PRESCRIBING PATTERNS AND AVAILABILITY OF ARTEMISININ BASED COMBINATION THERAPY ANTIMALARIALS COMPARED TO MONOTHERAPHY IN KIRINYAGA DISTRICT, CENTRAL PROVINCE, KENYA.

BY

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Kenya

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Fig. 1 Artemisia annua

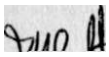
DECLARATION

This project *is* ni> original work and has not been presented for a degree in any other University.

Signature_____Date

l)r. Titus Muhu Kaluga, B. Pharm (U.O.N)

l itis disseiiation has been submitted with my approval as a university supervisor



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Prof. David Scott,

ACKNOWLEDGEMENT

To my supervisor Prof. David Scott for his immense humanity, care, guidance and intellect in accomplishment of this work

To Prof. Julius Wanjohi Mwangi for Mentorship and Scholastic Vision

To Dr. J. W. Bururia for the assistance in the final reading of the document

To all my research assistants for working day and night to meet the deadlines

To Stephen Mirigo for secretarial work in typing this document

To all of you, who will remain silent heroes, but whom only the Almighty will continue to inspire.

To my loving wife, Millicent and children; Roy, James and Beatrice Muhu

DEDICATION

This work is dedicated to Government organizations, global organizations, companies (both private and public) who continue to research and contribute towards the eradication of malaria.

I am also dedicating this work to all those who have lost fathers, mothers, grandfathers, uncles, nephews to a preventable disease like malaria.

I want to say this to you: With innovation, persistence and endurance, we shall stop malaria.

TABLE OF CONTENTS

Title

ABBREVIATIONS

ACT	Artemisin-Based Combination Therapy
AL	Artemeter- Lumefantrine Combination
AQ	Amodiaquine
AS	Artesunate
AS+AQ	Artesunate+Amodiaquine combination
AS+SP	Artesunate+Sulfadoxine Pyrithemanine
C.I	Confidence Interval
CQ	Chloroquine
HIV	Human Immune Deficiency Virus
MQ	Mefloquine
SP	Sulfadoxine- Pyrimethamine
WHO	World Health Organization
AT	Artemisinin Based Monotherapy
ART	Artemisinin
IM	Intramuscular
IPT	Intermittent Preventive Treatment
IV	Intravenous
PPB	Pharmacy and Poisons Board
M.O.H.	Ministry of Health

ABSTRACT

Malaria, a protozoan infection with high mortality and morbidity, remains a major health concern in Kenya and the world. New therapeutic agents and combinations continue to be developed and researched on the treatment of malaria. The Ministry of Health in the Republic of Kenya has developed guidelines on the management of Malaria. However, no study has been done to assess the progress of this new initiative.

The aim of this study was to examine the prescriptions generated over a three months period for those suffering from malaria and the availability of the various anti-malarials. The study involved district hospitals, sub-district hospitals, dispensaries, health centres private clinics, nursing homes and pharmacies.

A total of 482 prescriptions were examined from 50 health facilities.

The centres were chosen randomly from a set of 102 facilities in Kirinyaga District of Central Province Kenya. The results showed that Artemisin-Based Combination Therapy is the most commonly prescribed and dispensed anti-malarial (45.2%) followed by amodiaquine and quinine, in that order. The younger children were however more likely to get amodiaquine preparations while in adults preference tilted towards Sulfadoxine-Pyrimethamine and Quinine. The results indicated that the ACT uptake has gone up from a previous study at 10.2% and is consistent with the reports of a baseline study undertaken by the Ministry of Health, WHO and Pharmacy and Poisons Board. Nevertheless, the results indicate that SP, chloroquine, amodiaquine and artemeter monotherapy are still available in our drug outlets to a significant extent.

Challenges revealed by the study included stock out in the Public Sector and quality of available anti-malarials. Emerging resistance to ACT anti-malarials will continue to pose a serious threat to the Ministry of Health and the drug regulatory authority. Again, the public sector is totally reliant on donor funding to sustain the ACT availability. A donor pull out would spell doom to our country from a disease that is responsible for 30% all of out-patient attendances and 19% of admissions to our public health facilities.

It is expected that results from this study represent what is likely to be the situation in other parts of Kenya. Suggestions have been made on solutions or interventions to this killer disease.

1.0 INTRODUCTION AND LITERATURE REVIEW

Malaria is a protozoan infection that is both preventable and curable, and is very common in nearly all parts of Kenya. It has high incidences in Western Province, Nyanza Province, Rift Valley and part of Central Province including Kirinyaga district. It is estimated that a child dies of malaria every 30 seconds in the World[1]

The infection is usually transmitted through a bite by an infected female anopheles mosquito. There are 4 common types of these parasites; these are *Plasmodium falciparum, P.ovax, P. malarie* and *P. vivax.* It is characterized by bouts of chills, fever and sweating It is estimated that more than one million people die of Malaria every year. Most of them being infants, young children and pregnant women

Indeed it is reported that between 1981-1996, there was an estimated death rate of 2.5 million due to HIV as compared to 20-30 million deaths caused by malaria. It is therefore a disease that causes great concern to governments across Africa and the World.

Treatment of Malaria has mainly relied on monotherapies which include chloroquine, amodiaquine, sulphadoxine-pyrimethamine combinations, and artemisinin based drugs.

However, due to increasing resistance to the available drugs, WHO has recommended the use of Artemisinin based combination therapies (ACTs)[2] in order to ensure high cure rates of the *Plasmodium falciparum* Malaria.

In Kenya, the Ministry of Health through the Division of malaria control programme in compliance with the WHO, issued National Guidelines for diagnosis, treatment and prevention of Malaria in June, 2006.[3] The overall goal of these guidelines was to improve malaria case management by health workers and to have a harmonized approach, to treatment and with the aim of reducing the morbidity and mortality of Malaria.

Through the U.N sponsored Millennium Development Goals, the International Community agreed to halt and to begin to reverse the spread of Malaria by 2015.[4]

1.1 PATHOGENESIS

The malaria transmission begins when the female mosquito bites a patient with malaria. This blood contains both female and male gametocytes. In the mosquito these go through a sexual phase (sporogony) to form zygotes. The zygotes move to the stomach of the mosquito where they became sporozoites. The sporozoites, then migrate to the mosquito salivary glands where they may be transmitted into a patient as mosquito draws blood.

Once in the patient's blood stream the sporozoites travel in blood and lymphatic system to the liver where they multiply asexually. After 10-14 days merozoites are released and invade red blood cells, initiating the erythrocytic stage of the disease

In the red blood cells they multiply asexually (schizogony) to produce new merozoites. The red blood cells rupture or burst to release merozoites into the circulating plasma which concides

with the bouts of fever. The merozoites released attack other red blood cells to repeat the erythrocytic cycle. Gametocyctes rather than merozoites are formed in Red blood cells .These gametocytes cannot replicate unless they are ingested by mosquito to move into the sexual phase of the cycle.

1.2 CLASSIFICATION OF ANT1 MALARIAL AGENTS

This is done through two ways

1) The stage of parasite cycle that the agents affect.
2) Clinical indications, treatment and prophylaxis

Some drugs may have both types of anti-malarial action

1. **Prut; used for prophylaxis**

   These agents work on the liver stages of the Plasmodium therefore blocking the erythrocytic stage. Examples of such drugs are proguanil (Paludrine) or Proguanil atavaquone combination and Primaquine.

2. **Drugs used to prevent relapse**

   These act mainly on the latent tissue forms of *P.vivax and P.ovale* which cause relapsing malaria months or years after the initial infection. The drugs are taken either before or after one leaves the malaria area. For terminal prophylaxis they are initiated shortly before or after one leaves the Malaria area, while for radical cure they are given during the latent period or during an acute attack where they are given in combination with drugs that act on the erythrocytic stage. An example of a drug for prevention of relapse is primaquine.

3. **Drugs used for clinical and suppressive cure**

   These act on the erythrocytic stage (asexual) stages to prevent schizogony, therefore preventing clinical attacks. They also produce suppressive cure, which is complete elimination of parasites through continued therapy.

   Two groups of drugs exist;

   1) Rapidly acting blood schizonticides; examples include chloroquine, quinine, quinidine and mefloquine.
   2) Slower acting agents: examples are anti-folates and antibiotics.

4. Gametocytocides

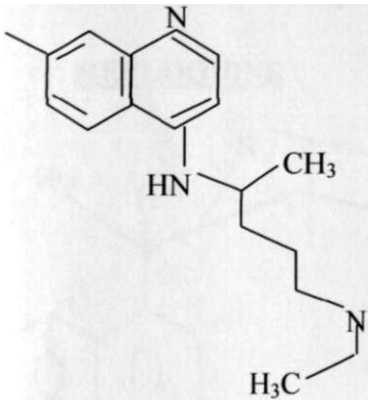
These agents act against sexual erythrocytic forms of plasmodia, thereby preventing transmission of malaria to mosquitoes. Chloroquine and quinine have gametocytocidal activity against *P. vivax, P. ovale*, and *P. malariae*, whereas primaquine displays especially potent activity against gametocytes of *P. falciparum.* However these anti-malarials are not used clinically just for their gametocytocidal action

5. Sporontocides

Such drugs ablate transmission of malaria by preventing or inhibiting formation of malarial oocysts and sporozoites in infected mosquitoes. Although chloroquine prevents normal plasmodial development within the mosquito, neither this nor other antimalarial agents are used clinically for this purpose.

1.3 DRUGS FOR MANAGEMENT OF MALARIA

a) CHLOROQUINE



First developed by Germans in 1934

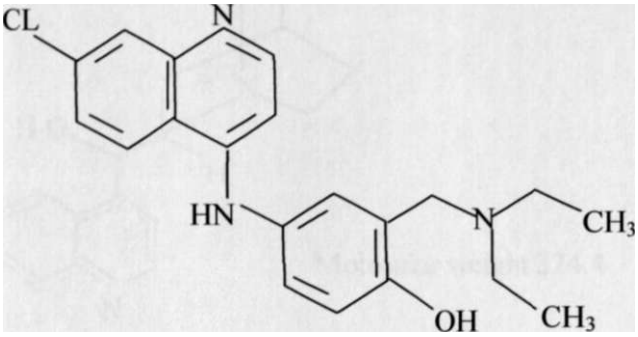
Molecular weight

436.0

Chloroquine (CQ) is a 4-aminoquinolone. It has been used for years for both treatment and prevention of malaria. However resistance has increased considerably making it virtually useless as an anti-malarial, especially against *P. falciparum* infection.Tablets containing both 100 mg and 150 mg of chloroquine base exist either as hydrochloride2 phosphate or sulphate.Chloroquine may be used for conditions other than malaria; these include use in hepatic amoebiasis, rheumatoid arthritis, systemic lupus erythematosus, discoid lupus, sarcoidosis etc.

b) AMOD1AQUINE

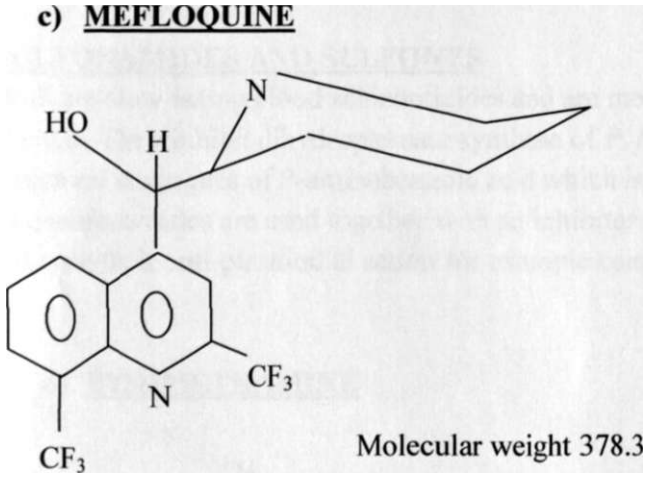
This is a congener of chloroquine developed by the Chinese in the 1970s and shown to be effective against both *P. falciparum* and *P.vivax.*



Molecular weight 355.9

Its shares the same mode of action with chloroquine but is effective against some chloroquine resistant strains of *P. falciparum.* There is some cross resistance with chloroquine. The amodiaquine exists as 200 mg tablets as a hydrochloride or 153.1 mg base as a chlorohydrate

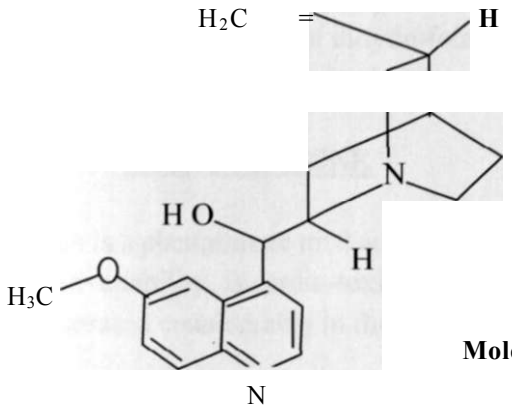
c) MEFLOQUINE



Molecular weight 378.3

It is a 4-quinoline methanol that is structurally related to quinine.and is, effective against all strains of malaria.Mefoquine exists as a racemic mixture of four optical isomers and is a blood schizonticide. It is taken orally because parenteral preparations cause severe local reactions. Absorption is enhanced by presence of food.

QUININE



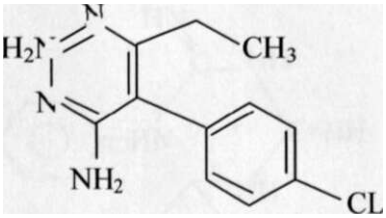
Molecular weight 324.4

The use of quinine dates back 350 years and is the chief alkaloid of, the bark of the cinchona tree. Four alkaloids can be derived from the bark; these are quinine, quinidine, cinchonine and cinchonidine. Quinine acts as blood schizonticide, and has little effect on sporozoites or pre-erythrocytic forms of malaria parasites. It is gametocidal for *P.vivax, P. malariae* but not *P. falciparum.* It cannot therefore be used for prophylaxis. It is useful for treatment of severe malaria caused by chloroquine and multi-drug resistant strains of *P. falciparum.*

SULFONAMIDES AND SULFQNES

Both are slow acting blood schizonticides and are more active against *P. falciparum* and *P.vivax.* They inhibit dihydropteroate synthase of *P. falciparum* competitively because they are structural analogues of P-aminobenzoic acid which is important in the synthesis of folic acid. The sulfonamides are used together with an inhibitor of the parasite dihydrofolate reductase to enhance their anti-plasmodial action for example combination with pyrimethamine.

d) PYRIMETHAMINE



Molecular weight 248.7

This is a 2, 4- diaminopyrimidine used in combination with a sulfonamide, usually sulfadoxine. It is a slow acting blood schizonticide. Its malarial action is through inhibition of plasmodial dihydrofolate reductase thus blocking the formation of nucleic acids in the malaria parasite.

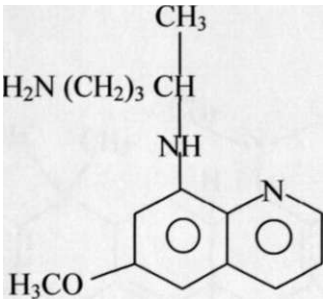
Pyrimethamine is effective against all the four human malaria parasites. There is synergism between pyrimethamine and sulfonamides through the blockage of two steps.

1) The utilization of *P*-amino benzoic acid used in the synthesis of dihydropteroic acid and catalysed by dihydropteroate synthase.
2) The reduction of dihydrofolate to tetrahydrofolate, catalyse by dihydrofolate reductase and inhibited by pyrimethamine.

e) HALOFANTRINE

This is a phenathrene methanol with blood schizonticidal activity. It shows erratic bioavailability, is cardio-toxic, and has extensive cross resistance with mefloquine. Its use has decreased considerably in the last few years.

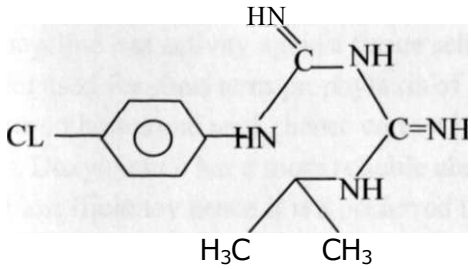
f) PRIMAQUINE



Molecular weight 259.4

It is an 8 amino quinoline that acts on the tissue stage (exo-erythrocytic stage) of both *P.vivax* and *P.ovale* to prevent and cure relapsing malaria. It can be used in combination with a blood schizonticide for erythrocytic parasite. It has also some gametocytocidal action against *P. falciparum.*

g) PROGUANIL (chloroguanide)

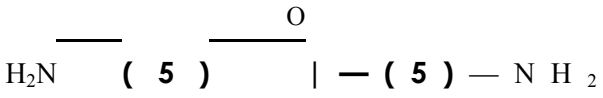


Molecular weight 253.70

This is a biguanide derivative whose activity is due to its active metabolite cycloguanil .It is a selective inhibitor of plasmodial dihydrofolate reductase-thymidylate synthetase. This causes inhibition of DNA synthesis and depletion of folate co-factors.

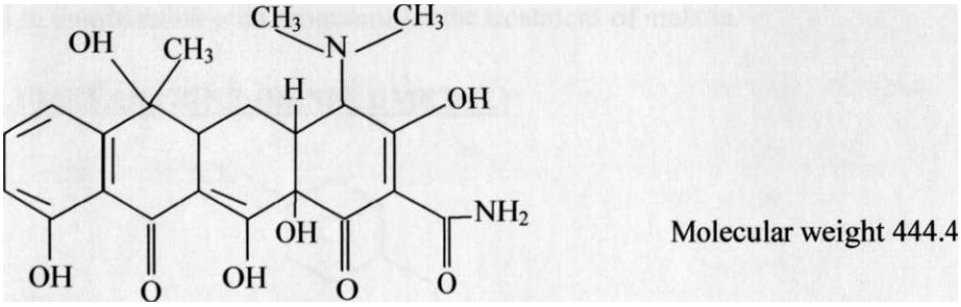
Progruanil is metabolized by cytochrome P450 enzymes, specifically CYP209 to cycloguanil .It has weak intrintic anti-malarial activities and has same activity against pre-erythrocytic forms of the parasite and is a slow blood schizonticide. It also has sporonticidal activity making the gametocytes non-infective to the mosquito vector.

h) DAPSONE



This is a sulfone, also used in treatment of leprosy and in prophylaxis of *Pneumocystis jiroveci pneumonia.* In malaria treatment it is given in combination with another anti-malarial e.g. chlorproguanil and inhibits dihydropteroate synthase.

i) TETRACYCLINE



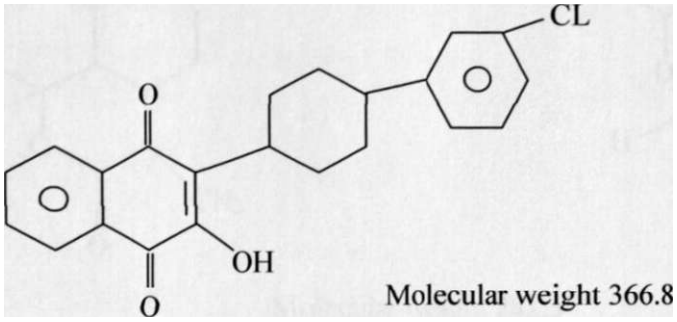
Tetracyclines are a group of antibiotics originally from *Streptomyces* species but made synthetically. They are useful in treatment of acute malarial attacks caused by multi drug resistant strains of *P. falciparum.* They can be administered orally or intravenously. They are inhibitors of aminoacyl-t RNA binding during protein synthesis. They are however slow-acting, making it desirable to combine with quinine for rapid control of parasitaemia. Tetracycline has activity against tissue schizonts of chloroquine resistant *P. falciparum.* They are not used for short term prophylaxis of multi-drug resistant strains. They have adverse effects on bones and teeth, hence cannot be given in pregnancy or to children below eight years. Doxycycline has a more reliable absorption and a better safety profile in patients with renal insufficiency hence it is a preferred tetracycline.

j) CLINDAMYCIN

This is a lincosamide antibiotic. It is very soluble in water and inhibits protein synthesis. It is given orally or parenterally.

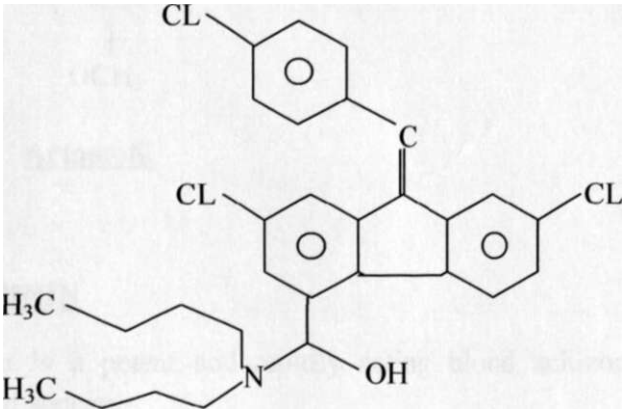
k) ATOVAOUONE

This is a hydroxynapthoquinone which is, active against all species of malaria parasite. It inhibits pre-erythrocytic development in the liver and oocyte development in the mosquito.



Atovaquone selectively interferes with mitochondrial electron transport and related processes such as ATP and pyrimidine synthesis in the malaria parasites
It is used in combination with proguanil for the treatment of malaria.

I) LUMEFANTRINE (BENFLUMETOL)

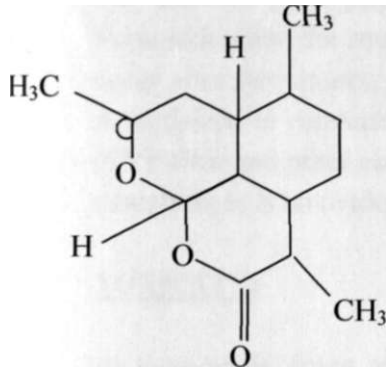


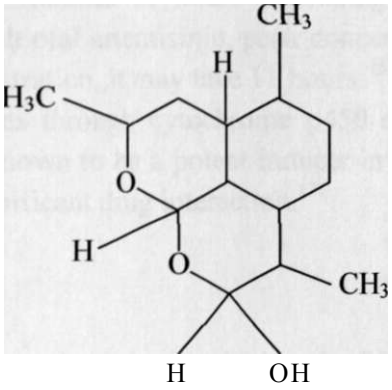
It belongs to the aryl-aminoalcohol group of anti-malarials, which include quinine, mefloquine and Halofantrine and share a similar mechanism of action. It is used in combination with artemether drugs. Oral availability is dependent on the presence of fatty foods and absorption increases considerably if taken with meals.

m) ARTEMISININ AND THE DERIVATIVES

Artemisinin is a sequitespere lactone and endoperoxide derived from the weed *Artemisia annua* (qinghaosu, sweet wormwood or annual wormwood). It has been used in China for over

2000 years for management of symptoms of malaria. In 1972 the Chinese extracted and crystallized artemisinin (Qinghaosu), the major anti-malarial ingredient. Four other synthetic derivatives were synthesized namely, dihydroartemisinin, artemether, artomotil and artesunate.

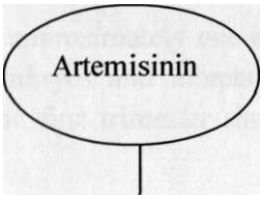




Molecular weight 282.3

Artemisinin **Dihydroartemisinin**

^rtemisini^



OCH_3 $OCO\ (CH_2)_2C0_2Na$

Artomotil **Artesunate**

ARTEMISININ

Artemisinin is a potent and rapidly acting blood schizonticide and is active against all Plasmodium species.

The endoperoxide moiety is required for anti-malarial activity. Substitution of lactone carbonyl group increases the potency.

These compounds have gametocidal activities but do not affect either the primary or latent tissue stage parasites. Artemisinin-based compounds are not used for chemoprophylaxis or for preventing relapses of *vivax* malaria

The mode of action of artemisinin compound is thought to involve a two-step process:-

1. The intra-parasitic heme iron of the infected erythrocyte catalyses the cleavage of the endoperoxide bridge.

2. Then intra-molecular rearrangement follows to produce carbon centered radicals that covalently modify and damage specific malarial proteins. Very few studies have been done on the pharmacokinetic profiles of artemisinin. This is due to problems in the preservation of biological samples and unreliable analytical samples.[5]

   The time to peak plasma levels varies from minutes to hours depending on the formulation and the route of administration; with oral artemisinin, peak concentrations occur after three hours, while with rectal administration, it may take 11 hours.[6]

   Artemisinin is converted to inactive metabolites through cytochrome p450 enzymes (CYP2B6) and other enzymes. Artemisinin is known to be a potent inducer in humans though there is no evidence of any clinically significant drug interaction/[7]'

TOXICITY:

At therapeutic doses artemisinin is safe [8]. There have been reports of mild gastro-intestinal disturbances, dizziness, tinnitus, recticulocytopaenia, neutropaenia and elevated serum aspartate aminotransferase. There are also cases of electro-cardiographic abnormalities including bradycardia and prolongation of the QT intervals.

Neurotoxicity has been reported in animal studies especially with high doses.

The most serious side effect is type 1 hypersensitivity reaction in approximately one in 3000 patients. Animal studies have also demonstrated death of embryos and morphological abnormalities in early pregnancy. [I()] Therefore its use during the first trimester should be avoided.

ARTEMETHER

This is the methyl ether of dihydroartemisinin. It has a high lipid solubility and is given as an oily emulsion intramuscularly or it can be given orally.

Peak plasma concentrations occur after two to three hours after oral administration. In IM administration; peak concentration occurs after six hours, but absorption is slow and erratic.[11]

Artemether is metabolized to dihydroartemisinin, which is the active metabolite.
Biotransformation is mediated through cytochrome P450 specifically CYP3A4.

Artemether is highly plasma bound (95%) with an elimination half life of one hour. However with I.M administration the elimination phase is prolonged because of continued absorption. No dose adjustments are required in renal or hepatic impairment.

In animal studies, neurotoxicity has been demonstrated following, I.M administration.[12]

ARTESUNATE

This is the sodium salt of the hemisuccinate ester of artemisinin. It is water soluble and has poor stability in aqueous solution. In the injectable form artesunic acid is drawn up in sodium bicarbonate immediately before injection. Artesunate may be given orally, rectally intramuscularly or intravenously.

It is rapidly absorbed with peak plasma levels at no more than three hours with all formulations.[13]
It is converted to dihydroartemisinin (DHA) entirely. The elimination is usually rapid and its potency is dependant on dihydroartemisinin (DHA) elimination half life of 45 minutes the toxicity and ADR profile resemble those of artemisinin.

DIHYDROARTEMISININ (DHA)

This is the main active metabolite of artemisin derivatives. It can be given both orally and rectally. It is water insoluble and requires formulation for optimum absorption. It can be co-formulated with their anti-malarials.

It reaches peak plasma levels after 2.5 hours; rectal absorption is slower (4 hours). Plasma binding is about 55%, elimination half-life is 45 minutes via intestinal or hepatic glucoronidation.[14]

ARTEMQTIL

Is also known as artether, this is the ethyl ether of artemisinin. It is given by intramuscular injection only. It is not water soluble

Absorption is poor and erratic, with patients taking nearly 24 hours for any detectable level in plasma. Other parameters resemble those of artemisinin

n) ARTEMIS1N1N-BASED COMBINATION THERAPY (ACT)

Artemisinin and its derivatives produce high and rapid clearance of malarial parasitemia, and hence rapid resolution of symptoms. However they are eliminated rapidly. They therefore require administration for up to seven days, if they are combined with drugs like tetracycline which are also rapidly eliminated,. They can however be combined with slowly eliminated drugs in a shorter course of treatment, hence can be given for three days.
The artemisinin drugs are active against all the species of malaria. They also can reduce the gametocyte carriage and thus the transmissibility of malaria.

The following combinations are recommended

1) Artemether- lumefantrine
2) Artesunate+ amodiaquine
3) Artesunate+mefloquine
4) Artesunate+sulfadoxine-pyrimethamine

Other combinations are still being evaluated for their clinical safety.

Combination of therapy

The aim of combination of therapy is two-fold:

1) To delay or stop the development of resistance.
2) To increase therapeutic efficacy by using two drugs with independent modes of action, and thus different bio-chemical targets in the parasite.

(o) JUSTIFICATION OF THE STUDY

The availability of a safe, effective anti-malarial therapy continues to be a big challenge to the ministries of Health in Kenya. The W.H.O in the year 2006 recommended the use of A.C.T as the first line treatment for uncomplicated malaria. Previously, in Kenya, several monotherapies were available but data showed a decrease in effectiveness.

The implementation of the new policy posed a big problem to medical practitioners and to the Government because medical workers needed to be trained in the new policy. Funds had to be availed to buy the new A.C.T combinations. The monotherapies available in both public and private sectors required time before they could be withdrawn. The purpose of this study was to assess the extent of the use of the new A.C.T. The study was also to check on availability of the monotherapies and the extent of their use.

The challenges of anti-malarial treatment include the provision of the best antimalarials at an affordable cost in a timely manner. The use of older, less-effective agents or the unavailability of recommended treatments quickly to all sufferers would increase morbidity and mortality.
To this end, national guidelines were issued in 2006 but the situation on the ground reflects failure of adherence to these guidelines. The extent of non adherence has never been studied in any region in Kenya. This study was undertaken to assess the magnitude in a cross section of facilities that offer malaria treatment in both private and public sectors

1.4 OBJECTIVES

General

To investigate and assess the prescribing patterns of the ACTs in comparison with other anti-malarial and to compare with the government policy and to measure the availability of anti-malarial drugs in both the private and public sector in Kirinyaga District.

Specific objectives

1. To sample a statistically significant proportion of facilities which either prescribe or dispense antimalarials and to examine retrospectively all the prescriptions dispensed at these facilities in a period of three months, from, December 2008, to, February 2009.
2. To analyze these prescriptions for frequency of use of different anti-malarial and compare and contrast the prescribing with the national policy guidelines.
3. To explore reasons for non-adherence to national policy and consider possible solutions.

2.0: METHOD

The study was conducted in Kirinyaga District, an area with high endemicity of malaria. It was across-sectional study which involved a sample of fifty facilities from the 102 public, private and faith- based organizations which dispense drugs. Prescriptions and supplies were considered for all patients suffering from malaria from all age groups and sexes.

2.1: SAMPLING PROCEDURE AND DATA COLLECTION

This_was a cross-sectional study from the total population of 102 facilities (The full list is in appendix IV). The only District hospital and the only two sub-district hospitals were included as well as the largest faith based facility .The rest of the facilities i.e. health centers and dispensaries were selected randomly from within the district while the private chemists and clinics were chosen randomly. The investigator piloted the procedure and then employed and trained research assistants who visited each facility by prior arrangement and inspected their records.

A questionnaire was filled by the research assistants for every prescription presented at the pharmacy. They also conducted a brief interview with the person in charge of drug supply in the facility.

The analysis was done on prescriptions written, or drugs dispensed in a period of three months from. December 2008, to February 2009

2.2 Sample size

Using Fischer's formula, if a drug is prescribed at a prevalence of 25%, to estimate this prevalence with a precision of 5%, the number of prescriptions needed is:

$$n = \frac{Z^2pq}{d^2} = 288 \text{ prescriptions}$$

Where;

n = Sample size

Z = 1.96 Standard normal deviate at required confidence level

p = 0.25 Estimated prevalence or proportion

q = 1 - p = 0.75

d = 0.05 Precision

Therefore, the study aimed to collect a minimum of 288 prescriptions but was able to collect 482

2.3 Ethical Considerations

Permission to carry out the study was sought from the Ethics and Research Committee at Kenyatta National Hospital. The review of prescriptions was done within the relevant facilities. Confidentiality was maintained on all the information and data collected.

Prescriptions used were kept confidential by using study numbers and register numbers and patient names were not entered into the data collection form. The data collected were stored securely under lock and key and in password-controlled computer files.

There were no risks to the patients during the study because this was a retrospective study and there was no direct patient contact

CHAPTER III

3.0 RESULTS

The total numbers of facilities in the districts that were analyzed were:

Table 1: District and Sub-District Hospitals

Facility	Total prescriptions analysed	Male	Female
Kerugoya District Hospital	104	47	57
Kimbimbi Sub-District Hospital	50	24	26
Kianyaga Sub-District Hospitals	46	23	23

Table 2: Faith based Dispensaries

Facility	Total prescriptions analysed	Male	Female
Kiaritha ACK Dispensary	5	3	2
St. John Thaita Dispensary	5	2	3
ACK Mbiri Dispensary	5	2	3
Kutus Dispensary	5	1	4
Kerugoya Catholic Dispensary	5	4	1

Table 3: **Government Dispensaries**

Facility	Total prescriptions analysed	Male	Female
Gathambi Dispensary	7	4	3
Gathigiriri Dispensary	5	4	1
Gatuto Dispensary	4	2	2
Gatwe Dispensary	3	1	2
Kagumo Dispensary	4	0	4
Kamweti Dispensary	3	1	2
Kandongu Dispensary	2	0	2
Kang'aru Dispensary	3	1	2
Kiangai Dispensary	5	2	3
Kiang'ombe Dispensary	4	2	2
Kianjogu East Dispensary	4	3	1
Kiaragana Dispensary	5	2	3
Kibirigwi Dispensary	4	3	1
Mutithi Dispensary	6	2	4
Nguka Dispensary	4	2	2
Njegas Dispensary	4	3	1
Wamumu Dispensary	2	2	0

Table 4 **Health Centers**

Facility	Total prescriptions analysed	Male	Female
Baricho Health Centre	10	3	7
Ditatha Health Centre	5	2	3
Kabare Health Centre	5	1	4
Kangaita Health Centre	4	2	2
Kiamutugu Health Centre	5	4	1
Kiumbu Health Centre	10	4	6
Mutithi Health Centre	11	5	6
Sagana Health Centre	10	4	6
Uceru Community Health Centre	10	4	6

Table 5 **Nursing Homes and Clinics**

Facility	Total prescriptions analysed	Male	Female
ACK Mt. Kenya Nursing Home	5	2	3
Karira Mission Hospital	14	7	7
Kagio Nursing Home	10	5	5
Kerugoya Nursing Home	7	0	7
CCS Wang'uru Clinic	5	2	3
Baraka Clinic	8	6	2

Table 6 **Pharmacies**

Facility	Total prescriptions analysed	Male	Female
Fountain Pharmacy Mwea	3	1	2
Glawar Chemist Sagana	5	5	0
Kamu Hills Chemist	6	3	3
Medikam Chemist Kerugoya	5	1	4
Sagala Pharmacy	2	0	2
Tabere Pharmacy Mwea	2	2	0
Jade Pharmacy Sagana	2	0	2
Kerugoya Family Pharmacy	4	3	1
Mwea Plains Pharmacy	3	3	0
Sesuma Chemist Sagana	2	1	1

3.1 Demographic characteristics

The study reviewed **482** patient prescriptions of which **52.5%** belonged to female and **47.5%** male patients. Majority of patients were 13 years and above **(45.2%)** and 31.3% were five years and below. The figure **2** below illustrates the age distribution of the patients.

Table 7: Demographic characteristics

Variable	Frequency (%)
Sex	
Female	253 (52.5)
1 Male	229 (47.5)
Age group	
0 - 5 years	151 (31.3)
6 - 12 years	35 (7.3)
13 years & above	218 (45.2)
Missing	78 (16.2)

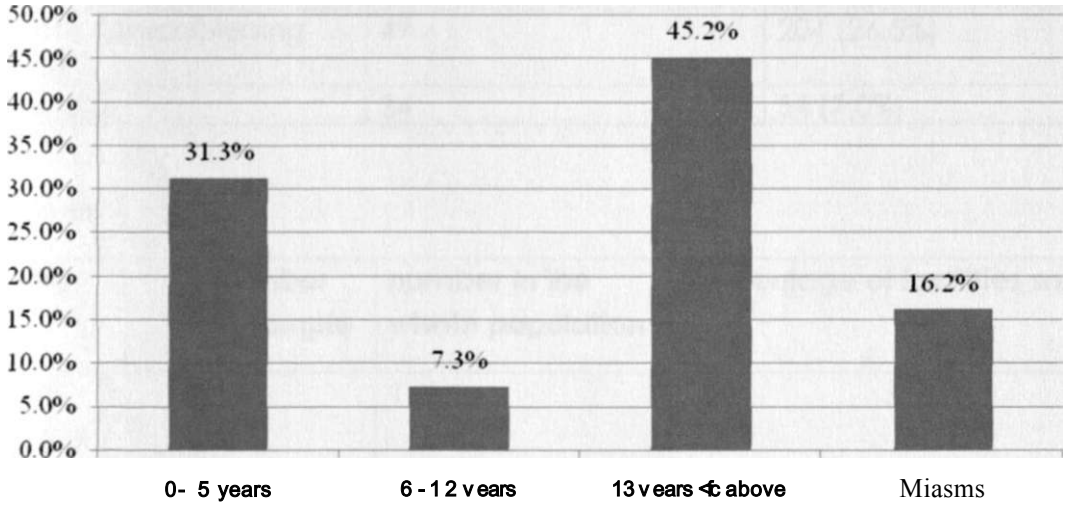


Figure 2: Age distributions of the patient

3.2 Health Facilities

Majority of the prescriptions were given at dispensaries/health centres (36.7%), district (23.3%) and sub-district hospital (21.4%). Private clinics/nursing homes and private chemists accounted for 11.0% and 7.6 % of the prescriptions respectively (Table 8a). However the sample was biased towards hospitals(District and Sub-district,-) in order to capture the large institutions and if the results are extrapolated to the whole population then the proportion is as shown in Table 8b .The proportion of facilities sampled is also shown in table 8c

Distribution of prescriptions per health facility

Table 8a:

Health facility	Frequency (%)
Dispensary/health centre	164 (36.7).
Private/Nursing homes	49 (11.0)
Private chemists	34 (7.6)
District hospital	104 (23.3)
Sub-district hospital	96 (21.4)

Table 8b:

Health Facility	Prescriptions in the sample	Extrapolated to the whole population
District Hospital	104	104 (13.5%)
Sub District Hospitals	96	96(12.5%)
Dispensaries/Health Centres	164	312 (40.5%)
Private Clinics/Nursing home	49	204 (26.5%)
Chemists	34	54 (7.0%)

Table 8c:

Facility	Number in sample	number in the whole population	Percentage of facilities sampled
District Hospital	1	1	100
Sub district hospitals	2	2	100
Health centers and dispensaries	31	58	53.4
Private Chemists	10	16	62.5
Nursing home and clinics	6	25	24

3.3 Types of antimalarial prescribed and given to the patients

The drugs prescribed differed slightly from those supplied (table 9) partly because 3.3% of prescriptions did not indicate the anti-malarial to be given and 4.6% of supplies were not specified.

Nearly half of the prescribed and supplied drugs were ACT but SP, Quinine and Amodiaquine were also used frequently.

Table 9: Distributions of antimalarial prescriptions

Variable	Frequency (%)	
Prescribed drug		
ACT	218	(45.2)
SP	71	(14.7)
Amodiaquine	94	(19.5)
Quinine	72	(14.9)
Artemesinin monotherapy	\ 1	(2.3)
Not indicated	16	(3.3)
Drugs dispensed		
ACT	223	(46.3)
SP	74	(15.4)
Amodiaquine	91	(18.9)
Quinine	64	(13.3)
Artemesinin monotherapy	7	(1.5)
Lonart injection	1	(0.2)
Not indicated	22	(4.6)
Dosage form dispensed		
Solid	336	(69.7)
Liquid	68	(14.1)
Injection	60	(12.4)
Solid & Injection	5	(1.0)
Not indicated	13	(2.7)

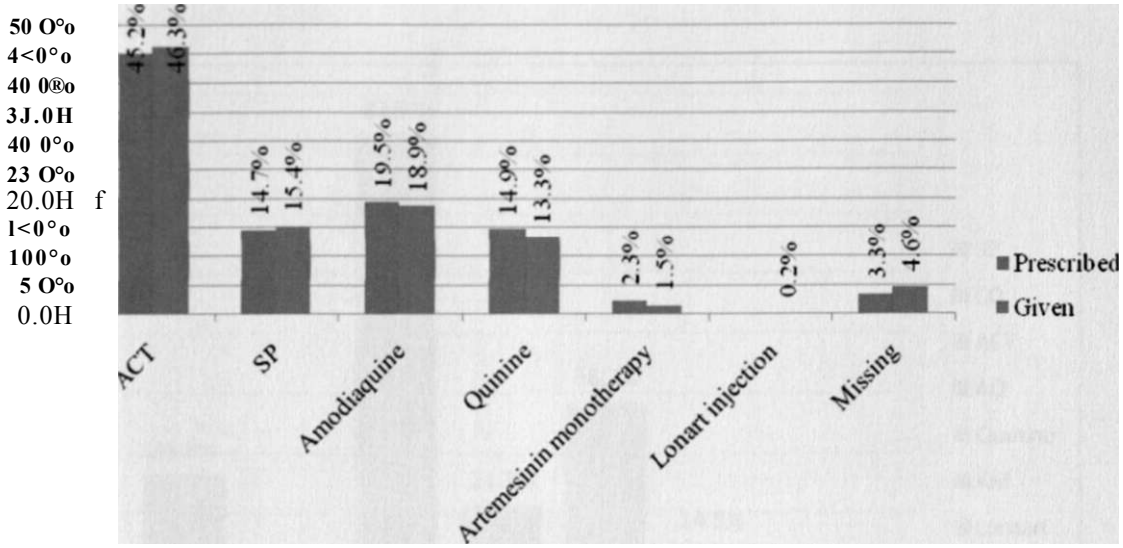


Figure 3: Distribution of drugs prescribed and supplied

3.4 **Dosage form**

Majority of the prescriptions were given in solid form (69.7%) while the others were given as liquid (14.1%) and injection (12.4%). Few prescriptions (1%) were given both as solid and injection.

3.5 Preference of antimalarial prescriptions

The providers had preferences of more than one drug for malaria. However, most of the providers preferred issuing ACT (82.9%). Besides issuing ACT, some providers also preferred giving quinine (38.2%), SP (26.3%) and amodiaquine (21.1 %).

Table 10: Preference of antimalarial prescriptions

Preference	Frequency (%)
SP	20 (26.3)
Chloroquine	6 (7.9)
ACT	63 (82.9)
Amodiaquine	16 (21.1)
Quinine	29 (38.2)
Artemesinin monotherapy	11 (14.5)
Lonart injection	1 (1.3)

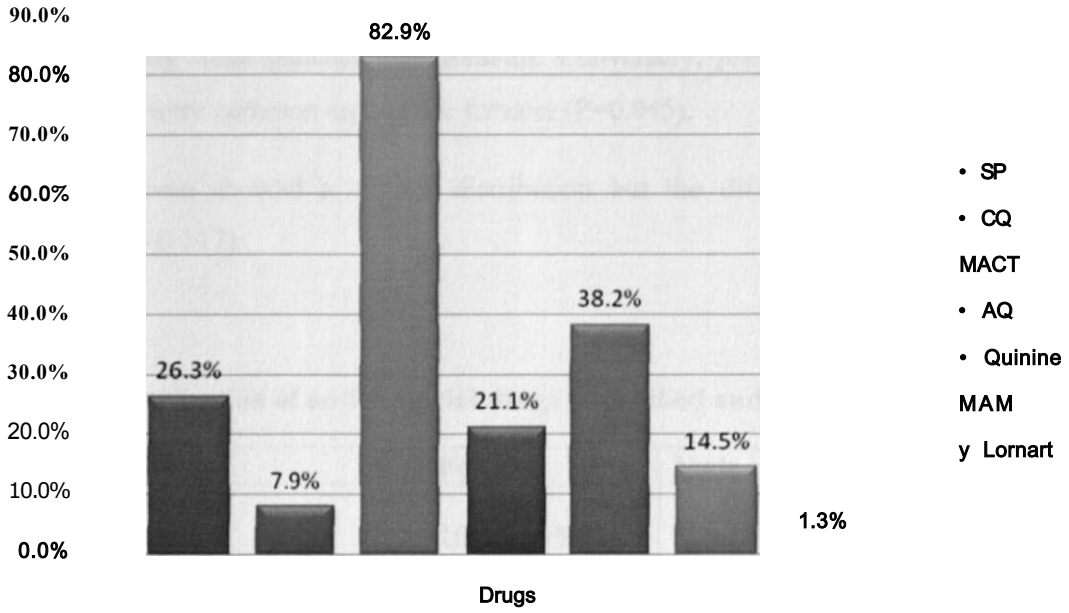


Figure 4: Preference of anti-malarial drugs

3.6 Shortages of antimalarial drugs

Out of the 55 respondents interviewed, 80% agreed that there were occasional stock outs of antimalarial drugs. Most of the respondents (72.7%) were not specific on when the drugs were out of stock. However, 5.5% reported 2weeks out of stock per month while 1.8% a few days in a month

Table 11: Anti-malarial drugs stock variations

Variable	Frequency (%)
Out of stock at the time of visit	
No	11 (20.0)
Yes	44 (80.0)
When out of stock	
1/2 Month	3 (5.5)
A few days	1 (1.8)
Not specific	40 (72.7)
Not indicated	11 (20.0)

3.7 **Prescriptions of antimalarial drugs and gender of the patients**

As indicated in Table 12, ACT, SP and artemesinin monotherapy prescriptions were more common among male patients than females. Conversely, prescriptions of amodiaquine and quinine were more common among the females (P=0.045).

The drugs given showed a similar distribution but the differences were not statistically significant (P=0.117).

Table 12: Distribution of anti-malarial drugs prescribed and supplied by gender

Variable	Female	Male	P value
Prescribed drug			
ACT	109 (44.1%)	109 (49.8%)	0.045
SP	33(13.4%)	38(17.4%)	
Amodiaquine	57(23.1%)	37(16.9%)	
Quinine	45(18.2%)	27(12.3%)	
Artemesinin monotherapy	3(1.2%)	8 (3.7%)	
Drugs dispensed			
ACT	111 (45.5%)	112(51.9%)	0.117
SP	35(14.3%)	39(18.1%)	
Amodiaquine	55 (22.5%)	36(16.7%)	
Quinine	40(16.4%)	24(11.1%)	
Artemesinin monotherapy	2 (0.8%)	5 (2.3%)	
Lonart injection	1 (0.4%)	0 (0.0%)	

3.8 **Prescription of antimalarial drugs and age of the patients**

ACT and artemesinin monotherapy were a greater proportion of prescriptions for six to twelve year-olds (80%) compared to the other age groups (Table 13). Younger children were more likely to get amodiaquine and adults were more likely to get SP or quinine.

Table 13: Distribution anti-malarial prescriptions by age

Variable	0 - 5	6 - 1 2	13 & above	P value
Prescribed drug				
ACT	61 (43.6%)	24 (68.6%)	90 (41.9%)	0.001
SP	4 (2.9%)	2 (5.7%)	54 (25.1%)	
Amodiaquine	53 (37.9%)	2 (5.7%)	25(11.6%)	
Quinine	20(14.3%)	3 (8.6%)	44 (20.5%)	
Artemesinin monotherapy	2(1.4%)	4(11.4%)	2 (0.9%)	

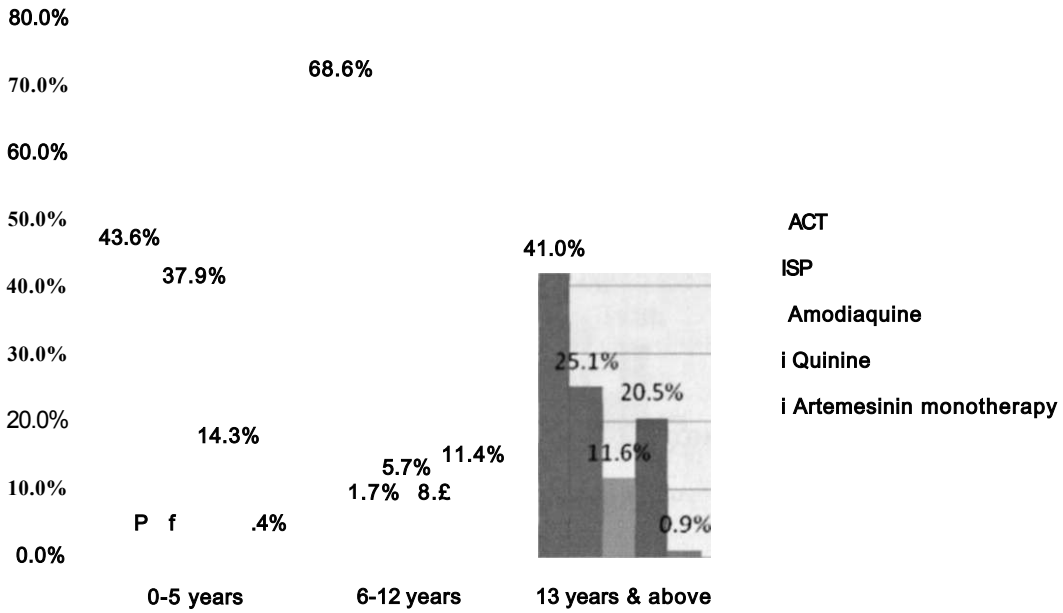


Figure 5: Prescription by age group

3.9 Anti-malarial drugs given and age of the patients

Similar trends were seen amongst drugs supplied (Table 14)

Table 14: Distribution anti-malarial drugs given by age

Variable	0 - 5	6 - 1 2	13 & above	P value
Drug given				
ACT	64 (46.4%)	25 (73.5%)	90 (42.5%)	
SP	6 (4.3%)	2 (5.9%)	54 (25.5%)	
Amodiaquine	52 (37.7%)	2 (5.9%)	24(11.3%)	0.001
Quinine	16(11.6%)	2 (5.9%)	42(19.8%)	
Artemesinin monotherapy	0 (0.0%)	2 (5.9%)	2 (0.9%)	
Lonart injection	0 (0.0%)	1 (2.9%)	0 (0.0%)	

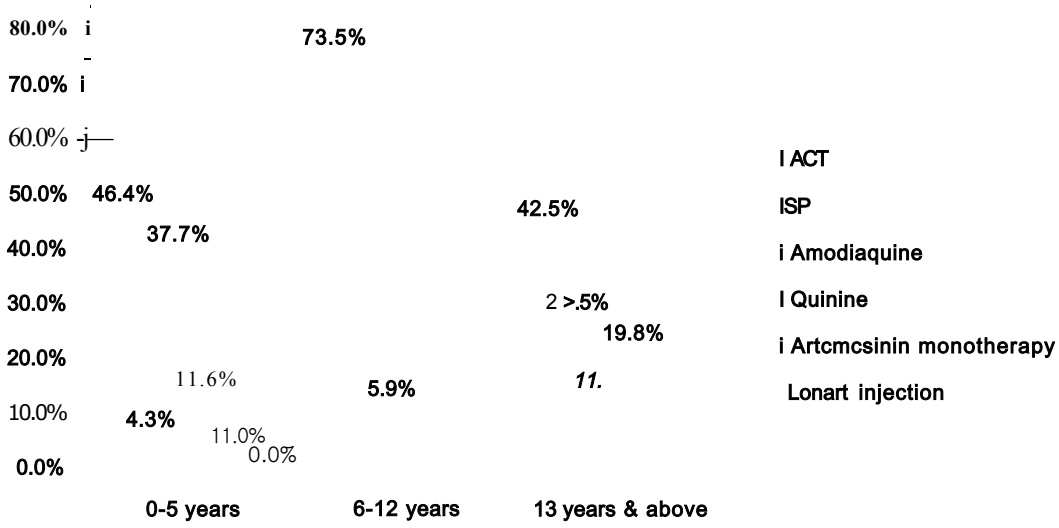


Figure 6: Distribution of antimalarial drugs given by age group

3.10 Anti-malarial drugs prescribed by health facility

The prescriptions of anti-malarial drugs varied according to the type of facility (P=0.001). Private clinics and nursing homes used a lot of ACT and artemesinin monotherapy (93%) whereas private chemists used a higher proportion of SP drugs (28.9%), sub-district hospitals used more amodiaquine than others (41%) and the district hospital has high quinine usage (52.9%) compared to the other facilities.

Table 15: Anti-malarial drugs prescribed by health facility

Prescribed drug	Dispensary /health centre	Private/ Nursing homes	Private chemists	District hospital	Sub-district hospital	P value
ACT	67 (42.4%)	55 (80.9%)	20 (52.6%)	48 (47.1%)	28 (28.0%)	0.001
SP	38 (24.1%)	3 (4.4%)	11 (28.9%)	0 (0.0%)	19(19.0%)	
Amodiaquine	50 (31.6%)	0 (0.0%)	3 (7.9%)	0 (0.0%)	41 (41.0%)	
Quinine	3(1.9%)	2 (2.9%)	2 (5.3%)	54 (52.9%)	11 (11.0%)	
Artemesinin monotherapy	0 (0.0%)	8(11.8%)	2 (5.3%)	0 (0.0%)	1 (1.0%)	

CHAPTER IV

4.0 DISCUSSION

In this sample dispensaries and health centers contributed to the highest proportion of prescriptions given for malaria in Kirinyaga District. District and sub-district hospitals were also significant facilities that prescribed antimalarial drugs over the three months study period.

Overall, ACT was the most prescribed and issued drug in the facilities studied. Though ACT was the drug of choice in all the facilities, prescription of ACT was comparatively higher in private clinics and nursing homes than the other facilities. Prescriptions of other antimalarial drugs such as SP, amodiaquine and quinine were comparatively high in private chemists, sub-district hospitals and district hospitals respectively. It is apparent that there is a proportion of Government facilities that do not adhere to the guidelines. The reasons for this position may include the fact that new medical workers are employed periodically and who may not have benefited from the previous training. Another possibility is the periodical stock out of supplies, either because of the logistics of procurement or transport issues. There may also be a class of prescribers which will not change and there is currently no method of enforcement. Patients too may have preferences, after all they have been used to using antimalarials and they certainly know what work best with few side effects. In private facilities, prescription writing and supply is more liberalized. The medical worker is more likely to give what fits the "pocket" whereas in public facilities these considerations are never entertained. . The pharmacy (where drugs are dispensed) and the diagnosis point, in a public facility are physically separate, in a private set up, it may be the same room, which allows instant consultation on what a patient can afford. In a previous study to investigate the use of artemether -lumefantrine (AL) in some districts in Kenya, the proportion of febrile children who received first-line recommended AL within 48 hours was 10.2%, compared to only 4.6% of children receiving sulphadoxine-pyrimethamine first line therapy in 2001[16]

Prescriptions of ACT, SP and artemesinin monotherapy were more common among the male patients compared to the female populations, although no distinction is made in the Government guidelines regarding males or females. Reasons for this discrepancy are not clear. It is possible that men can influence the prescribers in terms of what they consider better for them based on previous experience. For women, safety considerations may also influence what type of drug is to be prescribed. If breast feeding or pregnant, prescribers would be constrained

on what to prescribe. Policy on safety in breast feeding is not yet fully understood by medical workers. The standard statement giving prescribes discretion on the benefit versus risk is too open ended, especially for certain categories of medical workers who are less educated it would be prudent for the government to produce explicit guidelines.

Purchasing from the private sector is price dependent, with the cheaper drugs (SP, CQ) being preferred. In addition, age was found to determine the type of drug prescribed with six to twelve year-olds being more likely to get ACT and artemesinin monotherapy than the other age groups. While amodiaquine was commonly prescribed among those up to five years, age group, quinine and SP was common among the ages of 13 years and above. The age related differences are due to the fact that within the public health facilities, the liquid ACT is not available. Amodiaquine which has been used for a long time is readily available alternative. Amodiaquine also has an easy dosing schedule (a single dose, or a once daily dose for three days) SP use is even better with only a single dose, and it is cheaper (at KES 20 a dose at the time of the study). It was also easily available over the counter (it is not a prescription drug). SP was available in supermarkets and kiosks which were not a part of this study because they are unregulated and not registered.

Solid dosage forms are more stable, are available and are cheaper than liquids hence they are dispensed most of the times. The cadre of prescribers ranged from nurses (mostly at health dispensaries) to clinical officers (mostly at health centers) and Medical Officers (mostly at Sub-district and District hospitals)

The understanding of the malarial policy would follow the level of current medical knowledge. It may be argued that whereas nurses would be more conservative in the change from what they have traditionally used, medical officers being mostly younger practitioners would take a risk and try something new. They are also more recently trained and have access to internet. One may want to imagine that they can appraise their knowledge more frequently. However one may be curious to study whether this is totally true. Most of the dispensaries have experienced nurses and clinical officers who are likely to be more conservative. The private health facilities are certainly more liberal, they would give a compromise of what works best for patient and what the patient can afford.

The most preferred antimalarial drug prescribed by most of the healthcare providers was ACT which accounted for 82.9% of preferences. Quinine and SP were also prescribed to a

significant extent according to the respondents. It was also interesting to find that chloroquine is still a preference in treating malaria to some of the providers despite publicity and guidelines.

It was apparent that there were periods of stock outs, the respondents were however non-specific on the duration. This may be as a result of fear of publicity, or intimidation by their seniors. It is of course worrying what options are available during these stock outs periods with the low purchasing abilities of patients, one can only conclude that they would go to either alternative medicine or use the cheaper SP or CQ.

There are often delays in the Government procurement procedures. It is governed by statutes and involves a long process that is specifically dictated by the Procurement and Disposal act 2006. Once the drugs are in the procurement entity warehouse, the distribution is undertaken through the malaria program at the Ministry which has to authorize both the facilities and the quantities to be given This bureaucracy often leads to supply gaps.

The out of stock state, may lead to the use of whatever is available. It is known that quinine is being used when the A.C.T are not available in both health centers and dispensaries. This poses a huge safety risk because of its documented side effects (cinchonism). If the patients do not respond to quinine, then the situation would be alarming. But as a medical worker, one is in a total therapeutic dilemma. You may not allow the patient to go home and die of malaria and so you will prescribe whatever is available. The Government has a responsibility to its citizens. Health budgets must be given more priority than political budgets. Again, donors need more compassion as they deal with Governments on health matters. The procurement procedures need to be more liberalized to allow easier procurement of medical supplies. More often the developing countries like Kenya feel that the other world pushes it to into a begging corner, to accept "anything" and to depend on them for "everything" and may remove financial support without any notice. Health matters need to be separated from political matters. Currently there is a push to have a few companies to manufacture A.C.T at affordable prices to all sectors but this is yet to be actualized .There are complains that this is meant to give monopolies to a few companies to flood the market with the drugs. The consequence would be a loss of efficacy and effectiveness of the A.C.T due to development of resistance

The malaria endemic however remains a leading cause of mortality and morbidity. Fifty years ago, some countries eliminated malaria, and indeed any cases they experienced are an

"imported **form".** Certainly Kenya should learn from such states. Malaria is however a global problem, it has to be prioritized by many countries in the world. It needs a new thrust of energy that goes outside the traditional approaches. Perhaps a multiple pronged approach that re-looks at every part of the **Plasmodium** life cycle, (current interventions and possible options), re looks at the science of resistance development, looks at the body's vulnerability and in each of these, considers other optional interventions. Reports coming in from the South East Asia of resistance to A.C.T are a shock to medical workers globally. This, seen against a background of lack of any new anti-malarial, in the pipeline, is worrisome. Kenya and the world cannot keep waiting and watching.

Government needs to redirect research into more appropriate vector control; its needs to accelerate the on- going research in vaccinations, even consider providing incentives to scientists to join malaria research. As a country we need to walk more cautiously on massive use and campaigns on A.C.T especially where within our setup, every headache, stomach-ache, or fever is perceived as malaria. We are increasingly getting cases of heart diseases and our population needs to be educated appropriately. We need as a country to re-examine our communication strategies, especially on the training. How to translate training into practice will remain a challenge. We need to look at the guidelines and suggest ways of improving them to promote greater adherence. Finally a study to assess who influences prescription patterns may be necessary. This would be important even in other disease conditions where therapeutic interventions are to be made

CHAPTER V

5.0 CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

A high proportion of malaria cases at Kirinyaga district are treated with ACT. However, other antimalarial drugs such as quinine, SP and amodiaquine are common in treating malaria in the area. Different health facilities give different prescriptions. However, ACT prescriptions were found to be common in all types of health facilities. According to this study, ACT prescriptions were relatively high in private clinics and nursing homes compared to the other facilities. Also, prescriptions of antimalarial drugs were found to be different according to sex and the age of the patients. The male populations seemed to use ACT more than the female populations and the drug was more prescribed among ages six to twelve years compared to the other age groups.

It is apparent from the study that more training to the health workers is necessary to improve A.C.T uptake. Medical workers also need to be alerted on the possible side effects on the use of A.C.T. The out of stock issue deserves direct government intervention and the staff need to be guided on what to do when they lack the A.C.T. The availability of monotherapies is a testimony of weak enforcement by the regulating agencies, which would require strengthening. It is a fact that no drug can legally be imported without the approval of the National Drug Regulatory Authority. A recent survey by ministry of health and W.H.O. indicated that monotherapies, fake and counterfeit drugs do indeed exist in our drug supply chain. [16] The availability of the monotherapies in spite of the policy is then a wake up call to them.

A therapeutic dilemma arises, in areas where resistance to available monotherapies is low. Should we not use the cheaper monotherapy? What should our people do if they cannot afford the A.C.T and the Government cannot provide? Some acceptable options need to be availed to patients and medical workers. An acceptable and stable liquid preparation should also be available for children. The study also opens up possible areas of research in terms of the sex difference where men's uptake of A.C.T is higher than in women.

The use of ACT combinations is evidently justifiable scientifically but there is concern on safety especially of the lumefantrine; it resembles halofantrine which, is now not in much use. These two drugs belong to the same class of aryl-amino-alcohols. They are known to be

cardio-toxic and their absorption is dependent on gastric pH. The changing lifestyles and poor settings would make the Kenyan population very vulnerable to these adverse effects. It would be recommended that research on any cardio-vascular events so far in Kenya resulting from ACT use be undertaken.

5.2 Recommendations

Malaria is a major obstacle to economic development in Kenya. Kenya loses up to 170 million working days annually due to problems associated with malaria. Kenyans spend a lot of time seeking malaria treatment and it is certainly a major contributor to poverty.

From the study, it is apparent that gaps do indeed exist between policy formulation and implementation. Perhaps a continuous monitoring and assessment by Government should be done as a standard practice. Effective communication between medical workers and their trainers should be emphasized. New policies should also take into recognition the existing traditions and laws in order to gain wide acceptability. In this study, it is apparent that the removal of the older monotherapies was not efficient or proper, such that three years after policy guidelines were adopted; the monotherapies still exist in both private and public facilities. The stock out situation is particularly grave and has a variety of causes and consequences. Most certainly, the procurement and distribution challenges need to be optimized to mitigate against this.

A national platform comprising practitioners, researchers, universities, politicians and the highest authorities in the country need to urgently look into the malaria control, eradication and treatment issues. It would be recommended that a multidisciplinary team of professionals be involved in this fight, because medical workers alone have been too stereotyped in their approach to malaria research. Engineers may give a physical barrier; entomologists may come up with novel approaches to stop gametocytes production, *ad infinitum.* This may be through the new private-public sector partnerships. Globally, initiatives like Medicines for Malaria Venture (MMV), the Malaria Vaccine Initiative (MVI) need to be domiciled in Kenya. These would accelerate the development and deployment of effective and efficient malaria control tools for the population.

Quite certainly, the fight against malaria in Kenya must involve radical new approaches that would complement the existing methods. It would require malaria focused scientists, malaria focused funding, malaria supported political infrastructure if as a country we have to win this battle. The search for new chemical entities with different mechanisms of action with an acceptable safety profile must be intensified. Old molecules like chloroquine which have done well in the past; needs to be re-engineered to mitigate against the resistance. Counterfeits and fakes needs to be fought off by relevant arms of government.

Whatever the method, an all round understanding of both the human and the vector is mandatory. The whole world must congregate around this disease.

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7.0 APPENDICES

APPENDIX 1; SAMPLE OF QUESTIONNAIRE

Patient Name (: CODED) Age: Sex:

Date:

A. **ANTIMALARIAL PRESCRIBED, *(please circle or tick)***

1.SP, 2. CQ 3. ACT 4. Amodiaquine 5. Quinine

6. Artemisinin based Monotherapy 7. Any other, state details

B. ANTI MALARIAL GIVEN

1.SP, 2. CQ 3. ACT 4. Amodiaquine 5. Quinine

6. Artemisinin Monotherapy 7. Any other, state details

C. **DOSAGE FORM GIVEN**

1.Solid 2. Liquid 3. Injection 4. Suppository

D. ANY PREFERENCE OF ANTI -MALARIAL?

1.SP, 2. CQ 3. ACT 4. Amodiaquine 5. Quinine

6. Artemisinin based Monotherapy 7. Any other, state details

If yes give reasons

E. Any periods when the anti-malarial are out of stock.

(a) When

(b) Period out of stock ,and what was supplied instead

F. Which anti-malarial do you give on the counter?

1) SP

2) CQ

3) ACT

4) Amodiaquine

5) Quinine

6) Artemisinin Monotherapy

7) Any other, state details

Give reasons

APPENDIX II: KNH-IRB APPROVAL LETTER

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SC IENCES
SCHOOL OF PHARMACY

DEPARTMENT OF PHARMACEUTICS & PHARMACY PRACTICE
P.O. BOX 19676-00202, Tel: 054 020 2721215
NAIROBI, KENYA.

6th May, 2009

The Hospital Superintendent,
Nyeri Provincial Hospital,
P.O Box 27-10100,
Nyeri.

Dear Sir/Madam,

REF: DR. T.M. KAHIGA (REG.NO. U59/70421707^ RESEARCH ON PRESCRIBING PATTERN? AND AVAILABILITY OF ARTEMISININ BASED COMBINATION THERAPY ANTIMALARIALS COMPARED TO MONOTHERAPY IN KIRINYAQA:

Dr. Titus M. Kahiga is a bona fide Master's Degree student in the School of Pharmacy, University of Nairobi. He is carrying out a research on **"Prescribing Patterns and Availability of Artemisinin Based CombinationTherapy Antimalarials"** as part of his masters degree in clinical pharmacy programme. Your institution is among the institutions he will be carrying out his research.

Please *accord* him the necessary assistance.

Dr. Kimani. A. M. Kuria
Chairman Dept. of Pharmaceutics and Pharmacy Practice
School of Pharmacy

c.c. Dean,
School of Pharmacy

APPENDIX 111 - LETTER OF INTRODUCTION

e s s e

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP", Nairobi.
Email: KNHplan@Ken.Healthnet.org

Ref: KNH/UON-ERC/A/213

29th April 2009

Dr. Titus Muhu Kahiga
Dept. of Pharmaceutics and Pharmacy Practice
School of Pharmacy
University of Nairobi

Dear Dr. Kahiga

Research proposal: "Prescribing patterns and availability of Artemisinin Based Combination therapy Antimalarials compared to Monotherapy in Kirinyaga District, Central Province, Kenya"(P42/2/2009)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above revised research proposal for the period 29th April 2009 -28th April 2010.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to *minimize* chances of study duplication.

Yours sincerely

PROF. A N GUANTAI
SECRETARY, KNH/UON-ERC

c.c. The Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
The Dean, School of Pharmacy, UON
The Chairman, Dept. of Pharmaceutics & Pharmacy Practice, UON
Supervisor: Dr. David Scott, Dept. of Pharmaceutics & Pharmacy Practice, UON

APPENDIX IV: TABLES

Table 1 HEALTH FACILITIES IN KIRINYAGA DISTRICT AS AT 1ST SEPTEMBER 2008

	DISTRICT	PROVINCE	HEALTH FACILITY NAME	TYPE OF HEALTH FACILITY	STATUS
1	Kirinyaga	Central	Kerugoya D.H	District Hospital	MoH
2	Kirinyaga	Central	Kimbimbi S.D.H	Sub-District Hospital	MoH
3	Kirinyaga	Central	Kianyaga S.D.H	Sub-District Hospital	MoH
4	Kirinyaga	Central	Baricho Health Centre.	Health Centres	MoH
5	Kirinyaga	Central	Difathas Health Centre.	Health Centres	MoH
6	Kirinyaga	Central	Kabare Health Centre.	Health Centres	MoH
7	Kirinyaga	Central	Kangaita Health Centre.	Health Centres	MoH
8	Kirinyaga	Central	Kiamutugu Health Centre.	Health Centres	MoH
9	Kirinyaga	Central	Kiumbu Health Centre.	Health Centres	MoH
10	Kirinyaga	Central	Mutithi Health Centre.	Health Centres	MoH
11	Kirinyaga	Central	Sagana Health Centre.	Health Centres	MoH
12	Kirinyaga	Central	Uceru Community Health Centre.	Health Centres	MoH
13	Kirinyaga	Central	Ciagini Dispensary	Dispensaries	MoH
14	Kirinyaga	Central	G.K. Prison (Gathigiriri) Dispensary	Dispensaries	MoH
15	Kirinyaga	Central	Gaciongo Dispensary	Dispensaries	MoH
16	Kirinyaga	Central	Gathambi Dispensary	Dispensaries	MoH
17	Kirinyaga	Central	Gathigiriri Dispensary	Dispensaries	MoH
18	Kirinyaga	Central	Gatithi Dispensary	Dispensaries	MoH
19	Kirinyaga	Central	Gatugura Dispensary	Dispensaries	MoH
20	Kirinyaga	Central	Gatwe Dispensary	Dispensaries	MoH
21	Kirinyaga	Central	Kagumo Dispensary	Dispensaries	MoH
22	Kirinyaga	Central	Kamweti Dispensary	Dispensaries	MoH
23	Kirinyaga	Central	Kandongu Dispensaiy	Dispensaries	MoH
24	Kirinyaga	Central	Kang'aru Dispensary	Dispensaries	MoH
25	Kirinyaga	Central	Karumandi Dispensary	Dispensaries	MoH
26	Kirinyaga	Central	Kiangai Dispensary	Dispensaries	MoH
27	Kirinyaga	Central	Kiangombe Dispensary	Dispensaries	MoH
28	Kirinyaga	Central	Kianjege Dispensa/y	Dispensaries	MoH
29	Kirinyaga	Central	Kiaragana Dispensary	Dispensaries	MoH
30	Kirinyaga	Central	Kibirigwi Dispensary	Dispensaries	MoH
31	Kirinyaga	Central	Kutus Dispensary	Dispensaries	MoH
32	Kirinyaga	Central	Mumbuini Dispensary	Dispensaries	MoH
33	Kirinyaga	Central	Murinduko Dispensary	Dispensaries	MoH
34	Kirinyaga	Central	Nguka Dispensary	Dispensaries	MoH
35	Kirinyaga	Central	Njegas Dispensary	Dispensaries	MoH

36	Kirinyaga	Central	Rukanga Dispensary	Dispensaries	MoH
37	Kirinyaga	Central	Thiba Dispensary	Dispensaries	MoH
38	Kirinyaga	Central	Wamumu Dispensary	Dispensaries	MoH
39	Kirinyaga	Central	Gatuto Dispensary	Dispensaries	Gaz
40	Kirinyaga	Central	Joshua Mbai Memorial Dispensary	Dispensaries	Gaz
41	Kirinyaga	Central	Kairini Dispensary	Dispensaries	Gaz
42	Kirinyaga	Central	Kajiji Dispensary	Dispensaries	Gaz
43	Kirinyaga	Central	Kangu Dispensary	Dispensaries	Gaz
44	Kirinyaga	Central	Kiamanyeki Dispensary	Dispensaries	Gaz
45	Kirinyaga	Central	Kiburu Dispensary	Dispensaries	Gaz
46	Kirinyaga	Central	Kirogo Dispensary	Dispensaries	Gaz
47	Kirinyaga	Central	Kiumbu Dispensary	Dispensaries	Gaz
48	Kirinyaga	Central	Mutitu Dispensary	Dispensaries	Gaz
49	Kirinyaga	Central	Rurii-Kiandegwa Dispensary	Dispensaries	Gaz
50	Kirinyaga	Central	Baricho Dispensary	Dispensaries	KEC
51	Kirinyaga	Central	Kianyaga Dispensary	Dispensaries	KEC
52	Kirinyaga	Central	Difathas Dispensary	Dispensaries	KEC
53	Kirinyaga	Central	Kagio Dispensary	Dispensaries	KEC
54	Kirinyaga	Central	Kerugoya Dispensary	Dispensaries	KEC
55	Kirinyaga	Central	Kutus Dispensary	Dispensaries	KEC
56	Kirinyaga	Central	Sagana Dispensary	Dispensaries	KEC
57	Kirinyaga	Central	C.C.S Wang'uru Clinic	Dispensaries	CHAK
58	Kirinyaga	Central	Gatumbi SDA Dispensary	Dispensaries	CHAK
59	Kirinyaga	Central	Kiandegwa Health Clinic	Dispensaries	CHAK
60	Kirinyaga	Central	St. John's Thaita Dispensary	Dispensaries	CHAK
61	Kirinyaga	Central	Kariko Dispensary	Dispensaries	MoH
62	Kirinyaga	Central	A.C.K Mbiri Dispensary	Dispensaries	CHAK
			TOTAL	**62**	

»KEC - Kenya Ecumenical Conference(catholic)

*CHAK - Christian Health Association of Kenya

*SUPKEM - Supreme Council of Kenya Muslims

GAZ — Gazetted facilities

SUMMARY:

1 DISTRICT HOSPITAL

2 SUB-DISTRICT HOSPITALS

9 HEALTH CENTRES

37 GOK DISPENSARIES

12 FBO DISPENSARIES

1 GOK DISPENSARY - NOT OPERATIONAL

Table (2) - PRIVATE CHEMIST AND CLINICS WITHIN K1RINYAGA DISTRICT

Kerugoya Family Pharmacy		Kerugoya .Kutus Road	Opposite general Hospital	
Frajoy Health Services	Frajoy Building	Kutus - Mijini Road		
Semuma Chemist		Sagana - Muranga Road		
Exodus Drug Store	Plot No 14	–	Kianyaga (Karumande)	-
Baragwi Outreach Clinic	Plot No 216		Kamugunda	
Charity Clinic	–		–	-
Glorious Cosmetics			Plot No - Own land	-
Baragwi Maternity Home	Plot No 79			H I S
St Ann Medical Clinic	Plot No 108		Kianyaga	
Highway Health Facility	Plot No 29		Mururi	
Jonakam Chemist	–	–	Kimunye	-
Kangaita Medical Clinic	Plot No 321 Kangaita A		Kangaita A	m
Mwihoko Clinic	Plot No.A13		Kangaita-Nyagituchi Market	m
Victory Clinic	Plot No.18B		Nyagithuchi	
			ACK Mugumo Church CPD	–
Jade Heathcare Ltd	Plot A63 Hotel Chakaka Building	Sagana-Murang'a Road		–
Fadhili Pharmacy		Sagana - Kutus Road		§ m §
Kagco Nursing Home		Sagana - Kutus Road		
Kerugoya Pharmacy		Along Sagana-Kutus Road		
Chimo Pharmacy	Plot 94 B	Along Karatina - Kerugoya Road	Kagumo Market	H i
ACK Mt. Kenya Hospital		Along Kerugoya - Kagumo Road		
Flawar Chemist		Along Sagana Muranga Road		Sag*ana* Town
Kiangai Medical Clinic	Plot 8	Along Karatina - Kagumo Road	Kiangai	–
Bigems		Kutus, Ndumba Road		
Kahama Chemist	Plot No. 1304	–	Kangari	-
Makutano Medicare Clinic			Makutano, Mbeere District	I I I I
Kerugoya Catholic Dispensary			Opposite Telcom	
Twin Peaks			Opposite Kimbimbi Subdistrict Hospital	–
Kawakim Shop Clinic				Mwea Town

Jaima Chemist			Kimbimbi Opp sub-district hospital	
Arbedare Pharmaceuticals	Plot 2576		Kangari	
Woodstreet Pharmacy	Plot No 72	Off Makutano - Mwea Road		
Mumu Health Services Clinic		Sagana - Murang'a Road		
Kirinyaga Community Pharmacy		Kagio- Kandongu Road		Kagio Town
Sagana Medical Clinic	Chewa House, Plot No 270	Behind Sagana Muranga Road		
St Peters Medical Clinic	Plot 56 Kagumo		Kagumo	
Mutira Community Pharmacy	Plot No 45	Along Kerugoya - Karatina Road	Kagumo Market	
Sunrise Medical Clinic			Matithi trading Centre	
Fort Hall Chemist			Wanguru Mwea	
Baraka Clinic			Mutithi	
Tebebere Rural Pharmacy	Isamwaka Building		Isamwaka Building	

SUMMARY

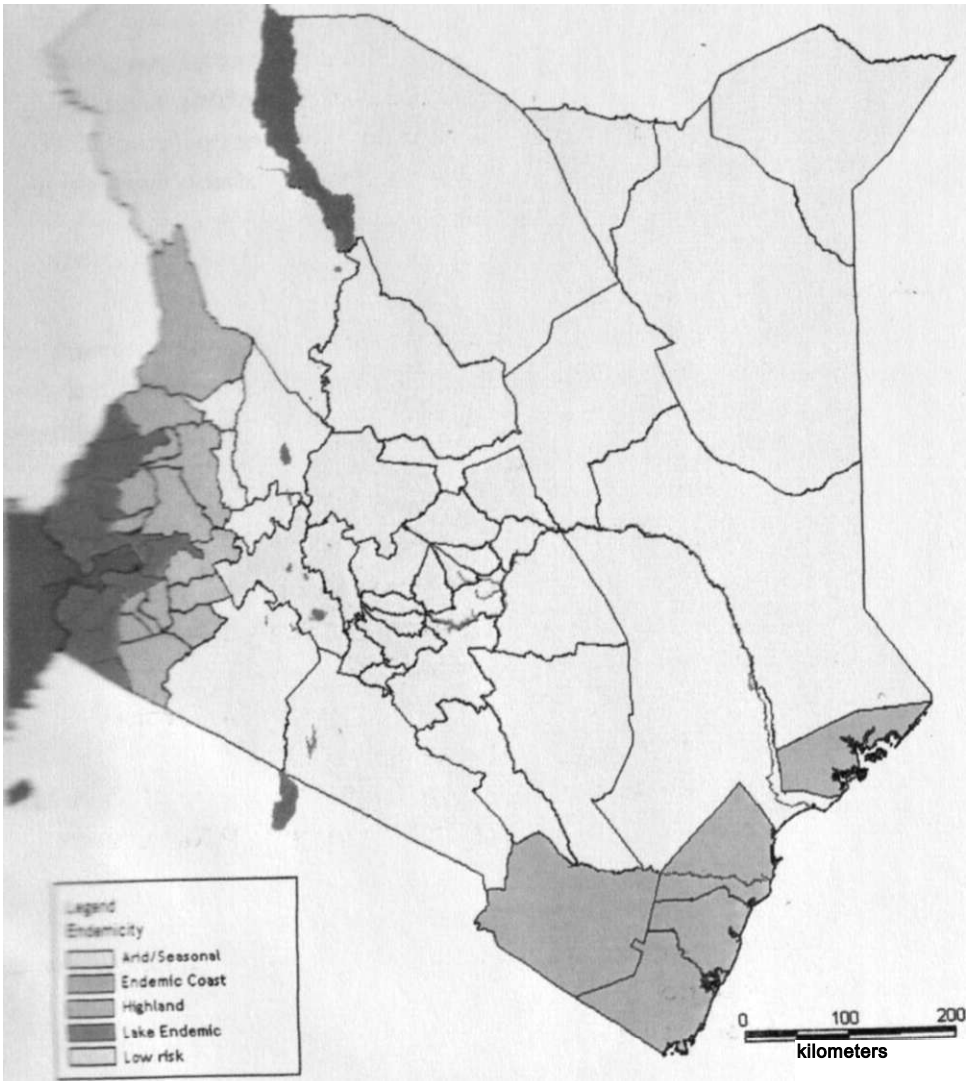
District Hospitals	**1**
Sub-District Hospitals	**2**
Health Centres	**9**
Dispensaries (G.O.K)	**37**
Faith Based Dispensaries	**12**
Pharmacies/ Chemists (PRIVATE)	**16**
Private Clinics/ Nursing Homes	**25**
Total	**102**

FACILITIES AND PRESCRIPTIONS THAT WERE TO BE ANALYSED

	Facilities	No. of prescriptions
District Hospitals	**1**	**100**
Sub-District Hospitals	**2**	**100**
Health Centres	**9**	**50**
Dispensaries (G.O.K)	**20**	**30**
Faith Based Dispensaries	**6**	**30**
Pharmacies/ Chemists (PRIVATE)	**10**	**30**
Nursing Homes and Clinics	**12**	**30**
Totals	**60**	**370**

APPENDIX V

i ENDEMIC1TY OF MALARIA IN KENVA



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0F *NAIROBI*