deaths due to these infections is over a million [1, 2] from 109 countries, representing a total at-risk population of over three billion. This is approximately half of the global population [3]. Thirty five countries account for 98% of the global malaria deaths, 30 of them being in sub-Saharan Africa and 5 in Asia among the countries at risk for malaria.

Malaria morbidity represents a significant part of the global health burden of malaria with estimates ranging from 247 to 515 million cases worldwide per year [1, 4]. An accurate count of the annual number of clinical malaria cases is however hindered by poor surveillance, inconsistent recording and reporting methods, and little to no parasitological diagnosis. It has even been argued that, considering average episodes per year in endemic areas and average rates of parasitemia among the exposed, well

over two billion febrile episodes resembling malaria can be expected annually, with the majority of these being positive for the malaria causing parasite [5].

Malaria morbidity is responsible for 2.2% of the global disease burden in terms of disability-adjusted life years (DALYs). This is according to the 2004 World Health Organization (WHO) estimates [6] which equates to over 35 million years of life lost to morbidity attributed to malaria infection. Malaria can also contribute to the development of a host of other syndromes, further increasing the impact on mortality and morbidity. Complications of *Plasmodium* infection, particularly with *P. falciparum* in cases of severe malaria, include severe anaemia, transient immune suppression, increased risk of HIV mortality, hypoglycemia, cerebral malaria, adverse events from malaria drugs, and death [5]. Other indirect contributions to morbidity are ascribed to malaria infection in addition to these direct effects. These include increase in maternal anaemia during pregnancy, low birth weight, intrauterine growth retardation, immune suppression, bone marrow suppression, and nutritional deficiencies [5].

A challenge is posed by the fact that many diseases have similar presentations. Many illnesses present with fevers and other signs that malaria would present with and many of these are treated with antimalarials. Non-malarial acute undifferentiated fever (NMAUF) refers to a group of febrile illnesses with no indication of an organ-specific disease after diagnosis of malaria has been excluded and is one such condition which is difficult to differentiate or specifically diagnose as a given illness [7]. In the developing countries, the empirical treatment of NMAUFs with antimalarial drugs continue to introduce overtreatment and the risk of developing resistance to antimalarials.

Integrated Management of Childhood Illnesses (IMCI) is an innovative approach which was started in 1995 by WHO and UNICEF with the aim of introducing a comprehensive and timely management of malaria, pneumonia, diarrhoeal diseases, measles and malnutrition which are the 5 most common causes of ill health and death among the under-fives[8]. World Health Organization also states that in developing countries, about half of all childhood deaths – 4.9 million – are caused by no more than four conditions namely pneumonia, diarrhoeal diseases, malaria and measles with malnutrition being associated with them[9]. Children brought for medical treatment in health facilities are often suffering from more than one condition, making a single diagnosis impossible hence the integrated approach. To manage these diagnoses, oral antibiotics are used in many health facilities with more than one type of antibiotic being available. First line antibiotics are prescribed first and the second line antibiotic will only be prescribed if the first-line one is not available or the illness does not respond to the first-line one. These are the cotrimoxazole and amoxicillin. Use of more than one antibiotic is also recommended with multiple illnesses especially if one antibiotic is not effective on both illnesses otherwise one antibiotic can be used as a broad-spectrum antibiotic and for a longer duration. Antimalarials on the other hand are used for malaria and these vary from country to country with Kenya using the ACTs. Other antimalarials used are chloroquine, quinine and sulfadoxine-pyrimethamine [8].

Resistance by *P. falciparum* to earlier antimalarial drugs has strongly laid setbacks on strategies for malaria control and elimination. One of the major aims of the World Health Organisation's new malaria control strategies is the rational and appropriate use of antimalarial drugs and in particular of artemisinin-based combination therapy (ACTs), currently used for the treatment of uncomplicated malaria; in order to delay

the appearance of drug-resistant parasites. The un-prescribed use of antimalarial drugs which includes self- medication and parental administration to children which are bought over the counter is a key component in the development of antimalarial drug resistance and must be controlled among patients living in malaria-endemic areas [10].

The un-prescribed use of the antimalarials introduces over-treatment hence bringing in a serious public health concern. Over prescription is exacerbated by presumptive treatment practices that assume most febrile illnesses are caused by malaria. The poor specificity of a clinical diagnosis for malaria [11], due to signs and symptoms that can be caused by other diseases [12], leads to significant over diagnosis of febrile illness as malaria and an over prescription of antimalarials [13]. Over diagnosis, over prescription of costly antimalarials, increased burden on health facilities, and loss of time and productivity from school or employment that result from misdiagnosis of untreated disease all contribute to the economic burden of malaria. In Sudan, the estimated cost of diagnosis and treatment of malaria was USD 100 million in 2000, but the cost of actual malaria cases which needed treatment was estimated to be closer to USD 14 million. In Uganda a study revealed that withholding antimalarial treatment in febrile children with negative blood smears was safe and saved 1,600 antimalarial treatments in 601 children over an 18-month period [14, 15].

In a review of studies looking at the misdiagnosis of malaria in Africa, it was found that an average of 67% of patients clinically diagnosed with malaria have illnesses attributable to other causes [10]. A study in Ghana showed that, in a typical rural health facility that does not have diagnostic capability, 90.1% of patients with negative blood slides received a clinical diagnosis of malaria and were wrongly treated with antimalarials [16]. In 1998, Kenya changed its first line antimalarial

policy from chloroquine to sulfadoxine-pyrimethamine (SP), and by 2003, resistance to this drug was already noted. In just four years, from 1998 to 2001, treatment failure was reported throughout Kenya. In Kisumu, failure rates were noted to be between 11 and 42%, and between 3 and 27% in Bondo [17]. This development of resistance to SP led the Kenyan Ministry of Health to change the first line antimalarial policy to artemisinin-based combination therapies (ACTs) in 2006. With this new treatment recommendation in place, delaying drug resistance development to ACTs became even more of a priority. The practice of presumptive diagnosis of malaria often leads to treatment of non-malaria fevers with antimalarials, thus increasing the risk of spreading drug resistance to antimalarial medications [10, 16, and 17]. Drug resistance is further exacerbated by the misuse of antimalarials. Over prescription, as well as incomplete dosing, can expose the parasite to the drug without eradicating it, thereby increasing the risk of developing resistance.

In resource-constrained settings such as western Kenya, where the burden of malaria is high and the need for accurate diagnosis and appropriate treatment is critical, it is important to maximize efforts by focusing interventions on areas where it is most needed, and that are positioned to have the greatest benefit for the smallest cost. Antimalarials therefore should only be given to those patients who test positive or who have confirmed malaria while those who test negative should be done further investigations so as to confirm underlying conditions and treat them appropriately.

The Facility Incentive Study implemented by the Academic Model Providing Access To Health care (AMPATH) was put in place with the primary objective of testing whether financial incentives offered at the facility level improve targeting of antimalarials to patients with parasitologically diagnosed malaria. To achieve this,

two specific aims were proposed, namely; Establish quality assurance/quality control surveillance of clinical microscopy in government health facilities (These received training in malaria diagnosis and clinical management as well as necessary capital investments in laboratory equipment), and comparing the effectiveness of clinical and technical training in diagnosis of malaria (group 1) to clinical and technical training in the diagnosis of malaria plus financial incentives linked to prescription practices (group 2) in improving diagnosis and treatment of malaria and non-malaria fevers. This proposed to test a novel strategy to introduce financial considerations into decision-making at the level of the facility in order to increase diagnostic testing, improve prescription practices and increase adherence to the results of diagnostic tests. For this large study, each public facility enrolled into the two groups, received training in malaria diagnosis and clinical management as well as necessary capital investments in laboratory equipment.

These facilities are found in two distinct regions of Kenya, Western and Rift Valley Provinces with varying malaria endemicity. The shores of Lake Victoria in Bunyala District as well as the districts in Western Province form the high malaria endemic zones. This is the zone with the highest malaria risk with transmission being perennial and peaks from June to August and in November. The average number of clinically diagnosed cases of malaria for those individuals under five years of age from January 2012 to March 2012 was 514 cases while the average for under-five, microscopically-confirmed cases of malaria was 226 cases in the same period (January 183 and 82, February 195 and 82 and March 136 and 62 respectively). The Kenyan highlands represented by the districts in Rift Valley province form the regions with low endemicity. This is a highly populated region with low disease risk in an average year, but the rainfall and temperature variations leads to the epidemics affecting large

population [18]. The average number of clinically diagnosed cases of malaria for those individuals under-five years of age from January 2012 to March 2012 was 264 cases while the average under five, microscopically-confirmed cases of malaria was 98 cases (January 101 and 28, February 93 and 41 and March 70 and 29 respectively) [19].

DISTRICT	**FACILITY**	**ENDEMICITY**
ELDORET WEST	Railways Dispensary	Low
	Moi's Bridge Health Centre	Low
	Sosiani Health Centre	Low
	Soy Health Centre	Low
BARINGO CENTRAL	Tenges Health Centre	Low
	Kiptagich Health Centre	Low
	*Kituro Health Centre	Low
KEIYO NORTH	Kapteren Health Centre	Low
	Msekekwa Health Centre	Low
BUNGOMA EAST	Sinoko Dispensary	High
	Milo Health Centre	High
BUTULA	Bumala A Health Centre	High
	Bumala B Health Centre	High
BUNYALA	Mukhobola Health Centre	High
	Budalangi Dispensary	High
TESO NORTH	Angurai Health Centre	High
	Moding Health Centre	High
	Malaba Dispensary	High

Most facilities in the study have a clinical officer, except for Kapteren Health Centre and Budalangi Dispensary. All facilities have at least three nurses with Moi's Bridge having nine nurses posted during the day. At least one laboratory technician is posted during the daytime hours of operation in each of the facilities.

Sinoko Dispensary, Moi's Bridge Health Centre and Mukhobola Health Centres are the only facilities that have a pharmacy technician. A nurse covers the pharmacy in Soy Health Centre, Msekekwa Health Centre, Kituro Health Centre, Bumala B Health Centre, and Budalangi Dispensary. In Bumala A Health Centre however, a casual covers the pharmacy and assists in the dispensing of drugs. Bumala A Health Centre, Kituro Health Centre, Malaba Dispensary, Angurai Health Centre, Mukhobola Health Centre, Budalangi Dispensary and Moding Health Centre do not have a cashier or records clerk. A few of the facilities have students on attachment [19].

This particular study was a sub-study of the above described study which highlighted the role of antibiotics and antimalarials in the management of fevers among children in order to reduce morbidity and mortality.

1.2 Problem Statement

The treatment of malaria as proposed by WHO, is treatment with antimalarials for positive tests, i.e. test to treat. Despite this, the practice in Kenya is that whenever a patient comes to the health facility with any kind of fever, he/she may be sent to the laboratory for tests but may still be treated for malaria despite having a negative result from the laboratory. This is done for both adults and children**.** Most febrile illnesses are often treated as malaria without laboratory confirmation. This can lead to resistance to the available antimalarials, ACTs, due to their continued use on non-malaria cases which would mean that there will no cheap alternatives once this occurs. Other diseases have febrile episodes e.g. pneumonia and correct diagnosis of these will reduce the use of ACTs and lead to proper use of antibiotics. Kenya changed its first line treatment of malaria from chloroquine to Sulfadoxine-

Pyrimethamines (SPs) in 1998 and by 2003 resistance to the SPs had already been noted. With a few studies conducted and evidence of this given, it led to the change to ACTs in 2006. Delaying resistance to these drugs then becomes a priority with the assistance of laboratory confirmation of malaria. Proper use of antibiotics in accordance to IMCI is also necessary.

1.3 Justification

Kenya's population according to the 2009 national census was at 38.3 million of which 19.15 million were children [20]. This figure represents roughly half of the entire population. According to the Kenya Demographic and Health Survey (KDHS) of 2008/2009, the under 5 mortality rate was 74/1000 live births or approximately 1 in 13 children die before their fifth birthday in Kenya [21]. These deaths are related to communicable childhood illnesses including malaria which have common signs and symptoms including febrile episodes. Nearly all child deaths occur in developing countries with almost half of them in Africa [22]. Appropriate treatment of these diseases would contribute to the reduction of these deaths and directing antimalarials to confirmed malaria cases would be a step at achieving this. This study provides information on whether clinicians adhere to IMCI guidelines on the management of childhood illnesses by reducing the unnecessary use of antimalarials and antibiotics and making sure that other conditions are treated so as to reduce morbidity and mortality.

1.4 Research Question

1. What is the role of antibiotics in the management of febrile illnesses among children in public health facilities in western Kenya?

1.5 Hypotheses

1.5.1 Null Hypothesis

Healthcare workers in the intervention group use antibiotics in the management of febrile illnesses to the same level as healthcare workers in the control group.

1.5.2 Alternative Hypothesis

Healthcare workers in the intervention group do not use antibiotics in the management of febrile illnesses to the same level as healthcare workers in the control group.

1.6 Objectives

The main objective of this study is to describe the prescription habits of both antimalarials and antibiotics in the management of febrile illnesses.

Specific objectives include the following:

1. To determine the slide positivity rate for the under 5s who visit the laboratory in public health facilities in western Kenya.
2. To describe antibiotic prescription patterns in the management of febrile illnesses.
3. To describe antimalarial prescription patterns in the management of febrile illnesses.

CHAPTER TWO

LITERATURE REVIEW

2.1 Childhood deaths in the world

Mortality among the under 5s is still an issue worldwide but more so in Africa. According to W.H.O. estimates, 73% of deaths are attributed to 6 causes, mostly communicable diseases [22], namely pneumonia (19%), diarrhoea (18%), malaria (8%), neonatal sepsis or pneumonia (10%), preterm delivery (10%) and asphyxia at birth (8%).

Malaria presents clinically as fever and flu-like illness with chills, headaches, muscle and joint pain and fatigue. Nausea, vomiting and diarrhoea can also occur. Due to the loss of red blood cells as they rupture, anaemia and jaundice (yellowing of the skin and conjunctiva of the eyes) may occur. Infection with P. falciparum, if not promptly and appropriately treated is fatal as it causes kidney failure, seizures and mental confusion, when the parasite penetrates the blood-brain-barrier (BBB), coma and death [1, 23].

Pneumonia which is the inflammation of the lungs due to infection presenting with cough and/or fast or troubled breathing, lethargy or tiredness and fever [24]. A recent study in USA found that 26 percent of children with fever and leukocytosis (a white blood cell count greater than 20,000 per mm3 [20 × 109 per L]) had pneumonia, even in the absence of respiratory symptoms [25].

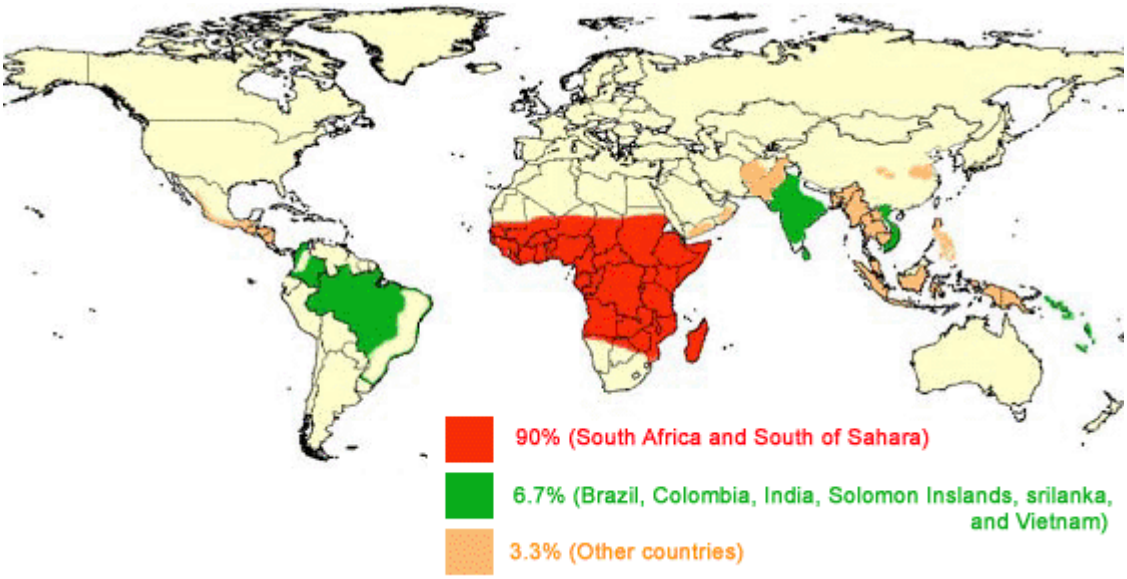
Diarrhoea on the other hand can be described as an abnormal increase in the frequency, volume or liquidity of stool. This may last from a few hours to a couple of days. It is typically associated with abdominal cramps with signs and symptoms including frequent loose, watery stools, abdominal pain, fever, bleeding and light

headedness or dizziness from dehydration [26]. All these diseases have fever as a common sign. A report from UNICEF states that 18% of deaths seen in under-five children in Africa are due to malaria, while diarrhoeal diseases and pneumonia account for 40% of child deaths [27].

Non malarial acute undifferentiated fever (NMAUF) refers to a febrile illness with no indication of an organ-specific disease after diagnosis of malaria has been excluded. Empirical treatment of NMAUFs with antimalarial drugs continues even in the era of highly specific rapid diagnostic tests (RDTs) for malaria in developing countries including Kenya [7].

2.2 Malaria in Africa

A large proportion of malaria deaths occur in Africa, specifically Sub Saharan Africa, where it is associated with poverty, (a disease of poverty and a disease causing poverty) [3]. Most of these infections in Sub Saharan Africa are caused by P. falciparum, the most severe and life-threatening form of the disease and is home to the most efficient vector, the anopheles mosquito [3]. With the map of malaria distribution in the world below, it is clear that malaria burden is borne by Africa with 90% in Sub Saharan Africa [28]



Malaria also has a direct impact on Africa's human resources. Of the estimated annual deaths from malaria, over 90% of these are borne by Africa alone [2].

Nearly 31 million of the over 35 million DALYs attributed to malaria, are suffered in Africa [6] making malaria the fourth-highest contributor to disease burden on the continent.

The economic burden resulting from malaria is considerable. Malaria-related costs in the region total USD 12 billion annually, equating to an average loss of 1.3% of gross domestic product (GDP) growth per year across some countries on the African continent. This financial burden impacts families as well. The average household expenditure on malaria is 10% of their yearly spend [3]. Exacerbating the healthcare costs that directly impact local and national economies are indirect costs resulting from the malaria burden. Not only does malaria result in lost life and lost productivity due to illness and premature death, but it also hampers schooling of children and their social development [3]. Lost productivity due to illness and time in patient care, lost education for students, teachers, and facilitators, costs related to long-term physical

disability, and even increased family size due to increased fertility compensation for high child mortality all contribute to the economic impact of malaria [3, 13].

2.3 The state of Malaria in Kenya

The burden of malaria is particularly high in Kenya with a 67% (2009) being at risk of malaria [29] and the estimated annual malaria deaths at 12/100,000 population (2008) [30]. Nineteen percent of all deaths in Kenya during the year 2006 were attributable to malaria [31] and 20% of all deaths in children under five. Between 30-50% of all outpatient attendance and 20% of all health facility admissions are due to malaria [32]. The morbidity associated with malaria has a significant impact on the country, which ranks fifth in the world in annual malaria incidence [3].

The economic burden contributed to the prevention, treatment, and management of malaria in Kenya is great. Over USD 61 million was spent on malaria control in 2008 [31], not including the costs to health systems and human resources, which are considerable. Kenya loses an estimated 170 million working days due to malaria infection annually [32].

Kenya is one of nineteen countries in the President's Malaria Initiative (PMI). This a five-year, US$ 1.2 billion program led by USAID in conjunction with the Department of Health and Human Services (Centers for Disease Control and Prevention), the Department of State, the U.S. Peace Corps and the U.S. Military's Walter Reed Malaria Research Unit. In Kenya PMI has committed an estimated $80 million towards the control of malaria by supporting four key interventions by the Division of Malaria Control (DOMC) namely the indoor residual spraying (IRS), provision of Insecticide-treated nets for mosquito control (ITNs), diagnosis and treatment in

conjunction with buying and distributing of life-saving drugs e.g. ACTs and delivering treatment for pregnant women (intermittent presumptive treatment - IPTp). PMI also supports the appropriate diagnosis and treatment of malaria by assisting in the improvement of government laboratories and laboratory personnel.

The first line treatment of malaria in Kenya since the change in 2006 has been artemether-lumefantrine (AL) which is an ACT. Currently, PMI has procured about 10 million treatment doses that were distributed to government health facilities and provided free of charge to the end user since its initiation [33].

2.4 Malaria diagnosis and treatment

WHO recommends parasitological diagnostic testing before treatment of malaria. When microscopy is not available, RDTs are the alternatives which have been demonstrated to perform equally well. Clinical diagnosis of malaria by use of signs and symptoms is still carried out especially in resource-constrained countries. This employs the use of integrated management of childhood illness (IMCI) guidelines. Mothers also understand the signs and symptoms of malaria with symptom recognition, with proper management of childhood illnesses as addressed by the IMCI strategy. The implementation of IMCI programmes in government health facilities has significantly improved health seeking for childhood diseases [34].

The mainstay treatment for malaria is ACTs. A large multicenter trial aimed at collecting information that would assist national malaria control programs in sub-Saharan African countries in choosing the most appropriate ACTs found that ACTs showed excellent efficacy, up to day 63 post-treatment, with the risk of recurrent infections being significantly low, even in areas of high transmission [35]. Another study carried out in Kenya found that stock-outs of AL coupled with low microscopy

and RDT availability in health facilities are a setback in malaria treatment. The microscopes and RDTs are more often available in high level facilities than in the lower levels where majority of the people get their treatment. The same study however found that over two-thirds of facilities lacked RDTs in areas where RDTs had been supplied since 2006 [36]. Low reports of stock-outs of antimalarial drugs and malaria diagnostic services is a basic prerequisite for effective implementation of the new malaria case-management policy recommended by W.H.O.

Despite the IMCI guidelines and WHO recommendations, people still do self-diagnosis and treatment. This treatment is done using over-the-counter medication due to the ease in availability and cost. A study carried out in western Kenya found that most people access these drugs and use them since retailers stock them with quinine being the most frequently stocked variety at 61% followed by SPs at 57% and ACTs at 44%. Accessing these drugs was also easier since the distance to the retailer was roughly half the distance to the nearest health facility. Prices for these also varied with SPs being the cheapest [37]. These findings coupled with the time spent while searching for this treatment would make people to utilize over-the-counter medication rather than to go for health facility services.

With the overlap of signs and symptoms of malaria and bacterial infections like pneumonia, treatment guided by diagnostic tests may miss few true cases i.e. false negatives but these could be followed up and treated. A question that would come to mind is “If it is not malaria, then what is the cause of the fever?” The use of RDT's and microscopy to direct the use of antimalarial drugs in young children has been proved as a safe strategy as it did not result in any missed diagnoses of malaria.

Microscopy has even better sensitivity and specificity hence better case management [38, 39].

A systematic review of studies conducted in 16 different African countries between 1986 and 2007 and published between 1989 and 2009 revealed a considerable reduction of the proportion of malaria among fevers over time in Africa. This decline provides evidence for the policy change from presumptive antimalarial treatment of all children with fever to laboratory diagnosis and treatment upon result which WHO recommends currently. Using RDTs as an alternative when microscopy is unavailable also reduces over-treatment with antimalarials significantly. Thus, with declining malaria prevalence, RDTs and microscopy will potentially identify majority of febrile cases with parasites and lead to improved management of malaria and non-malaria fevers insuring appropriate care of non-malaria fevers and rationale use of antimalarials [40, 41].

Confirmed malaria cases have better prognosis as compared to clinically diagnosed cases. A study carried out in Uganda found that the diagnosis of malaria in the absence of microscopic confirmation was associated with significantly increased mortality in hospitalized paediatric patients and concluded that inpatient diagnosis of malaria should be supported by microscopic or rapid diagnostic test confirmation. After adjustment for age, malaria complications, and co-morbid conditions, children who did not have microscopy performed or had a negative blood smear had a higher risk of death than those with a positive blood smear [odds ratio (OR): 3.49, 95% confidence interval (CI): 2.88-4.22, $P < 0.001$; and OR: 1.59, 95% CI: 1.29-1.96, $P < 0.001$, respectively] [42]. Outpatients should also have confirmed diagnoses.

Despite efforts to expand the provision of malaria diagnostics like RDTs and microscopy, they continue to be underused and patients with negative test results frequently receive antimalarials since people tend to treat presumptively. Provision of new tools to reduce inappropriate use of new expensive antimalarial treatments must be accompanied by a major change in clinical treatment of patients presenting with fever but lacking evidence of malaria infection reducing overtreatment of malaria [43]. A study done in an urban setting in Uganda found that with-holding antimalarial drugs from febrile patients with negative malaria slides was safe. Malaria was responsible for only 32% of febrile episodes. This saved over 1,600 antimalarial treatments in 601 children over an 18-month period. In this era of expensive ACT, directing resources towards improving diagnostic and treatment practices and interventions may provide a cost-effective measure for promoting rational use of antimalarial therapy and reduction of case fatality [44]. This could prompt clinicians to consider alternative diagnosis and increase prescription of antimicrobials.

A study carried out in a rural teaching hospital in central India showed that 88% of all hospitalized adults with acute undifferentiated fever tested for malaria did not have evidence of malaria by light microscopy or by RDT. Overtreatment of malaria was common despite the availability of the rapid diagnostic test for malaria in the hospital. Forty percent of the patients with a negative test for HRP-2–based RDT received treatment for malaria despite the negative RDT results [28].

Appropriate and prompt management of malaria cases employs health workers prescribing antimalarial drugs according to evidence-based guidelines. In sub-Saharan Africa, the guidelines for use in outpatient settings generally recommend that febrile illness in children should be suspected to be malaria and be treated with an

antimalarial drug with low levels of adherence to national guidelines. With interventions such as the Integrated Management of Childhood Illness (IMCI) strategy, the treatment of not only malaria but also other potentially life-threatening illnesses which include febrile illnesses, will improve [45].

Numerous technical, behavioral and management issues impede implementation of sustainable antimalaria efforts which include: rapid spread and intensification of resistance by P. falciparum to most commonly used antimalarial drugs including SP leading to the contributions to the change to using ACTs; lack of diagnostic facilities at district and peripheral health services, resulting in the adoption of a defective policy of treating all febrile cases with anti-malarial drugs. This has led to treatment of non-malaria conditions as malaria hence not treating underlying conditions; inadequate coverage of the health services that excludes a large portion of the residents of endemic countries, forcing them to rely on self-medication and treatment with over-the-counter drugs leading to inappropriate treatment of underlying conditions and resistance to anti malarials; wide-spread use and availability of locally produced or imported sub-standard or imitation anti-malaria drugs due to an absence of laboratories that would perform quality assurance and to poor enforcement of basic standards by regulatory agencies; and inadequate knowledge and practice relating to timely treatment-seeking behavior for children and full compliance for the use of prescribed drugs which result in resistance [46].

CHAPTER THREE

METHODOLOGY

3.1 Study area

The study was carried out in 7 districts in the western region of Kenya (Eldoret West, Baringo Central and Keiyo North in Rift Valley Province and Bungoma East, Butula, Bunyala and Teso North in Western Province).

The Western Province of Kenya borders Uganda and is one of the 8 provinces. It is found west of the eastern part of Rift Valley Province and is inhabited mainly by the Luhya community. In 2009, the total population was of 4,334,282 inhabitants within an area of 8,361 km² with 904,075 households. Children aged 15 years and below are approximately 650,143 while those aged below 5 years are approximately 216,715.

Western Province has diverse physical features, from the Kakamega Rain Forest to the plains bordering Lake Victoria in Bunyala District which is the lowest point. These affect the climate which is mainly tropical, with variations due to the altitude. The hot, rainy parts of western Kenya has rainfall throughout the year, the heaviest usually during April, when as much as 200mm may be recorded, and the lowest in January, with an average of 40mm. Temperatures range from a minimum of 14°C to 18°C to a maximum of 30°C to 36°C throughout the year. Bungoma East District is cold and wet while Bunyala, Butula and Teso North Districts are warm. The entire province experiences very heavy rainfall all year round, with the long rains in the earlier months of the year.

Rift Valley Province is bordered by Uganda on the west and is the largest and one of the most economically important provinces in Kenya. It is dominated by the Kenya Rift Valley which passes through it and gives the province its name. According to the

2009 Census, the province covers an area of 173,854 square kilometres and has a population of 10,006,805 inhabitants with 2,137,136 households, making it the largest and most populous province in the country. Children aged 15 years and below are approximately 1,501,021 while those aged 5 years and below are approximately 500,341.

The Great Rift Valley runs south through Kenya from Lake Turkana in the north and has several unique geographical features, including the Kerio Valley in Keiyo North. The highlands provide adequate rainfall for farming and agriculture which is the economic base of the residents of the Rift Valley. The temperate Rift Valley has good climate with average temperatures varying from a minimum of 10°C to 14°C to a maximum of 22°C to 28°C. Rainfall varies from a minimum of 20mm in July to 200mm in April, falling in essentially two seasons – March to the beginning of June (the 'long rains') and October to the end of November (the 'short rains').

Rift Valley is cosmopolitan with different tribal identities, and the Kalenjin and the Maasai are two of the best known ethnic groups.

3.2 Study population

Children aged 5 years and below attending the selected public health facilities.

3.3 Study design

This was a comparative, records-based cross-sectional study. It was based on a larger study which was a randomized control field trial implemented by Moi University and Duke University, put in place with the primary objective of testing whether financial incentives offered at the facility level improve targeting of antimalarials to patients with parasitologically diagnosed malaria (chapter 1, pg. 4). Eighteen government

health facilities in a malaria endemic region of western Kenya were randomly selected for the trial with the health facilities being the primary sampling units. These were randomly allocated to the intervention and control groups. In this particular study, records from October 2012 to September 2013 of seventeen government facilities were included in the analysis of the study.

3.4 Sample size determination

We calculated sample size and power based on a cluster-randomized, difference-of-proportions test with the primary outcome being the proportion of antibiotics used in each group [47]. The sample size required was determined by using a 95% confidence interval and a sampling error of 5% using the following formula;

$$n = \frac{2(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

$$n = \frac{2(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

Where:

p_1=0.5 (proportion of antibiotic use in one group)

p_2=0.5+ε (proportion of antibiotic use in the second group)

ε is the difference that we wanted to detect, also called effect size (10)

$\bar{p}$ (bar) = average of p_1 and p_2

$Z_{\alpha/2}$ is the critical value corresponding to the confidence level (95%/0.95) = 1.96

Z_{β} is the critical value corresponding to the desired power (90%/0.9) = 1.282

The study was powered to detect a 10 % point difference in antibiotic use between the control and intervention groups with a 90% power and 95% confidence level.

Substituting

$$n = \frac{2(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

$\bar{p} = (0.5 + 0.6)/2 = 0.55$

$$= \frac{2(0.55)\ (1 - 0.55)\ (1.282+1.96)^2}{(0.5 - 0.6)^2}$$

$$= \frac{2(0.55)\ (1 - 0.55)\ (1.282+1.96)^2}{(0.1)^2}$$

$$= \frac{2(0.55)\ (0.45)\ (3.242)^2}{0.01}$$

$$= \frac{2(0.2475)\ (10.510564)}{0.01}$$

$= 5.20272918/0.01$

$= 520.2272918$

$= 521$

Therefore there were 521 individuals on each group.

Since we are using a clustered sample the children were grouped by health facility (the facility being our ‘cluster’).

Applying design effect DE = 1+ICC (m-1)

Where ICC is the inter-cluster correlation = 0.002

m= n/k

Where n = sample size = 521 and k = number of clusters on each group = 9

DE = 1+0.002(521/9-1)

= 1+0.002(57.9-1)

=1+0.002(56.9)

=1+0.1138

=1.11

Adjusting the sample by 11% = 111/100*521

=578.3

=579

Therefore 579 individuals were needed in each group.

We managed to use the records of all the under 5s after considering the inclusion and exclusion criteria and ended up with a sample size of 6086. (The sample size was calculated as a guide to the minimum number of records we would need in each group. However, we decided to analyse all the available observations).

3.5 Sampling techniques

Multistage sampling (simple random sampling with the health facilities being the primary sampling units, stratified sampling in terms of high and low endemicity then cluster sampling to get actual number of participants per facility. This was weighted based on the number of cases seen during the months of January, February and March 2012).

From the pre-implementation survey report [19], this was as follows:

FACILITY	**MONTH**			**AVERAGE**	**PROPORTION**	**SAMPLE**
	JAN	**FEB**	**MAR**			
RIFT VALLEY						
Soy HC	46	68	47	54	0.09 (9%)	51
Msekekwa HC	120	39	52	71	0.11 (11%)	67
Moi's Bridge HC	132	138	157	143	0.23 (23%)	134
Kapteren HC	98	92	121	104	0.17 (17%)	98
Sosiani HC	66	54	42	54	0.09 (9%)	51
Railways Disp	172	151	70	131	0.21 (21%)	123
Tenges HC	74	109	0	61	0.10 (10%)	58
Kiptagich HC	-	-	-			51
*Kituro HC	-	-	-			51
AVERAGE	101	93	70	TOTAL = 618		
WESTERN						
Milo HC	93	16	10	40	0.03 (3%)	15
Bumala A HC	99	72	20	64	0.04 (4%)	24
Bumala B HC	201	156	102	153	0.10 (10%)	58
Sinoko Disp	0	14	24	13	0.01 (1%)	5
Malaba Disp	501	420	247	390	0.25 (25%)	147
Angurai HC	0	445	397	281	0.18 (18%)	106
Mukhobola HC	86	79	100	89	0.06 (6%)	34
Budalangi HC	209	229	116	185	0.12 (12%)	70
Moding HC	457	323	208	330	0.21 (21%)	124
AVERAGE	183	195	136	TOTAL = 1545		

Below is a table with the facilities, (the intervention facilities versus the control facilities).

INTERVENTION	CONTROL
Sinoko Dispensary	Milo Health Centre
Bumala A Health Centre	Bumala B Health Centre
Mukhobola Health Centre	Budalangi Dispensary
Angurai Health Centre & Malaba Dispensary	Moding Health Centre
Sosiani Health Centre	Railways Dispensary
Soy Health Centre	Moi's Bridge Health Centre
Msekekwa Health Centre	Kapteren Health Centre
*Kituro Health Centre & Kiptagich Health Centre	Tenges Health Centre

*Kituro Health Centre was excluded due to non-compliance to the study requirements/study protocol. (They did not save the malaria slides for the study and were not updating their AL register as expected due to absence of laboratory technician; hence the facility was not participating meaningfully in the study)

3.6 Inclusion and exclusion criteria

3.6.1. Inclusion criteria

- All records of children aged below 5 years in the MOH laboratory register in the participating facilities.

3.6.2. Exclusion criteria

- Records of patients from facilities that did not follow research protocol.
- Records of facilities that had stock-outs of both cotrimoxazole and amoxicillin during the same month.

3.7 Study variables

Age, gender, group, diagnosis, treatment regimen, blood smear result, region.

3.8 Data collection techniques

Data collection followed the procedures of the larger study where records from the facilities were scanned and reviewed. A checklist (appendix 1) was used to get the necessary data on the variables. There were monthly facility visits to review the under-five OPD registers, the antibiotic use registers, the AL use registers and the laboratory registers. Data was obtained from:

- Under five OPD register: Date, age, OPD number, diagnosis, gender
- Antibiotic use register: Date, age, OPD number, antibiotics given
- AL use register: Date, age, OPD number, dosage
- Laboratory register: Date, OPD number, age, gender, blood smear result.

A random sample of patients was selected from each facility in each month and data on their malaria testing and treatment extracted from the facility registers. My additional data collection included scanning the antibiotics registers and identifying the study subjects from these registers and the medication they were given. Starting with the laboratory register all entries were counted for that month and divided to get the sampling interval ‘n’ then starting at 1 and sampling every nth, we recorded the OPD number, gender, age and BS results. If the patient did not have a BS, the next consecutive entry was used and counting continued from there. If the OPD number was missing, the next consecutive entry was selected. If fewer than 30 negative BS for children under 5 were picked we would go back to the beginning and find the consecutive negative BSs for under 5s until we got 30. The AL register was used to check for AL prescription by OPD number and the OPD register was used to register

the diagnosis according to the clinicians. The antibiotics register was used to record any antibiotics given to the selected patients. All the registers were used to countercheck the variables like date and age.

Stock outs of medication were extracted from the drugs register used by the study. The availability of AL, quinine tablets, quinine injections and SPs for malaria and septrin (cotrimoxazole), amoxicillin, doxycycline and erythromycin in the antibiotics were recorded during each visit. Clinicians' diagnoses were grouped into 4, namely malaria, respiratory tract infections (RTIs), abdominal infections and others. This was based on the common illnesses according to IMCI; malaria, pneumonia, diarrhoea.

3.9 Data processing and analysis

Use of descriptive statistics to calculate proportions were used. Measures of central tendency were used to describe the data. This was then presented in prose and in form of tables and graphs. Logistic regressions (crude and adjusted) were used to analyse the variables that affect the use of antibiotics. The use of STATA statistical analysis packages was employed. The Pearson's Chi Square test was used to generate the P values with a 95% confidence interval.

3.10 Limitations

These are records of children who were sent to the laboratory so they are either slide negative or slide positive. We cannot describe from these data the prescriptions for children with unknown malaria status.

Prior antibiotic treatment was not identified only antimalarial treatment was identified as this may affect the clinician's prescription decision.

Stock outs of antibiotics may have had an impact on the results.

Follow-up and patients outcome data was not assessed.

3.11 Results dissemination

The results of this study will be shared with the participating facilities through reports as well as presented to the defence panellists of Moi University, College of Health Sciences. A manuscript will be prepared for publication in prestigious journals like the Malaria Journal. Presentations to be made in related conferences and workshops as well.

3.12 Ethical considerations

Ethical approval was sought from Moi University/ Moi Teaching and Referral Hospital Institutional Research and Ethics Committee (IREC). (Formal Approval reference IREC/2012/203, Approval Number: 000991).

Permission to use the facilities was gotten from the respective PMOHs and DMOHs. Approval from the health facility in-charges was also sought where the facility in-charge signed a consent form describing the study and its purpose. IREC contacts were also provided.

All data was handled with utmost confidentiality. This included password protection for all computer records and locking up all forms in a secure location. This information will only be accessible to the investigators, her supervisors and the academic committee that will be involved with the student's thesis and only upon approved written request.

CHAPTER FOUR

RESULTS

A total of 6086 children under the age of 5 years were included in the study. These were selected from 17 facilities in the western part of Kenya.

Table 1: Baseline characteristics

	Intervention (n=3278)		Control (n=2808)	
Age, Mean (SD)	2.0	(1.41)	2.0	(1.39)
Gender, n (%)				
Female	1662	(50.7)	1455	(51.8)
Male	1616	(49.3)	1353	(48.2)
Region, n (%)				
Western	2373	(72.4)	1687	(60.1)
Rift	905	(27.6)	112	(39.9)

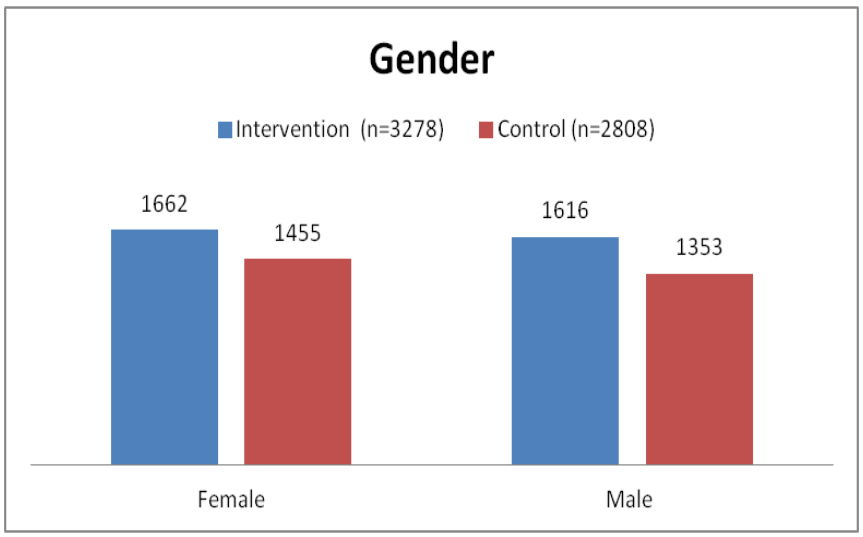


Figure 1: Gender characteristics

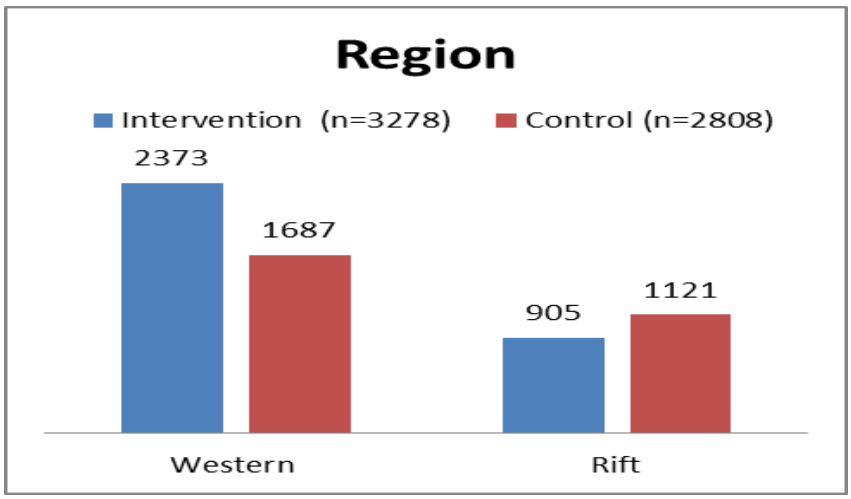


Figure 2: Regional Characteristics

The mean age of the study subjects was 2 years in both the intervention and control groups with a standard deviation of 1.41 and 1.39 respectively. 50.7% and 51.8% of these were female while 72.4% and 60.1% were from Western Province in the intervention and control groups respectively. Population in the catchment area of the facilities in Western Province is dense. Almost 700 more study subjects were in the intervention group compared to the control group in the facilities in Western Province since there were 5 intervention facilities and 4 control facilities.

Table 2: Hypothesis: Antibiotic use between groups

	Intervention (n=3278)		Control (n=2808)		P-value
Antibiotics given					<0.001
Yes	1230	(37.5)	894	(31.8)	
No	2048	(62.5)	1914	(68.2)	
Antibiotics type (n=2124)					
Amoxicillin	478	(38.9)	357	(39.9)	0.618
Cotrimoxazole	534	(43.4)	432	(48.3)	0.025
Doxycycline	3	(0.24)	4	(0.45)	0.464
Erythromycin	50	(4.1)	18	(2.0)	0.008
Other	165	(13.41)	83	(9.28)	0.054

A total of 2124 study subjects received prescriptions of antibiotics and other medication like paracetamol, zinc sulphate, ORS and piriton. Antibiotics like metronidazole, ciprofloxacin, benzyl penicillin and flucloxacillin were included in the group of other. 57.9% were in the intervention group while 42.1% were in the control group with 37.5% of those in the intervention group and 31.8% of those in the control group (P-value <0.001) getting the prescriptions. Based on the P value, we therefore reject the null hypothesis and say that the healthcare workers in the two groups do not use antibiotics to the same level. This may have been so because of the restriction to use AL only for those patients who had positive malaria slides in the intervention group hence they would probably prescribe antibiotics to treat the cases of the fever.

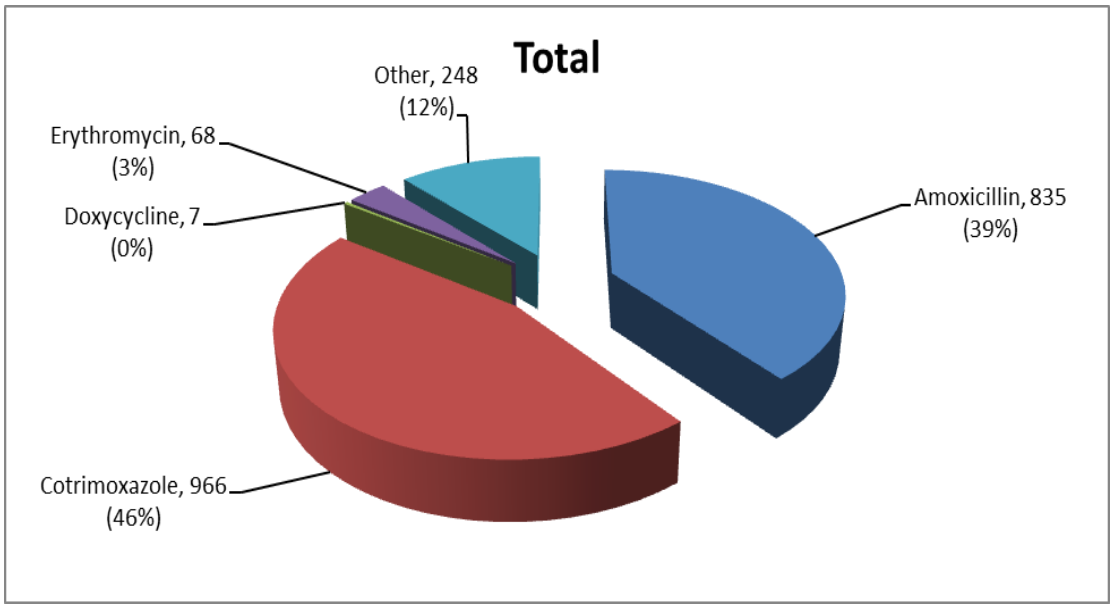


Figure 3: Overall antibiotics used

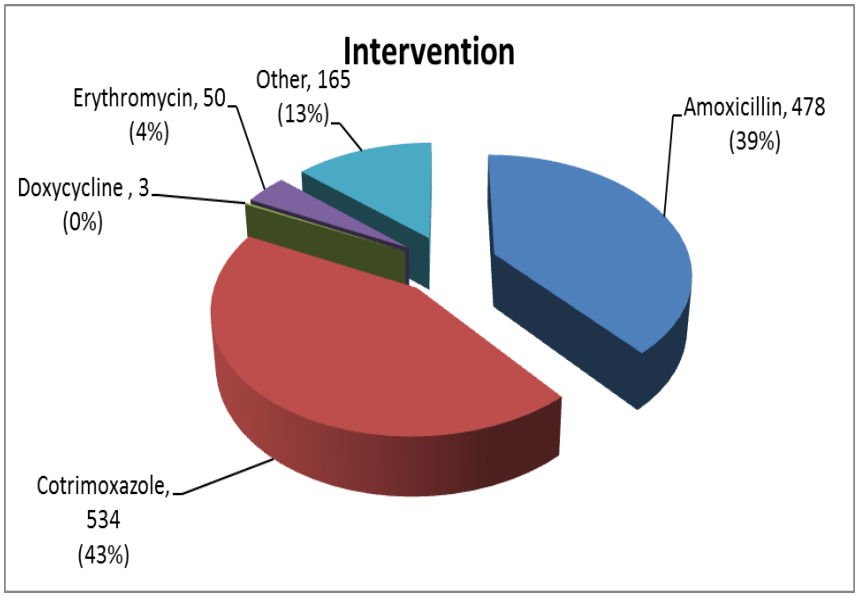


Figure 4: Antibiotics used in intervention group

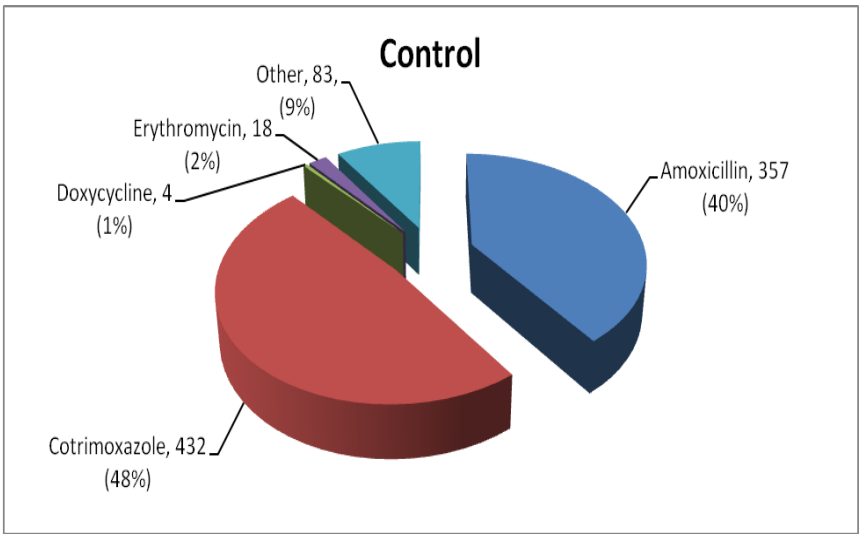


Figure 5: Antibiotics used in control group

Cotrimoxazole was highly dispensed to these study respondents with 46% of those given antibiotics getting it. This was also seen in the two groups (intervention, 43% and control, 48%). Doxycycline was the least used antibiotic due to its contra-indication in paediatric treatment while erythromycin was used at a rate of 3% due to its constant stock-outs in the health facilities.

Table 3: Laboratory characteristics of patients

	Intervention (3277)		Control (n=2808)		Total (6085)	
Blood smear result						
Negative	2606	(79.5)	2171	(77.3)	4777	(78.5)
Positive	671	(20.5)	637	(22.7)	1308	(21.5)
Region	Negative	Positive	Negative	Positive	Negative	Positive
Western	1791	582	1195	492	2986	1074
Rift	815	89	976	145	1791	234
Diagnosis type (n=5239)						
Malaria	854	(35.1)	654	(23.3)	1508	(28.8)
RTI	986	(40.5)	950	(33.8)	1936	(37.0)
Abdominal	263	(10.8)	170	(6.1)	433	(8.3)
Other	387	(15.9)	1179	(42.0)	1566	(29.9)
No Diagnosis	213	(8.8)	0	(0.0)	213	(8.8)

Patients were diagnosed by the clinicians to be having RTIs (37%), malaria (28.8%), abdominal diseases (8.3%) and other diagnoses like burns and skin rashes (29.9%). Those who had no diagnosis specified were few (8.8%).

Table 4: Laboratory characteristics by region

		Intervention		**Control**		**Total**
		1791	(60.0)	1195	(40.0)	**2986**
	Negative	(75.5)		70.8358		**(73.5)**
		582	(54.2)	492	(45.8)	**1074**
	Positive	(24.5)		29.1642		**(26.5)**
Western	**Total**	**2373**		**1687**		**4060**
		815	(45.5)	976	(54.5)	**1791**
	Negative	(90.2)		(87.1)		**(88.4)**
Rift		89	(38.0)	145	(62.0)	**234**
	Positive	(9.8)		(12.9)		**(11.6)**
	Total	**904**		**1121**		**2025**
Grand Total		**3277**		**2808**		**6085**

26.5% of the study subjects from the facilities in Western Province had blood smear results positive for malaria while 11.6% of the study subjects from the facilities in Rift Valley blood smear results positive for malaria.

Table 5: Characteristics by medication type given

	Medication type(n=3241)				P-value
	AB	AL	AL and AB	No AL/AB	
Blood smear result					<0.001
Negative	1543 (95.1)(^{e}1274)	405 (36.3)(^{e}877)	246 (49.1)(^{e}393)	2583 (90.8)(^{e}2233)	
Positive	80 (4.9) (^{e}349)	712 (63.7) (^{e}240)	255 (50.9) (^{e}108)	261 (9.2) (^{e}611)	
Diagnosis					
Malaria	156 (9.9)	731 (67.2)	327 (58.9)	294 (12.1)	<0.001
RTI	830 (52.6)	117 (10.8)	128 (23.1)	861 (35.4)	<0.001
Abdominal	169 (10.7)	30 (2.8)	18 (3.2)	216 (8.9)	<0.001
Other	386(24.4)	178 (16.4)	68 (12.3)	934 (38.4)	<0.001
No Diagnosis	38 (2.4)	31 (2.9)	14 (2.5)	130 (5.3)	<0.001

^{e}X = expected value

The difference in prescription to slide negative and slide positive patients was significant (Chi-square test, p<0.001). Patients with a positive malaria test were more likely to get AL or AL with an antibiotic, but less likely to get only an antibiotic. AL was overprescribed to the slide positive patients as 712 and 255 were given AL and AL and an antibiotic compared to an expected 240 and 108 respectively. Fewer patients with negative malaria tests got AL than expected based on a random distribution.

52.6% of patients given antibiotics alone had an RTI, 67.2% of patients given AL alone had malaria, 58.9% of patients given both antibiotics and AL had malaria and

38.4% of patients who got no medication had other diagnoses like burns and skin rashes.

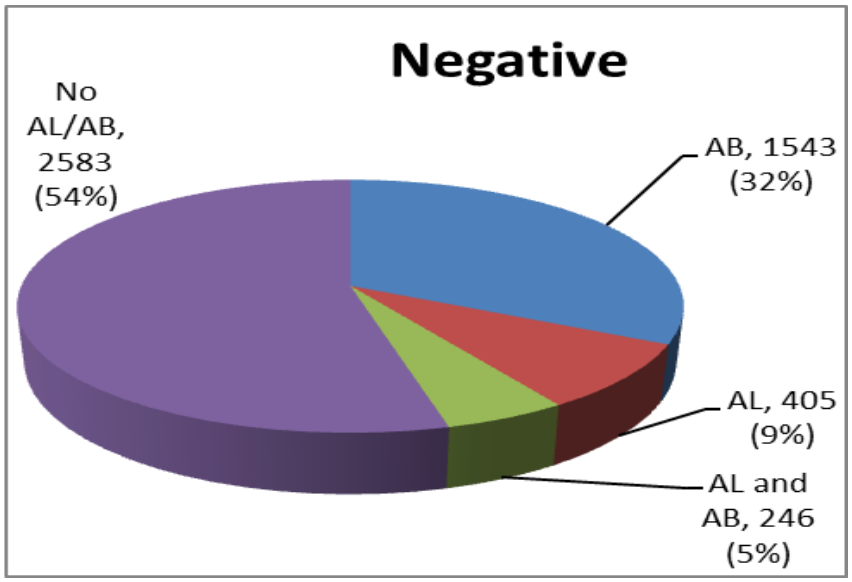


Figure 6: Total medication in negative

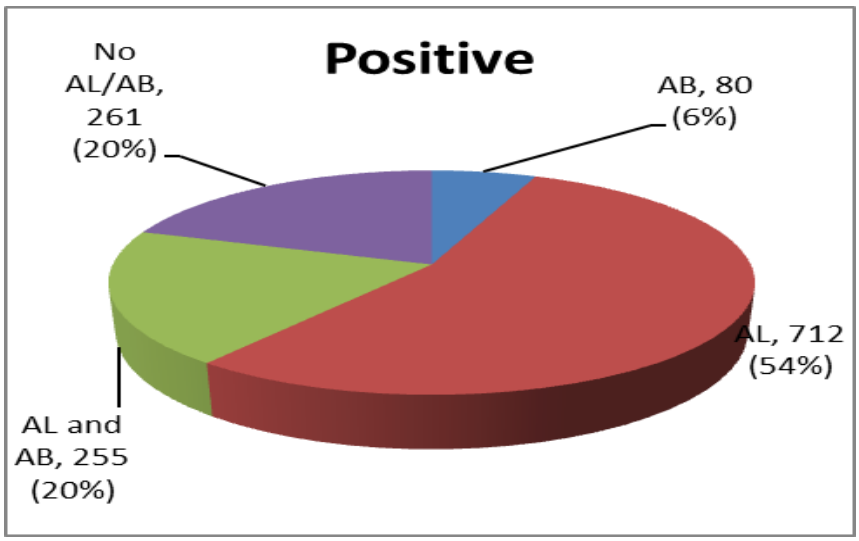


Figure 7: Total medication in positive

Of the 6086 study subjects, results for 6085 were included since one study subject had no blood smear result indicated. 54% of those who had a negative blood smear result did not receive any medication while 54% of those who had a positive blood smear result received AL.

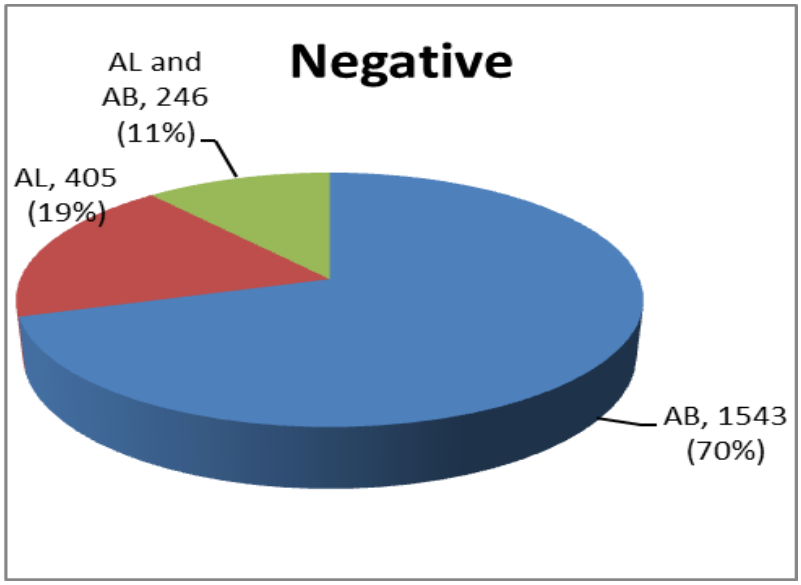


Figure 8: Antibiotics and AL in negative

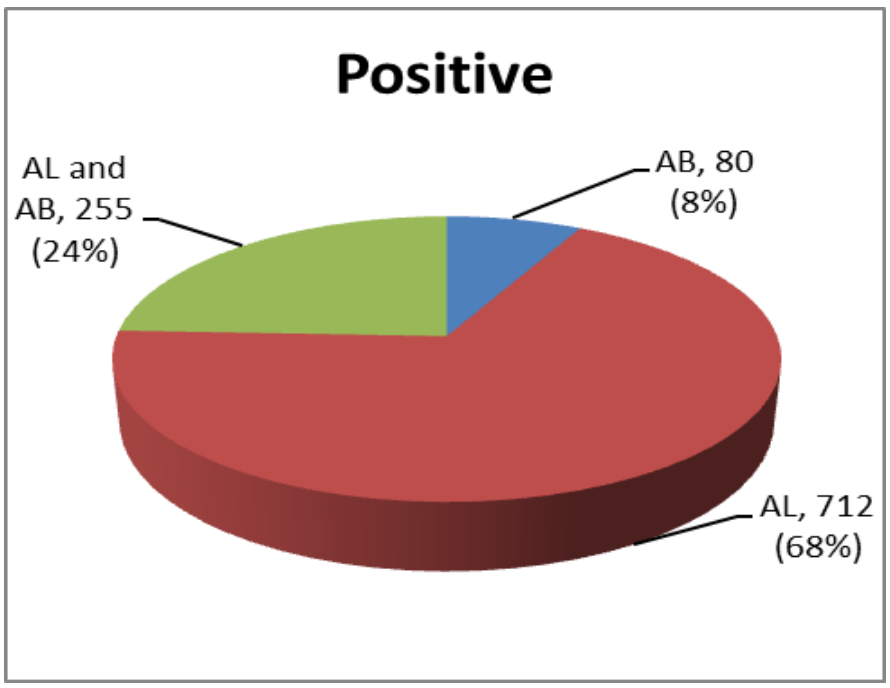


Figure 9: Antibiotics and AL in positive

Among those who received medication, 70% of those with a negative blood smear result were given antibiotics and 68% of those with a positive blood smear result got AL.

Table 6: Logistic regression of effects of patient's laboratory and baseline characteristics on antibiotic use

	Antibiotics use (n=6086)		
	OR	**P-value**	**95% CI**
Unadjusted analyses			
Age	0.95	0.007	0.91-0.99
Gender (Male)	0.93	0.159	0.83-1.03
Blood smear result (positive)	0.58	<0.001	0.50-0.66
Study group (Intervention)	1.29	<0.001	1.16-1.43
Region (Western)	1.77	<0.001	1.58-1.99
Diagnosis (No)	0.36	<0.001	0.32-0.41
AL Given (Yes)	0.79	<0.001	0.70-0.89
Diagnosis type (n=5239)			
Diagnosis type (RTI)	2.40	<0.001	2.06-2.81
Diagnosis type (Abdominal)	1.92	<0.001	1.53-2.42
Diagnosis type (Others)	1.01	0.869	0.86-1.20
Diagnosis type (No diagnosis)	0.80	0.200	0.57-1.12

	Antibiotics use (n=5239)		
	OR	**P-value**	**95% CI**
Fully adjusted analysis			
Age	1.02	0.735	0.93-1.11
Gender (Male)	0.93	0.121	0.84-1.02
Blood smear result (positive)	0.68	0.017	0.50-0.93
Study arm (Intervention)	1.40	0.311	0.73-2.71
Region (Western)	1.98	0.155	0.77-5.08
AL Given (Yes)	0.95	0.695	0.74-1.22
Diagnosis type			
Diagnosis type (Malaria)	0.97	0.862	0.71-1.34
Diagnosis type (RTI)	2.51	<0.001	1.86-3.38
Diagnosis type (Abdominal)	1.64	0.043	1.01-2.64
Diagnosis type (Others)	1.06	0.727	0.76-1.49

On the use of antibiotics various variables were significant both in increasing and reducing their use. From the crude logistic regression, the study group was a positively significant variable (OR 1.29, P value <0.001) with those in the intervention group having a 1.29 times higher odds of being given antibiotics than those from the control group. The region was also a positive variable (OR 1.77, P value <0.001) with patients from the facilities in Western Province having 1.77 higher odds of being given antibiotics more than those from the facilities in Rift Valley Province. Other significant variables were on the diagnosis type with those having either RTI or an abdominal disease (ORs and P values of 2.40 and <0.001; 1.92 and 0.001) increasing the odds of being given antibiotics by 2.4 and 1.92 times compared to those with malaria and other diseases. The negatively significant variables were the blood smear result (OR 0.58, P value <0.001) with those having a positive blood smear result having their odds of being given antibiotics reduced by 0.42 compared to those with negative blood smear results, AL being given (OR 0.79, P value<0.001) with those getting AL having their odds of being given antibiotics reduced by 0.21 compared to those who did not get AL and diagnosis (OR 0.36, P value <0.001) with those patients with no specific diagnosis given by the clinician having their odds of being given antibiotics reduced by 0.64 compared to those with RTIs and abdominal diseases.

From the fully adjusted logistic regression, some variables were significant both in increasing and reducing their use. One positively significant variable was the diagnosis type (Adjusted OR 2.51 and P value of <0.001) with patients having an RTI having two and a half times more odds of being given antibiotics more than the other

patients when we adjust for the other predictors in the model. Another significant variable was blood smear result (Adjusted OR 0.68 and P value of 0.017) with those having a positive blood smear result having a decreased probability or odds of being given antibiotics by 0.32 after adjusting for the other predictors in the model.

CHAPTER FIVE

DISCUSSION

Malaria is a global tropical disease associated with high morbidity and mortality, especially among the children. The treatment of malaria as proposed by WHO, is treatment with antimalarials for positive tests, i.e. test to treat but despite this, most febrile illnesses are often treated as malaria without laboratory confirmation. This can lead to resistance to the available antimalarials, ACTs, due to their continued use on non-malaria cases. Correct diagnosis of these will reduce the use of ACTs and lead to proper use of antibiotics. Delaying resistance to these drugs then becomes a priority with the assistance of laboratory confirmation of malaria. Proper use of antibiotics in accordance to IMCI is also necessary.

This study described the prescription habits of both antimalarials and antibiotics in the management of febrile illnesses in children with known malaria slide results. Almost a third of the study subjects from the facilities in Western Province had blood smear results positive for malaria while a little over 1/10 of the study subjects from the facilities in Rift Valley had blood smear results positive for malaria. 4 main malaria eco-epidemiological zones have been identified namely endemic, seasonal transmission, epidemic-prone and low risk zones due to the variations in malaria parasite prevalence across these zones. Endemic zones have a prevalence of 17%, areas of seasonal transmission have 1.4%, epidemic-prone zones have 1% and low risk transmission zones have 0.4%. Districts have also been grouped into 4 strata namely Lake stable endemic and Coast seasonal stable endemic with a risk equal to or greater 20% which include Nyanza and Western Provinces; Highland epidemic-prone districts with risk of 5-<20% which include Rift Valley Province; Seasonal low transmission including the arid and semi-arid districts with a risk less than 5% which

include Eastern Province and low risk districts with a risk less than 0.1% which include North Eastern Province [48]. The study findings may be lower than the actual figures due to the data collection technique (selecting consecutive negative slides to reach a minimum sample of 30 negative slides) but they do agree with this information.

When you compare the two groups, there seems to be no big difference in the slide positivity rates due to randomization.

According to the Kenya Malaria Indicator Survey (KMIS) 2010, the prevalence of malaria in children below five years increased from 4% in 2007 to 8% in 2010 with the lake endemic zone having the highest prevalence of malaria overall (38 per cent), while other zones have less than 5% [49].

There was a higher use of antibiotics in the intervention group compared to the control group because of the restriction to use AL only for those patients who had positive malaria slides. The healthcare workers would probably prescribe antibiotics to treat the cases of the fever as alternatives. A study done in Afghanistan reported antibiotic prescription being more common with microscopy rather than clinical diagnosis and more common among patients with negative malaria slide results than positive [50]. This agrees with our findings as microscopy determined whether to use AL or alternatives in the intervention group. For both groups, slide positive results reduced the odds of being given an antibiotic. Nearly half of the children in this study were prescribed AL and an antibiotic whether or not they tested positive for malaria. A study by Njozi et al in Tanzania found no significant difference in antibiotics co-prescription with anti-malarial between those who tested positive for malaria and those not tested in febrile children [51]. This high antibiotic use in the intervention

group supports the test-to-treat policy since proper use of AL is going to be implemented and the broad spectrum antibiotics are likely to treat the underlying cause of the fever.

Cotrimoxazole and amoxicillin may have been dispensed in large quantities since these are the first and second line antibiotic treatment for many infections and they are easily available in the health centres and dispensaries in Kenya. Since most of the diagnoses were in the group of respiratory tract infections, cotrimoxazole and amoxicillin were dispensed to treat most of these since they are broad spectrum antibiotics. A diagnosis of an RTI increased the odds of being given an antibiotic. This was seen in both groups and overall. According to the integrated management of childhood illnesses, oral antibiotics are given to children diagnosed with various conditions including pneumonia and dysentery [52]. Stock outs affected the use of antibiotics especially with erythromycin. ACTs or AL is the first line treatment of malaria in Kenya. Those diagnosed with malaria were given AL hence the high percentage. A positive blood smear result also reduced the odds of receiving antibiotics since this would lead to a diagnosis of malaria and a subsequent AL prescription. A large multicentre trial aimed at collecting information that would assist national malaria control programs in sub-Saharan African countries in choosing the most appropriate ACTs found that ACTs showed excellent efficacy, up to day 63 post-treatment, with the risk of recurrent infections being significantly low, even in areas of high transmission with their use [35]. Similarly, Ugandan patients who received an antibiotic had lower odds of not being prescribed anti-malarials as reported by a study done by Sears et al [53].

Negative patients may have been given AL since “the presence of signs and symptoms of disease with negative blood smear does not preclude the diagnosis of malaria”. [54]. Although most of the patients with a positive blood smear result were treated with AL, about a third of the patients given AL had a negative result and about half of those given both AL and antibiotics also had negative blood smear results. This information agrees with a study done in Kenya which showed that prescribers, who more often than not are the clinicians, may view blood slide diagnosis more as a tool to confirm their clinical suspicion or diagnosis rather than to rule out malaria, a malaria diagnosis and treatment may be simply a ‘convenient’ clinical strategy avoiding the more complicated search for other causes of the presenting illness and, the same clinicians may doubt the quality of microscopy or the skills of the microscopist leading to a lack of confidence when a negative malaria slide result is reported [55]. A study done in Afghanistan reports similar results where patients with negative malaria slide results were given antimalarials or combinations of antimalarials and antibiotics since clinicians do not rely solely on malaria slide results [50]. A small percentage of those with negative blood smear results may have also been given AL especially in the western facilities of the control group due to the high prevalence of malaria in that region. The conflicting guidelines by IMCI and WHO may also affect the prescription habits of the clinicians by use of test-to-treat and syndromic approach [52].

This study however has some limitations. First, the results are from records of children who were sent to the laboratory so they are either slide negative or slide positive. We cannot describe from these data the prescriptions for children with unknown malaria status. Second, prior antibiotic treatment was not identified only antimalarial treatment was identified as this may affect the clinician’s prescription

decision. Third, antibiotic stock outs in some facilities may have had an impact on the results. Finally, follow-up and patients outcome after treatment was not assessed.

From this study, antibiotics are used according to IMCI guidelines with most patients receiving cotrimoxazole or amoxicillin and AL being used for the malaria patients. The healthcare workers in the intervention group use these antibiotics in the management of febrile illnesses more than healthcare workers in the control group which could have been positively influenced by the incentives. A follow up study to find out the final outcome of the patients after completing the treatment regimen should be carried out as clinicians ensure the proper use of all medication especially the AL so as to delay resistance.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. Antibiotics are used according to IMCI guidelines especially in patients with RTIs, with most patients receiving Cotrimoxazole or amoxicillin which are the first and second line antibiotics.
2. Healthcare workers in the intervention group use antibiotics in the management of febrile illnesses more than healthcare workers in the control group.
3. Twice as many children had positive malaria smears in the public health facilities in Western Province compared to the public health facilities in Rift Valley Province.
4. Patients with positive blood smear results receive AL while those with other diseases receive antibiotics.

6.2 Recommendations

1. Clinicians should ensure proper use of medication e.g. anti-malarials (Western Province due to higher slide positivity rate) so as to delay resistance.
2. The Ministry of Health should enhance the support it gives the public health facilities by providing adequate supplies of antibiotics and anti-malarials.
3. A study to find out the final outcome of the patients after completing the treatment regimen should be carried out.

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APPENDICES

APPENDIX 1 - DATA COLLECTION TOOL

			OUTPATIENT REGISTER (UNDER 5)					**LAB REGISTER**		**AL REGISTER**	**ANTIBIOTIC REGISTER**	**OTHER DRUGS**
Month	Health Facility #	Study ID #	Visit Date	OPD #	Age	Dx	Drugs prescribed (If available)	Blood smear taken	Blood smear result	Coartem (AL) given	Antibiotics given	Any other drugs given
		1										
		2										
		3										
		4										
		5										
		6										
		7										
		8										
		9										
		10										
		11										
		12										
		13										
		14										
		15										
		16										
		17 etc										

APPENDIX 2 – FACILITY CONSENT FORM
Health Facility Incentive Study

The health facility incentive study is a collaboration between Moi University School of Public Health, Moi University School of Medicine, the Division of Malaria Control and Duke University. The purpose of the study is to understand how to improve the diagnosis and treatment of fevers, especially malaria fevers.

I understand that _____ (name of health centre) has been randomly chosen for this study. Our staff will receive training in microscopic diagnosis of malaria and fever management. We will be enrolled in routine quality control quality assurance of our malaria diagnosis and receive regular feedback about the performance of our laboratory. We may be enrolled in the intervention group which would include quarterly incentives.

As one of the study sites, I understand that the study team will regularly review the routinely collected patient data in the facility, including outpatient registers, laboratory registers and pharmacy records. I understand that we will be asked to archive blood smears to be re-read by the study microscopist.

The objectives and the procedures of the research have been explained to me as well as the possible risks and potential benefits of participating in the study. I understand that I am free to contact the study investigators (Dr. Diana Menya 0733777500, Prof. Wendy O'Meara 0728306521) and ethical reviewing body (IREC – 053-33471/2/3) during normal business hours if there are further questions. I understand that I may withdraw from the study at any time, at which time any incentives (in the intervention group) or laboratory support (both groups) from the study will end.

I agree for _____ (name of health centre) to participate in this study. I have been provided with a copy of this document.

_____ _____

Signature of Authorized representative of Health Centre Date

_____ _____

Signature of Witness Date

BUDGET ALLOCATION

ITEM	**QUANTITY**	**UNIT COST (In Ksh.)**	**TOTAL (In Ksh.)**
STATIONERY			
Ream of foolscaps	4	350	1400
Ream of printing papers	5	500	2500
Folders	5	50	250
Pens	10	20	200
Pencils	10	25	250
Erasers	10	25	250
Paper clips (pkt)	1	80	80
Box files	2	250	500
Clip boards	4	150	600
Rulers	4	25	100
USB Flash Disks	2	1000	2000
Stapler	1	350	350
Staple pins (pkt)	2	250	500
REPORT PROCESSING			
Typing			2000
Printing			5000
Binding			1000
PRELIMINARY TYPING & PRINTING			3000
TRAVEL			10000
CONTINGENCIES			5000
GRAND TOTAL			**34,980**