EFFECT OF MISSED MASS DRUG ADMINISTRATION ON FILARIAL INFECTION IN MALINDI SUB-COUNTY, KENYA

MERCY LUSUNGU MKANDAWIRE

MASTER OF SCIENCE
(Medical Parasitology and Entomology)

JOMO KENYATTA UNIVERSITY OF AGRICULTURE AND TECHNOLOGY

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Effect of missed mass drug administration on filarial infection in Malindi Sub-County, Kenya

Mercy Lusungu Mkandawire

A thesis submitted in partial fulfillment for the degree of Master of Science in Medical Parasitology and Entomology in the Jomo Kenyatta University of Agriculture and Technology

2019
DECLARATION

This thesis is my original work and has not been presented to any other university or college.

Signature: ……………………………….. Date: ………………………………………

Mercy Lusungu Mkandawire

This thesis has been submitted with our approval as University appointed supervisors:

Signature: ……………………………….. Date: ………………………………………

Prof. Sammy Njenga

KEMRI, Kenya

Signature: ……………………………….. Date: ………………………………………

Dr. Charles Mwandawiro

KEMRI, Kenya

Signature: ……………………………….. Date: ………………………………………

Prof. Zipporah Ng’ang’a

JKUAT, Kenya
DEDICATION

For,

Eric

Naomi,

Nathan.

I am forever indebted, zikomo kwambiri!
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ABBREVIATIONS AND ACRONYMS

ADL  Adenolymphangitis
ADLA Acute Dermatolymphangioadenitis
CFA Circulating Filarial Antigen
CFML Community Microfilaria Load
CMR Center for Microbiology Research
DALY Disability Adjusted Life Years
DEC Diethylcarbamazine Citrate
ELISA Enzyme Linked Immunosorbent Assay
GAELF Global Alliance for Elimination of Lymphatic Filariasis
GMI Geometric Mean Intensity
GPELF Global Program to Eliminate Lymphatic Filariasis
GSK GlaxoSmithKline
ICT Immunochromatographic Card Test
IEC Information, Education, Communication
KEMRI Kenya Medical Research Institute
LF Lymphatic filariasis
MDA Mass Drug Administration
Mf  Microfilariae
MFD  Microfilaria Density
MOH  Ministry of Health
MDP  Mectizan Donation Program
MX  Molecular Xenomonitoring
NGDO  Non-governmental Development Organizations
NPELF  National Program to Eliminate Lymphatic Filariasis
PCR  Polymerase Chain Reaction
QBC  Quantitative Buffy Coat
SAEs  Severe Adverse Experiences
SSC  Scientific Steering Committee
STH  Soil Transmitted Helminth
TBSs  Thick Blood Smears
TPE  Tropical Pulmonary Eosinophilia
TAG-ELF  Technical Advisory Group for the Global Program to Eliminate Lymphatic Filariasis
WHO  World Health Organization
WHA  World Health Assembly
ABSTRACT

In 1997 Lymphatic Filariasis was identified as one of the Neglected Tropical Diseases that could be eliminated. The Global Program to Eliminate Lymphatic Filariasis, through national programs, depends on mass drug administration (MDA) of antifilarial and antihelminthic drugs to over 80% of the population at-risk for a period of 4 – 6 years to interrupt transmission of the disease and control morbidity caused by LF. National programs are responsible for the distribution, control and evaluation of MDAs. In Kenya, MDA was initiated in 2002 and MDA administered in 2002, 2003, 2005 and 2008. Parasitologic surveys were conducted in eight sentinel communities in Malindi sub-County after four annual MDAs with 6mg/kg of diethylcarbamazine in combination with 400mg albendazole. MDA was not administered to the targeted at-risk population in 2004, 2006 and 2007 due to insufficient funding. Analysis of Variance and Kruskal-Wallis tests were employed to determine quantitative differences in the study communities. The McNemars and Wilcoxon signed ranks test were used to test for the change in microfilaremia and antigenemia among the participants using paired data collection before and after the MDA at α=0.05. At baseline, 1447 participants were tested using the Immunochromatographic card test and night blood specimens were collected from all ICT positive participants. Prevalence rates were compared using a Chi-square test. Antigen prevalence among the communities ranged from 34.4% in 2002, 26.2% in 2003, 18.7% in 2004, 14.0% in 2007 and 11.4% in 2009 respectively, while the microfilaraemia prevalence’s measured 20.9% in 2002, 10.5% in 2003, 7.1% in 2004, 1.9% in 2007 and 0.9% in 2009. By 2009, after four rounds of treatment, the number of mf positive individuals were 10 compared to the 297 in 2002 was statistically significant (p < 0.001). The mean value for the microfilaria count among the eight communities was at a steady decrease from 43.6 in 2002 to a 0.1 in 2009. Despite the missing of two rounds of treatment, there was a general decrease in the overall microfilaraemia and antigenemia over time but no interruption of transmission. There is need for evaluation and further surveillance. There may also be need to extend the 4 – 6 year recommended period of mass treatment.

Key words: Lymphatic Filariasis, Mass Drug Administration, Microfilaria, Neglected Tropical Disease.
CHAPTER ONE
INTRODUCTION

1.1 Introduction

Lymphatic filariasis (LF) also referred to as elephantiasis, resulting from infection with the mosquito-borne filarial parasitic nematode Wuchereria bancrofti. This parasite is widely distributed in tropical and subtropical areas of the world, where it results in considerable suffering and debilitating clinical disease (McMahon and Simonsen, 1996; Cano et. al., 2014). LF is the fourth leading cause of disability in the world (WHO, 1996).

In Kenya LF is endemic to the coastal region (Wamae et al., 2001). The area along the River Sabaki in Malindi sub-County, Kenya is one of the main LF foci (Wijers and Kaleli, 1984; Njenga et al., 2007). The disease is diagnosed by demonstration of the parasites in the blood/body, antibody testing, antigen detection, molecular diagnosis and vector testing (McCarthy et al., 2012). LF is treated with a single annual dose of diethyl carbamazine (DEC) co-administered with Albendazole in endemic areas. In areas where LF is co-endemic with onchocerciasis or loasis, Ivermectin and Albendazole are used to counter severe adverse reactions cause by the drug, worm and patient interactions (Klion, 2018).

Elephantiasis is a major poverty-associated cause of morbidity occurring primarily in poor communities where the disease further aggravates the situation by affecting the people’s livelihoods (Tan, 2003). Lost productivity due to LF runs into billions of dollars across the world each year (WHO, 2000). The World Health Organization (WHO) reported Disability Adjusted Life Years (DALYs) and the years of life lost due to disability to the disease are estimated at 4.9 million (WHO, 2001), (Hotez et al., 2014). Medical treatment for the disease imposes a tremendous burden on the infected individuals as well as healthcare systems as treatment can be costly.
The 50th World Health Assembly (WHA) in 1997 identified LF as one of the neglected tropical diseases (NTDs) that could not only be controlled, but, could be eliminated from public health problems by the year 2020 through careful planning, implementation and monitoring (WHO, 2005a). Subsequently, WHO initiated the Global Program to Eliminate Lymphatic Filariasis (GPELF) in 1998, which was officially launched in 2000 with MDAs being undertaken in a few initial endemic countries? The Global Alliance to Elimination LF (GAELF) was created in 2000, and, through various partners including drug companies and different foundations, allied with the GPELF (Global Alliance, 2018). Commitment on the national level is vital for the success of the program. There is need to integrate the GPELF programs with already existing control programs in the endemic countries to decrease the cost of operation and sustainability (Molyneux, 2008).

The rolling out of MDA programs since initiation has been commendable. Of the 73 countries classified as endemic to LF, 40 countries have completed MDA campaigns and are conducting post surveillance assessment to validate elimination. Mass drug administration is ongoing in 45 countries while 10 countries have not started MDAs or conducted pre-MDA assessments (WHO, 2018). Even with all the programs, many national programs to eliminate LF (NPELFs) are faced by difficulties in conducting MDAs mainly due to several challenges including, data collection and reporting or prevalences and intensities, weak health care systems in endemic countries, community participation and program logistics (Gyapong et al., 2017). The Technical Advisory Group for the Global program to Eliminate Lymphatic Filariasis (TAG-ELF) issued concerns and warned that if NPELFs do not concede to the essence of monitoring and evaluation, the current effort may not only divert programs away from success but also waste limited resources (Ichimori and Ottesen, 2011). The sequential patterns surrounding LF elimination raises other concerns over the effectiveness, cost-effectiveness, time and how all these impact on MDA progress and funding. Elimination of LF revolves around the premise that with 4 – 6 regular rounds of drug administration, infection may be interrupted and thus elimination eventually achieved (WHO, 2000;
The GPELF relies on two main pillars in their elimination program. The first is the mass drug administration (MDA) of antifilarial drugs to interrupt the transmission of the parasite and secondly by morbidity control and disability prevention (MMDP) (WHO, 2018). Mass chemotherapy employs the recommended co-administration of a single dose of either relatively low-cost diethylcarbamazine (DEC) or ivermectin and albendazole once a year for a recommended period of 4–6 years based on models that estimate the reproductive life span of the adult worms to be 5 years (Ichimori and Ottesen, 2011). DEC, however, cannot be given in areas co-endemic with onchocerciasis or the Loa loa (loaiaisis) eye worm due to the high frequency of severe adverse experiences (SAEs) among patients. Morbidity control involves lymphoedema management mainly through hygiene practice to reduce the occurrence of secondary bacterial and fungal infections and hydrocele surgery (Dreyer et al., 2002). Hydrocele surgery can be relatively costly (Turner et al., 2016).

As with every control program, up-scaling of deployment efforts is of great importance, and since the initiation of GPELF, there has been a rapid increase in the number of countries that have began national programs of elimination (NPELFs) and an increase in the number of people at-risk that have been targeted through MDAs (Hooper et al., 2014). No public health program has ever expanded as quickly as the GPELF (GAELF, 2007). The rapid expansion can be attributed to several factors, including; the generous drug donations and the fact that governments in endemic regions increasingly view the program as a tangible way to address poverty eradication and improve public health (Ottesen et al., 2008; Ichimori et al., 2014).

In addition, the global alliance is already seeing benefits beyond the primary program intent (Global Alliance, 2018). In integrating its work with other health programs, including the control of soil transmitted helminthes (STHs), malaria, schistosomiasis and African river blindness (onchocerciasis), among others, local health systems are able to
maximize resources leading to saving on costs (GAELF, 2007). Effective monitoring of implemented MDAs and morbidity control strategies to determine the effect of the national programs is of vital importance (WHO, 2018).

Although the success of the GPELF is evident, the program has experienced challenges, for instance, there has been a prolonged period of disease mapping out of target areas in those countries that are endemic (Baker et al., 2010; Chand et al., 2014). There has also been a slow rate of scaling up of national programs to cover all the at-risk populations. Another challenge has been setbacks in already active programs due to insufficient funding (Seniors, 2007; Chu et al., 2013; Brady and the GAELF, 2014). In already active programs, greater effort needs to be put into achieving and sustaining high therapeutic and increased treatment coverage (GAELF, 2007).

1.2 Statement of the Problem

Lymphatic filariasis is a disease of public health significance that causes high morbidity rates and exerts a negative impact on the fight against poverty (Tan, 2003; Cano et al., 2014). At the start of the GPELF over 120 million people were infected with LF and over 40 million people were disfigured and incapacitated by the disease (WHO, 2018). Lymphatic filariasis results in abnormal impairment of body parts causing severe pain, physical incapacitation, social stigma, mental disturbance and financial losses (WHO, 2018; Wynd et al., 2007).

Since 2000, 499 million people no longer require preventive chemotherapy due to successful implementation of WHO strategies. Despite more than 6.7 billion treatments having been delivered by 2018, 856 million people in 52 countries worldwide remain threatened by lymphatic filariasis and require preventive chemotherapy to stop the spread of this parasitic infection. In Kenya, baseline assessment date collected in 2002 indicated LF intensities and prevalences of over 25 mf/ul (Njenga et al., 2017).

The assessment of microfilariae (mf) and circulating filarial antigen (CFA) in sentinel communities/villages involved in NPELF is important because it provides valuable
information on the changes in the prevalence of community microfilaraemia and antigenemia after various rounds of MDA. This study assessed the impact of missing two rounds of annual treatments of antifilarial and antihelminthics on the overall mf and CFA prevalence trends in the affected population. MDAs on the overall success of interrupting transmission.

1.3 Justification

There is a need to put more effort towards its elimination. Sustaining annual treatment with high coverage of the population at risk for the recommended 4 – 6 consecutive years to be able to attain elimination has been a challenge for many NPELFs (Wamae et al., 2006). Even so, high treatment coverage and sustainable drug delivery is not easy to achieve for most endemic countries in Africa (Engels et al., 2002).

Missing regular treatment could have an impact in the overall success of an elimination program and it may result being a lot more costly to the government involved. In many resource poor countries, however, continued MDA every year for the recommended 4 – 6 years of the program may not be feasible.

The technical advisory group on the global elimination of lymphatic filariasis (TAG-ELF) warns that unless the current funding situation is looked into, there is a risk that eliminating LF as a public health problem by 2020 will not be achieved. There is also a concern that the efforts already made and the successes achieved could be abandoned in the poorer nations despite the generous donations of two of the three drugs, Ivermectin and Albendazole (WHO, 2005b).

The assessment of microfilariae (mf) and circulating filarial antigen (CFA) in sentinel communities in NPELF is important because it provides valuable information on the changes in the prevalence of community microfilaraemia and antigenemia after various rounds of MDA. This study assessed what impact missed annual treatments of antifilarial and antihelminthics has on the mf and CFA prevalence trends in a population that has missed two rounds of MDAs since the last treatment and if this has had any
effect on the vectors ability to transmit *W. bancrofti*.

1.4 Objectives

General Objective

To determine the effect of missed annual MDAs in the success of an LF elimination program in Malindi District.

Specific Objectives

The specific objectives:

i. To monitor the impact of MDA on the prevalence and intensity of LF in a highly endemic area.

ii. To determine the impact of missed annual MDAs on microfilaremia and antigenemia prevalence according to the gender and age of the study participants.

1.5 Research Questions

i. What are the effects of missing of annual MDA's on the overall success of an LF elimination program?

ii. What effect would missing MDA’s have on the prevalence and intensity of the antigenemia and parasitemia of the population at risk?

1.6 Hypothesis

1. $H_0$: Missing annual rounds of MDA has a negative effect on the overall success of an elimination program.

2. $H_0$: Missing annual rounds of MDA has no effect on the prevalence and intensity of the antigenemia and parasitemia of the population at risk.
CHAPTER TWO
LITERATURE REVIEW

2.1 Burden of Lymphatic Filariasis

Lymphatic filariasis is one of the Neglected Tropical Diseases (NTDs) of public health concern (WHO, 2018). As at 2017, over 54 countries were endemic to LF with over 1.2 billion people at risk of infection (GAELF, 2018; WHO, 2018). More than 120 million people were estimated to be infected and over 40 million of these infections manifested overt clinical manifestations of hydrocele, elephantiasis of the limbs and adenolymphangitis (ADL) (Michael et al., 1996). Currently, about 947 million people worldwide remain at-risk (WHO, 2017). In Africa alone, an estimated 406 million people are at-risk in over 39 LF endemic countries (WHO, 2015).

2.2 Neglected Tropical Diseases

Neglected tropical diseases are mainly diseases that are associated with poverty. These are the “forgotten” diseases of the poor. More than half of the world’s populations are at risk of being infected by an NTD with most of these individuals coming from among the world’s poorest populations (Hotez, 2011; Hotez, 2014). The overall global burden of NTDs put together is comparable to malaria and tuberculosis (Hotez and Kamath, 2009). The high morbidity rates associated with the diseases affect cognitive and physical development and in the long run overall productivity of an individual and society as a whole (Hotez and Kamath, 2009).

Unfortunately, the neglected tropical diseases are not priority diseases and so most often are ignored by policy-makers and politicians who selectively focus on other disease such as HIV, tuberculosis (TB) and malaria (Molyneux, 2008). Neglected tropical diseases cause immense suffering and often life-long disability but because the mortality rates associated with these diseases are low, they do not receive attention and funding like other tropical infections (Molyneux, 2004). In reality these diseases can be controlled or
eliminated by de-worming or mass treatment of at-risk populations (WHO, 2017).

Over the past two decades there have been significant achievements in the control of some NTDs through intervention by significantly reducing the prevalence and intensity of these diseases (Hoerauf et al., 2011). This has lead to a more integrated disease control approach with a lot of interest and intervention based on public/private partnerships and donations. In addition to the public and private partnerships involved in combating NTDs, the governments of endemic countries should in their own capacity develop strategies and funds dedicated to prioritize the control of NTDs in order to reduce poverty in their own countries.

2.2.1 Success of NTD Elimination

The reality of NTD control or elimination today is made more feasible with research and medical breakthrough leading to the success of different diseases in different countries (WHO, 2018). Many control programs have had success but it is also important to note that not all control programs have succeeded in elimination/eradication (Hoerauf et al., 2011).

One of the major NTD success stories is that of the efforts of 19 African countries comprising of the African Program for Onchocerciasis Control (APOC) set up to eliminate River blindness (Dunn et al., 2015). The program targeted about 62 million people in the endemic countries to control river blindness and treat skin disease using Ivermectin (donated by Merck and Co. Inc) (GAELF, 2018) through community-directed distributors (Molyneux, 2008). In the Americas, a similar program is close to achieving the interruption of transmission in several foci in six countries using twice-yearly treatments (Molyneux, 2008).

Another successful program aimed at eradicating the Guinea worm (Rwakimari, 2006; Callahan et al., 2013; CDC, 2017). With nearly 180 countries already declared free from the dracunculiasis and several countries previously endemic to dracunculiasis have been certified free of transmission (Molyneaux, 2017) with the number of cases has been
dramatically reduced from over 1 million in 1988 to some 25,000 in 2006 in the remaining nine endemic countries (Molyneux, 2008).

Further, the prevalence of schistosomiasis in some countries has been reduced from over 20% to less than 1 – 2% using praziquantel over the last two decades (Molyneux, 2009). There are now ongoing schistosomiasis and soil-transmitted helminth programs in other countries where 20 million people have been treated with praziquantel and albendazole (Molyneux, 2008).

Recent control programs to eliminate LF have been successful in countries like China, North America, Japan and Australia (Gordon et al., 2018). Filariasis has been successfully curtailed in several countries and has given optimism in the campaigns for global eradication (WHO, 2001). The transmission of LF has been interrupted and is no longer of public health concern in Thailand, Sri Lanka, Suriname, Solomon Islands, Trinidad and Tobago, Egypt and Costa Rica (GAELF, 2018; WHO, 2018). National programs to eliminate LF in 46 out of 83 endemic countries worldwide were ongoing by 2009 (WHO, 2018). The elimination strategy is based on annual mass drug distribution of albendazole and DEC/DEC fortified salt or Ivermectin/Mectizan. A WHO report stated that by 2005, 381 million treatments had been delivered (WHO, 2005). Success has been realized in many NPELF programs, but, it is important to note that the elimination of filariasis has not been achieved in some areas despite long – term control programs because of (Esterre et al., 2001; Lau et al., 2017).

2.3 Etiologic Agents and Vectors of Lymphatic Filariasis

Filarial infection is transmitted to humans by mosquito vectors (Famakinde, 2018; WHO, 2014). The vector species responsible for LF transmission are numerous and vary from region to region depending on the filarial worm that they transmit (Choi et al., 2011).
2.3.1 Filaroidea

Filaroids are tissue–dwelling parasitic worms (Kassis et al., 2014; Paily et al., 2009). According to Roberts and Janvoy (1996), they are “among the most highly evolved of the parasitic nematodes.” The super family Filaroidea belongs to the **Phylum:** Nematoda, **Class:** Rhabditea and **Order:** Spirurida (Goldsmid and Melrose, 2005). Most of the members of this family require an intermediate vertebrate host that deposits larvae on the definitive host. Most Filaroids are parasites of wild birds and mammals. Medically important parasites in humans belong to the family Onchocercidae with the ones of medical importance to humans belonging to the **Family:** Onchocercidae (Tanya et al., 2012).

In humans, LF is caused by three species of filarial worms namely; *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori* (Supali et al., 2006). Infection with *W. bancrofti* is referred to as bancroftian filariasis, while brugian filariasis refers to infection by either *B. malayi* or *B. timori*. Filariae are transmitted into the human host, by the female mosquitoes, which are the blood feeders, belonging to the genera *Culex, Anopheles, Aedes* and *Mansonina* (Roberts and Janvoy, 1996) in the course of a blood meal.

2.3.2 Principle Vectors of Lymphatic Filariasis

In Africa, LF vectors are members of the following species complex or group; *Anopheles gambiae* complex, *Anopheles funestus* group, and *Culex pipens* complex (Pedersen, 2008). In urban and semi-urban environments, *Culex pipens* complex, which are exophilic day feeders that breed in dirty polluted water, are the principle vectors where as in rural settings, the endophilic night feeders are the main vectors (Kaliwal, 2009). In areas where *Anopheles spp.* are LF vectors, they are also responsible for the transmission of the malaria parasite, *Plasmodium spp.* (Samdi, 2012).
2.4 Distribution of Lymphatic Filariasis

*W. bancrofti* is distributed throughout the tropical regions of Asia, Africa, the Americas and the Pacific and is prevalent in areas with hot and humid climates (Figure 1). *B. malayi*, on the other hand, is found in South-East Asia and in areas of South-West India and South and Central China, whereas *B. timori* occurs only on some small islands in Indonesia (Simonsen, 2003).

![Geographic MDA coverage against Lymphatic Filariasis in WHO African region (2016)](image)

**Figure 2.1: Overview of MF MDA programs in Africa**
2.5 Lymphatic Filariasis in Kenya

Lymphatic filariasis in Kenya has been reported since 1910 (Wamae et al., 2001) the disease remains endemic in the six foci of Kwale, Mombasa, Malindi, Kilifi, Tana River and Lamu in coastal Kenya where about 2.5 million people (CBS, 2001) are at risk of infection. Several studies conducted in the LF foci in recent years report microfilaremia prevalence of between 15- 25 % and antigenemia as 35% and above (Estambale et al., 1994; Wamae et al., 1998; Njenga and Wamae, 2001; Mukoko et al., 2004).

2.6 Life Cycle and Transmission of Lymphatic Filariasis

The disease epidemiology of lymphatic filariasis caused by W. bancrofti, varies in different regions depending on the local vectors and the periodicity (Molyneux et al., 2003) of the parasite. The adult filarial males are up to 40 mm in body length while the females range between 60-100 mm long (Roberts and Janvoy, 1996). The adult worms live in the lymphatic ducts and vessels of the human definitive host (Silva et al., 2002). The females release pre-larval forms known as microfilariae (mf), which retain the egg membrane as a sheath and unsheath ("hatch") after being ingested by the arthropod intermediate host.

The mf when released into the definitive host, migrate into the peripheral blood circulation where they exhibit periodicity (Silva et al., 2002). Periodicity favors the vectors feeding time and is thought to be due to the biological rhythm inherent in the mf but influenced by the circadian rhythm of the host (Cheesebrough, 2005). Depending on the parasite species, there are two main peak periods (nocturnal or diurnal periodicity) when the number of mf is highest in peripheral circulation (Silva et al., 2002). Periodicity favors the chances of the parasite to be picked up from the circulation by the intermediate host. At other times the mf are in deep tissue and pulmonary vessels (McSorley and Maizels, 2012). Sub-periodicity is expressed by other species where the number of mf in circulation remains relatively stable nocturnally or diurnally (McSorley and Maizels, 2012).
From the peripheral circulation, the microfilariae are picked up by the intermediate mosquito host where the mf enter into the mosquito gut and lose their sheath to become L₁ larvae. These then penetrate out of the digestive tract into the thoracic muscles of the mosquito where they molt twice through the L₂ stage and transform into the L₃ filariform larvae (also known as infective larvae) that migrate to the mosquito hemocoel and in to the mouthparts of the mosquito where they enter the human host through the puncture site that the mosquito is feeding from and move into the lymphatics where they mature (Figure 2.2).

Figure 2.2: Transmission and life cycle of W. bancrofti and Brugia sp.

Source: Adapted from http://www.dpd.cdc.gov/dpdx
Larval development into adult worms takes 3 to 15 months. Microfilariae can be found in peripheral blood 9 months after infection for *W. bancrofti* and after about three months for brugian filariasis (Cheesebrough, 2005). The average life span of the adult worms is generally between 4 - 6 years (Roberts and Janvoy, 1996). If not picked up by the mosquito vector from circulation, the mf will eventually die off. Development of the larvae in the mosquito vector into the infective L₃ larvae takes about 1 to 2 weeks.

### 2.7 Lymphatic Filariasis Pathology and Immunology

It is thought that the clinical features and pathology of the infection depend largely on the sites occupied by the mature worms, the number of worms present, and the duration of the infection and the immune response of the host. Symptoms of infection differ from one endemic area to another. Infection can be asymptomatic, acute or chronic. Several stages of the parasite persist chronically within the host and continuously release antigens. The type and magnitude of the chronic immune stimulation by these antigens contribute substantially to the spectrum of disease observed in LF (King *et al.*, 2004). However, the respective roles of innate and adaptive host immune responses still remains poorly understood.
2.7.1 Pathology

Most of the pathology in LF is associated with the adult worms and their habitation of the lymphatics. A spectrum of manifestations (Figure 2.3) has been observed in endemic areas (Ottesen, 1980).

Figure 2.3: Clinical manifestations of lymphatic filariasis in endemic areas

Source: Adapted from Ottesen, 1980.

Figure 2.3 shows a broad spectrum of symptoms that may be exhibited from having no visible symptoms to Pulmonary Eosinophilia. At one end of the spectrum (box 1 -2) are individuals with no obvious signs of infection or disease and asymptomatic microfilaremia-carriers. On the other end of the spectrum (box 3, 4 and 5) are individuals who develop signs of lymphatic responsiveness to the adult worms with fevers and later development of chronic lymphatic pathology (Simonsen, 2003).

Macrophages are associated with granulomatous lesions, composed primarily of eosinophils and macrophages, which form around the adult worms and microfilariae (Taylor et al., 2010). It is possible that partial immunity to mf may accelerate the clearance of mf, but that this accelerated clearance, although beneficial in reducing transmission, is achieved at the cost of an increased host immune response to dying mf (King et al., 2004). Immunologic responses that develop during chronic helminthic
infections can contribute to tissue injury and pathologic changes that are the primary cause of disease complications such as fibrosis, lymphoedema and hydrocele in LF (Rajasekaran et al., 2017; Narahari et al., 2016; Garcia and Fox, 2014).

2.7.2 Immunology of Lymphatic Filariasis

Most individuals in endemic areas mount an immunological response to filarial antigens because of the continued exposure to the filarial parasites (Hubner et al., 2014). Others have no detectable microfilaremia and antigenemia (which is the presence of circulating filarial antigens in the blood) or clinical manifestations (Nutting, 2015). Microfilaremia is the numeration of microfilaria in a host, while antigenemia is the measure of the level of microfilarial antigens present in the blood of the host. Individuals who have no clinical manifestations are referred to as endemic normals. Other individuals show clinical signs and are mf and antigen positive (Ottesen, 1984).

Adult worms residing in the lymphatics of the human host are able to employ anti-inflammatory strategies to enhance survival and evade the destructive host immune system (Finlay et al., 2014). Microfilariae in the blood are exposed to distinct components of the immune system. The distinguishing mark of infection with *W. bancrofti* is the cellular immune hypo-responsiveness (Maizels and McSorley, 2016; Wilson et al., 2010). The hypo–responsiveness that develops to mf is antigen specific, suggesting that there are either diminished frequencies of filarial antigen-specific T-cells or an increase in immunoregulatory T-cells (King et al., 1992; Nutman and Kumaraswami, 2001). The access that the parasites, and the products they excrete and secrete, have to the immune cells allows them to interfere directly with immune response such as T-Cell activation, antigen presentation and cytokine production leading to immunoregulation (King et al., 2004).

Hyper-responsiveness of the host’s immune response to mf accounts for the burden of parasite material in the host such that the exaggerated host response is thought to be the basis of the tropical pulmonary eosinophilia (TPE) syndrome, an allergy-like clinical
manifestation of LF where mf are rapidly cleared in the lung (Lobos et al., 1996; Choi et al., 2003).

The identification of Wolbachia spp. as an essential endosymbiont of filarial parasites present in all developmental stages has sparked greater interest in studying the role of Wolbachia spp. in innate immune responses as well as disease development (Saint et al., 2002; Taylor, 2002). Wolbachia spp. produce molecules capable of directly stimulating cells of the innate immune system and these may play a major role in the development of acute filarial lymphangitis (King et al., 2004).

Adaptive immune responses result in successful immunoregulation which limits the damage to the host (McSorley and Maizels, 2012). The mechanisms that initiate and sustain this immune regulation are still not well understood. According to cell-mediated immune responses, filarial infection is associated with enhanced type-two helper T-cells (Th-2) cytokine production and impaired type-one helper T-Cells (Th-1) response where the existence of a Th2-type response is important for the successful persistence of the parasites within the host (Maizels et al., 1995). Macrophages are effective at killing the larval stages of filarial parasites by sustained release of reactive oxygen species (peroxides and nitric oxides). Adult parasites are more resistant to these because they are able to produce antioxidant enzymes that protect them (Allen and Loke, 2001).

Cytokines lead to the production of IgE antibodies and the development and activation of eosinophils and mast cells (Hewitson et al., 2009). IgE antibodies bind to the surface of the parasite and eosinophils attach on to the IgE receptors and participate in antibody-dependent cell-mediated cytotoxicity by releasing enzymes from their granules to damage the worms’ tegument.

Humoral immune responses are dominated by the IgG4 antifilarial isotypes that are prominent in individuals with infection as opposed to IgG1 and IgG2 which increases to the same extent in individuals who acquire infection and among those who remain antigen negative (Jaoko et al., 2007).
2.8 Clinical Presentation of Lymphatic Filariasis

Common clinical manifestations of bancroftian filariasis include acute adenolymphangitis (ADL), scrotal hydrocele, lymphoedema and elephantiasis, chyluria and tropical pulmonary eosinophilia (TPE) (Gordon et al., 2018). Clinical diagnosis is achieved by detecting one of the mentioned symptoms (Simonsen, 2003).

2.8.1 Manifestations of Acute Lymphatic Filariasis

Acute manifestations are often referred to as adenolymphangitis (ADL) (Gordon et al., 2018). These are characterized by episodic attacks of malaise, fever and chills, enlarged, painful lymph nodes that drain into affected limbs (Simonsen, 2003). This is followed by an acute warm and tender swelling and regression of the swelling after an ADL attack is commonly followed by excessive skin exfoliation (Dunyo et al., 1998). Acute attacks commonly occur in individuals with chronic LF manifestations (Gasarasi et al., 2000).

Acute filarial lymphangitis (AFL), is caused by the death of the adult worms either spontaneously or after treatment, and acute dermatolymphangioadenitis (ADLA) may result from secondary bacterial and fungal infection in the legs of those with compromised lymphatics (Dreyer et al., 1999) are the two distinct syndromes of acute filarial attacks. Bacterial infections aggravate pre-existing pathology in animal models and lymphatic dysfunction in humans predisposes them to secondary infections that clinically accelerate lymphatic damage (Dreyer et al., 2000; Esterre et al., 2000).

2.8.2 Hydrocele Formation

The glands in the groin and lymphatics of the male genitalia are frequently affected by bancroftian filariasis. Inflammation and repeated attacks can lead to the blockage of the spermatic lymphatic vessels leading to the accumulation of fluid in the scrotal sac that becomes distended leading to formation of hydrocele. Dreyer et al. (2002) recently emphasized the distinction between lymphoedema of the scrotal and penile skin, which has the same pathogenesis as lymphoedema of the limbs, and swelling due to increased
fluid inside the *tunica vaginalis*.

Clinical research and observation in filariasis-endemic areas has revealed that the fluid inside the scrotal sac, which was considered as hydrocele, actually is comprised of several distinct entities: true hydrocele, lymphocele, chylocele, and hematochylocele (Addiss and Brady, 2005). In many filariasis-endemic areas, hydrocelectomy is able to reverse the effects although the surgery can be quite costly.

### 2.8.3 Lymphoedema and Elephantiasis

Elephantiasis is a complication resulting from chronic LF. It is seen as a coarse thickening, hardening and cracking of the skin over enlarged fibrosed tissues (WHO, 2013). In *W. bancrofti* endemic areas, the legs are more commonly affected than the arms (Chandy *et al.*, 2012; Lu *et al.*, 2009). Grossly enlarged limbs make walking and movement difficult. Secondary bacterial and fungal infections of the skin on the affected limbs are quite common (Palumbo, 2008). In this stage of infection mf may not be easily found in the blood of patients (Palumbo, 2008).

### 2.8.4 Chyluria

An uncommon complication of chronic bancroftian filariasis is chyluria which occurs when the uro-genital vessels, which are linked to those that transport chyle from the intestines, become blocked and rupture (Mortimer and Gordon, 2016; El-Sherbiny, 2008; El-Diasty and El-Sherbiny, 2007; Ansari, 2005). Little is known about the epidemiology, risk factors, or complications of chyluria (Addiss and Mackenzie, 2004).

### 2.8.5 Tropical Pulmonary Eosinophilia

Tropical pulmonary eosinophilia (TPE) is a form of occult filariasis in which there is a hypersensitive reaction to the destruction of microfilariae in pulmonary capillaries (Vijayan, 2007; Lobos *et al.*, 1996; Choi *et al.*, 2003). This condition is common in the filariasis endemic regions of India, and South-East Asia and males are more commonly affected than females (Checkley *et al.*, 2010). It interferes with breathing in infected
humans and can lead to chronic pulmonary fibrosis (Gordon et al., 2018). Other common systems include; increased eosinophilia, raised erythrocyte sedimentation rate and high levels of filarial antibodies including high titers of IgE (Cheesebrough, 2005).

2.9 Diagnosis Lymphatic Filariasis

There has been a shift from the trend of LF diagnosis at the individual level to the need to define populations eligible for mass treatment and to monitor the impact of mass drug distribution programs (Molyneux, 2009). Traditional diagnosis of LF was dependent on parasitological detection of mf through thick blood smears (TBSs), filtration and counting chambers techniques (mainly employed in Eastern and Southern Africa), and Knott’s method for observing the microfilariae (Cheesebrough, 2005). Other methods include; CFA and antibody testing assays are highly specific for LF with minimal to no cross-reactivity for gastrointestinal worms, PCR for parasite DNA, ultrasonography for adult worm detection and clinical manifestations (Simonsen and Dunyo, 1990; Simonsen, 2003). Acute and chronic manifestations in persons living in or visiting areas endemic to W. bancrofti, B. malayi, and B. timori are indication of LF infection (Simonsen, 2003).

2.9.1 Parasitological Diagnosis of Lymphatic Filariasis

Parasitological diagnosis is usually based on the detection of microfilaria worms in from the patient’s peripheral blood, urine or hydrocele sample (Eberhard and Lammie, 1991). Specimens should be obtained at the time of mf peak concentrations (Eberhard and Lammie, 1991). In some cases, adult worms are detected while in the lymphatic vessels of the scrotal area of infected males and in the female breast through ultrasonography (Simonsen et al., 1997).

Many techniques for demonstrating mf have been described and they include; the filtration method, Knott’s concentration technique and the fast, quantitative and cheap counting chamber technique (McMahon et al., 1979). Staining with Giemsa or haematoxylin dyes enables microfilaria differentiation in areas endemic to more than
one species of filariae (Walther and Muller, 2003; Moody and Chiodini, 2000). The diethylcarbamazine provocative day test mimics normally nocturnal mf available for testing during the day. The test is a sensitive method for detecting mf of nocturnally periodic W. bancrofti as in the examination of night blood (McMahon et al., 1979). This test has an important practical use in studying mf prevalence and densities in the target communities where it is difficult to obtain cooperation from the population for night blood surveys (Simonsen, 2003). This method will allow data to be collected during the day instead of having to collect a nocturnal sample.

Venous blood drawn at night and filtered through membrane filters, enables easy detection and quantification of microfilariae (Anitha and Shenoy, 2001). Microfilaria are usually seen in the early stages of the disease before clinical manifestations develop (Shenoy, 2008). Once lymphoedema develops microfilaria are generally absent in the peripheral blood (Kumaraswami, 2000). The Quantitative Blood Count (QBC) method can also be used to identify the microfilaria and to study their morphology in the blood drawn at night (Cheesebrough, 2005). Though QBC can be performed quickly, it is no more

2.9.2 Immunological Diagnosis of Lymphatic Filariasis

In the human host, filarial worms induce a wide range of immune responses (Maizels and Yazdanbakhsh, 2003). Several immunodiagnostic techniques that are antibody-specific to the host have been devised (Cooper et al., 2008). These techniques have, had limited success because; (i) most individuals are positive to crude filarial antigens as a result of constant exposure and (ii) these tests have suffered from cross-reactions to other nematode infections (Maizels et al., 1995) and this is coupled to their inability to distinguish old and new infections (Dickson et al., 2018).

The development of new, specific and sensitive immunodiagnostic tools has been a priority in LF research. Cross-reactions have been minimized through the discovery of specific IgG4 antibodies that are also viable markers for active infection (Simonsen,
2003). Such tests may be of particular value in brugian filariasis (Haarbrink et al., 1995; Rahmah et al., 2001) where progress of antigen detection-based diagnosis has been limited.

2.9.3 Circulating Filarial Antigens

Adult *W. bancrofti* release antigens that can be detected in human blood, plasma or serum by immunoassays (Morzaria et al., 1998). Highly sensitive and specific, circulating filarial antigens (CFAs) for bancroftian filariasis rely on the capture of filarial antigens in serum, plasma or blood specimens using specific monoclonal antibodies (Simonsen, 2003). An enzyme-linked immunosorbent assay (ELISA) (which detects Og4C3 antigen and is produced by TropBio, Australia) is highly sensitive and specific (More and Copeman, 1999). Another rapid-format ICT filariasis test, which detects AD12 antigen produced by Binax, USA) (Weil et al., 1997; Simonsen and Dunyo, 1999) which can directly test blood, serum or plasma in the field and provides a result in a few minutes.

The card test has the advantage that it can be performed on blood sample drawn by finger prick at any time of the day (Weil et al., 1997). This card test is limited by its inability to detect dead adult worms but only when they are alive in the circulation (Weil et al., 1997). At present no such test is available for *B. malayi* filariasis, where the detection of IgG4 antibodies is helpful.

The advantage of CFA-based testing is that they detect adult worm infections and not just microfilaremia. Additionally, their specificity appears quite high and only a few, if any, individuals with undetectable or ultra-low microfilaremia are undetected (Rocha et al., 1996). Another advantage is that because this test is not dependent on microfilarial periodicity, blood specimens can be collected and examined at any time of the day (Weil et al., 1997). Antigen testing can be challenging because the results often remain positive after treatment probably because most drug regimens are not completely effective in clearing adult worms, but it is also possible that even when all adult worms
are dead, antigen clearance from the circulating blood could take some time (Lammie et al., 2004).

2.9.4 Antibody Detection in LF

Antifilarial antibody responses can serve as sensitive markers of filarial exposure and transmission, providing evidence of infection prior to the development of antigenemia or microfilaremia, since antibody responses in an infected individual may develop within weeks to months following exposure to infective larvae (Lammie et al., 2004). Findings in a study by Njenga (2005) suggest that the use of antifilarial IgG1 should be used as a marker indicative pathogen of exposure rather than as a marker of active infection. Thus, assays for antifilarial antibodies can be used in for LF program monitoring aimed at of filariasis elimination.

The use of assays to detect circulating Og4C3 antigen and IgG4 antibody to a recombinant LF protein, designated Bm14, is becoming more popular for the purpose of identifying endemic populations to help in decision making for implementation and termination of MDA programs (Tisch et al., 2008). The Og4C3 antigen on which the ELISA and diagnostic card test are based is secreted by *W. bancrofti* spp but not *Brugia spp* adult worms (Tisch et al., 2008). Antibodies to Bm14 protein could be present in the persons with *W. bancrofti*, *B. malayi*, or *B. timori* infection (Lammie et al., 2004). The antigen and antibody assays have several advantages over microscopic identification of mf in blood because they are more sensitive and both have overcome the inconvenience of obtaining blood samples at night, for detection of mf that exhibit nocturnal periodicity (Weil et al., 1997).

Recent advances have led to improvement in the testing and standardization of immunoglobulin antibody assay for LF (Weil and Ramzy, 2007). Two recombinant antigen - based antibody tests using the (Bm14 and BmR1) antigens have been shown to be sensitive and specific for LF infection and exposure (Lammie et al., 2004). These assays can be useful tools for monitoring sentinel populations and detecting transmission
of filarial parasites (WHO, 2005). BmR1 antibody test that detects antifilarial IgG4 antibodies is more specific than IgG1 (Lammie et al., 2004).

Bm14 antibody may detect recent exposure to infective filarial larvae as well as the presence of adult worms, because animal studies indicate that the antibodies appear during the pre-patent period of infection (Lammie et al., 2004). Therefore Bm14 antibody testing could be more useful in interpreting the progress and long-term impact of MDA programs (Tisch et al., 2008).

2.9.5 Detection of Microfilaria by PCR Assays

Polymerase chain reaction (PCR) assays for the detection of microfilarial infections have been developed for screening blood samples and mosquito vectors both for *W. bancrofti* (Ramzy et al., 1997; Dissanayake et al., 2000) and for *B. malayi* (Fischer et al., 2000; McCarthy, 2000).

Gene-based molecular techniques appear to be effective tools for detection of microfilarial infection in vectors and for monitoring transmission (Ramzy et al., 1997). Polymerase chain reaction – based methods can be used with much better specificity and sensitivity than that of direct microscopic detection of mf (or for other larval stages in the mosquito vector) (Lammie et al., 2004). Though this method is quick and easy to perform, the disadvantage is that it requires sophisticated equipment and is available only in well-equipped research laboratories, hence they may not be applicable for use under normal field settings.

2.9.6 Ultrasonography for Adult Worm Detection

Studies have indicated that adult worms can be visualized in the lymphatic vessels and lymphatic nodes using ultrasound technology (Amaral et al., 1994). Ultrasonography is a non-invasive technique where the adult worms display characteristic movement known as the filarial dance sign (FDS) using a 7.5 or 10 MHz probe that helps to locate and visualize the movements of living adult filarial worms of *W. bancrofti* in the scrotal
lymphatics of asymptomatic males with microfilaremia (Amaral et al., 1994). Ultrasonographical monitoring has been a tool for in vivo assessment of the adulticidal efficacy of antifilarial drugs (Dreyer et al., 1995a; Dreyer et al., 1996; Hussein et al., 2004). Ultrasound has been used to study the effect of drug treatment on the adult worms and to retrieve them surgically from the dilated scrotal lymphatics (Anitha and Shenoy, 2001).

Ultrasonography is however not useful in patients with filarial lymphoedema because living adult worms are generally not present at this stage of the disease. Similarly ultrasonography has not helped in locating the adult worms of B. malayi in the scrotal lymphatics since they do not involve the genitalia (Shenoy et al., 2000). One study however excluded women from ultrasonography detection because ultrasonography was shown to be unreliable for detection of worms in women (Stolk et al., 2005).

2.10 Lymphoscintigraphy

This involves the assessment of the structure and function of the lymphatics of the involved limb (Freedman et al., 1994). After injecting radiolabelled albumin or dextran in the web space of the toes, the structural changes are imaged using a gamma camera (Anitha and Shenoy, 2001). Lymphatic dilatation, dermal back flow and obstruction can be directly demonstrated in the edematous limbs by lymphoscintigraphy (Anitha and Shenoy, 2001). Lymphoscintigraphy has proved that even in the early, clinically asymptomatic stage of the LF disease shows lymphatic abnormalities in the affected limbs of persons harboring microfilaria (Freedman et al., 1994).

2.11 Treatment of Lymphatic Filariasis

The currently used drugs and drug combinations for elimination of LF have benefits and limitations (Molyneux et al., 2003). Extended drug use promotes development of drug resistance. It is essential to design new drugs and evaluate how to use current drugs to their best effect. Introduction of single-dose treatment regimens of either diethylcarbamazine (DEC) or ivermectin with albendazole has been an important
breakthrough for the control of filariasis (Wamae et al., 2006). Findings from previous proposed that there is insufficient evidence to confirm or refute studies suggest that albendazole co-administered with DEC or ivermectin is more effective than DEC or ivermectin alone in clearing microfilariae or killing adult worms (Addiss et al., 2009).

2.11.1 Diethylcarbamazine Citrate (DEC)

The drug most commonly used drug or more than half a century, has been diethylcarbamazine citrate (DEC; Hetrazan, Banocide, Notezine). As a microfilaricide, it is also capable of killing W. bancrofti, B. malayi and B. timori adult worms (Ottesen et al., 1997). It has been shown in East Africa and that a single dose treatment of DEC given at half-yearly or yearly intervals can dramatically reduce the microfilarial load in the human blood (Simonsen et al., 2004). DEC exerts no direct lethal action on the microfilariae although its mechanism of action leading to its lethal effect on either mf or adult worms is poorly understood. Previous findings suggest that this drug may require cooperation with a functional host immune system to be optimally effective in killing microfilaria (Chandasekaran et al., 1980; King et al., 1983).

Therapy with DEC may prevent the development of lymphatic damage in the human host by reducing the adult worms though there is little or no effect on already induced lymphatic damage or on chronic obstructive disease (Freedman et al., 1995). The drug is administered orally with a recommended therapeutic single dose of 6mg/kg body weight annually for a period of 4–6 years (Molyneux et al., 2003; Ismail et al., 1998). The number of mf in the blood decreases rapidly after the initiation of treatment and then increases, at a reduced intensity after some months (Simonsen, 2003).

DEC treatment rapidly reduces the prevalence and intensities of mf. An alternative treatment strategy involving the use of DEC as a fortificant in table salt for a period of 1–2 years is currently used in just one country, but was a mainstay of the earlier, successful LF elimination program in China (Kumaraswami et al., 2004).
2.112 Ivermectin (Mectizan)

A single dose of ivermectin at 150μg/kg body weight effectively removes mf of *W. bancrofti* (Cao et al., 1997), but mf reappears in the blood faster than after treatment with a dose of DEC and there is no evidence of its macrofilaricidal action (Dreyer et al., 1996). Ivermectin is the drug of choice in onchocerciasis endemic areas (Gonzalez et al., 2012). Since 1998, ivermectin has been available free of charge for use in the control of lymphatic filariasis in African countries where Onchocerciasis is endemic, through the Mectizan Donation Program (MDP) (Simonsen, 2003). Ivermectin binds selectively and with high affinity to glutamate-gated chloride ion channels in invertebrate nerve and muscle cells (Yates et al., 2003). The glutamate gated chloride ion channels increases permeability of the cell membrane to chloride ions, resulting in hyperpolarization of nerve or muscle cells, causing parasite paralysis and death (Kumaraswami et al., 2004).

2.11.3 Albendazole

Albendazole was initially shown to be effective against lymphatic filariasis by a study conducted in laboratory animals infected with *B. malayi* (Mak et al., 1984). The combination of albendazole with either ivermectin or DEC gives a more effective sustained reduction in LF microfilaremia than either drug alone (Ottesen et al., 1997; Ottesen et al., 1999). The use of a higher dose (800 mg and 400 μg/kg) albendazole – ivermectin therapy completely cleared microfilaria (Dembele et al., 2010). The primary target for albendazole is tubulin, and this drug is observed to have a higher affinity for the tubulin of the parasite than for that of the host (Lacey, 1990). By blocking tubulin polymerization and microtubule formation, the drug inhibits mitosis, and therefore embryonation and egg hatching (Ottesen et al., 1999). It is very likely that albendazole exerts an effect on adult filariae in the same manner (Kumaraswami et al., 2004). Another advantage of albendazole is its effect on intestinal helminth infections (Beach et al., 1999). Albendazole destroys the worms in several different ways. It interferes with the worms skeletal structure and inhibits microtubule assembly by binding to its
colchicine – sensitive sites of β-tubulin (Albendazole, 2015). Albendazole inhibits glucose uptake by both the adult and larval stages of the helminths, blocks egg production and prevents egg hatching (Gerogiev, 1997). In higher concentrations Albendazole disrupts the cells metabolic pathways, leading to decreased energy production within the cell which causes paralysis and eventual death (Junquera, 2017).

2.11.4 Moxidectin

Studies to evaluate moxidectin as an alternative to ivermectin for the treatment of onchocerciasis have shown moxidectin to be more effective than ivermectin in most animal models (Tagboto et al., 1996). This drug has potent effects on mf and results in long-term sterilization of female adult worms (Kumaraswami et al., 2004), and resulted in t death of 49% of adult worms in vitro (Verma et al., 2014).

2.11.5 Doxycycline

Many species of filariae contain obligate endosymbiotic bacteria of the genera Wolbachia spp. (Taylor et al., 2005). These rickettsia-like organisms are essential for the survival and development of the filarial parasite (Simonsen and Meyrowitsch, 2008). Studies using antibiotics to eliminate the bacterial endosymbiont Wolbachia spp. have led to a new approach for treating filarial nematodes. Wolbachia spp. are obligate parasites that filarial worms need for their development, fertility and survival (Slatko et al., 2014). In arthropod hosts like the mosquitoes, Wolbachia spp. influence transmission of parasites and viruses.

More focus has been put on the study of potential of antibiotics as adult worm sterilants (Taylor and Hoerauf, 2001). Alternative approaches to classical chemotherapy have emerged as the Wolbachia spp. endosymbionts of filariae have been recognized as potential drug targets (Iturbe-Ormaetxe and O’Neill, 2010; Kumari and Blaxter, 2011; Nikoh et al., 2014). Wolbachia spp. have also been identified as potential contributors to disease pathology (Taylor et al., 2002) and promotes adverse reactions to treatment (Keizer et al., 2002; Cross et al., 2007). Many of these studies opened a new direction
for drug discovery that will target the *Wolbachia* sp. Doxycycline may also be capable of preventing or reversing lymphatic pathology (Kazura, 2010).

As used in onchocerciasis treatment, it has been established that treatment with doxycycline at 100 mg per day for six weeks leads to the long-term sterility of adult female worms (Townson *et al.*, 2000). Further research is being done to determine the effect of antibiotics on filarial infection. The effect of an intensive course of doxycycline at 200mg daily for 8 weeks in LF infected individuals resulted in microfilaremia decrease along with the number of adult worms detected by ultrasonography (Taylor *et al.*, 2002). Doxycycline is inexpensive but cannot be used in young children or pregnant women. More research is needed on the approaches of targeting the endosymbiont is needed (Stolk *et al.*, 2005).

### 2.11.6 Flubendazole

Flubendazole is a potential drug that can be used in filariasis treatment and is already widely used to treat worm infestations in animals (Mackenzie and Geary, 2011). In the 1980s, an oil-based formulation of the drug was given orally to human patients with filarial infection and it was ineffective and resulted in severe abscesses (Narahari *et al.*, 2016). Research is being done to develop a new way to safely administer the drug (Mackenzie and Geary, 2011). Formulating a new drug that can easily be administered can aid the WHO goal of eradicating LF.

### 2.12 The Global Program and the Global Alliance to Eliminate Lymphatic Filariasis

The Global Alliance to Eliminate Lymphatic Filariasis (GAELF), was created in 2000 together with several partners including WHO and GlaxoSmithKline each with a different mandate but all having the common goal of tackling the wide-ranging and complex process of science and practice that will result in the elimination of lymphatic filariasis as a global public health problem (WHO, 2001).
This alliance was mandated to coordinate the activities of partners and concentrate on political, financial and technical support geared towards elimination. The GAELF identifies partnerships with national and international organizations, local non-governmental development organizations (NGDOs), institutions and academia and pharmaceutical companies, mainly GlaxoSmithKline (GSK) and Merck and Co., Inc. through the MDP, who have agreed to donate free of charge all the albendazole and ivermectin (Mectizan) needed by endemic countries.

The WHO GPELF provides technical assistance to countries that are implementing mapping activities and MDA campaigns. It also coordinates the efforts to promote appropriate prevention and control of clinical symptoms of LF. Since the GAELF and the GPELF were initiated, their greatest achievement has been the enthusiasm of endemic countries to accept the challenge and strategies on elimination. Globally the GPELF has scaled up the target population more quickly than many other public health program established. Since 2000, 6.2 billion people have received preventive chemotherapy, and due to this, over 300 million people no longer require chemotherapy (WHO, 2017). Although all this enthusiasm is a positive step forward, it has posed several challenges both for the alliance and the endemic countries involved.

One of these challenges facing has been the prolonged period that it has taken for the individual countries to map out endemic areas that will be MDA targets. While some countries have begun elimination with multiple rounds already administered, others are yet to activate their national programs. For most countries that have already begun MDAs, up-scaling to cover the entire at-risk population has been a major challenge due to insufficient funding because those who are not treated will remain a source of infection for others (Hoerauf et al., 2011, De-jain et al., 2013). Even though one hundred percent coverage may not be possible, the more people treated the better.

The GPELF recognizes that to achieve the goals of interrupting transmission of infection and alleviating and preventing suffering and disability caused by LF, health systems in
endemic countries must play a critical role. It is also clear that there must be a convergence between the GPELF and global efforts to assess health systems performance (King et al., 2004). It is important for endemic countries to own their elimination programs. They need to partner with organizations, institutions and academia at the local, regional and global levels if possible as well as the integration of the program to other already existing public health programs (GAELF, 2007).

For a disease to be eligible for elimination, it has to first have an effective tool of diagnosis that will be able to clearly detect cases before and after intervention. LF diagnostic tools that are in existence today are thought to be adequate, but validation, refinement and additional experience with the available assay are needed (Zhong et al., 1996). Diagnostic tools are important at each step of the GPELF at the beginning, through the program and also for monitoring MDA to check for recurrence of the infection. During the key stages of the elimination program, different tools may be needed (Weil, 2005). The most common tools involve parasitological examination of mf and examination of clinical manifestations of elephantiasis of the limbs or organs.

The second thing that will determine whether an infection is eradicable is an effective intervention tool that will be able to break the cycle of transmission (Zhong et al., 1996). Drug administration for LF is able to drastically reduce the numbers of mf in the circulating blood of the infected individuals to be able to stop transmission from one person to the next. Once one dose is administered it is able to reduce the mf levels in circulation for a period of 8 months and after that, the adult worms will begin to release mf again (Kwarteng et al., 2016). During this period monitoring and evaluation in the elimination of LF transmission is essential (Goodman et al., 2003; Plichart et al., 2006; Boakye et al., 2007).

2.13 Lymphatic Filariasis Contribution to Poverty

Lymphatic filariasis is the second major cause of the highest DALYs, second to malaria (Bockarie et al., 2008). The amount of manpower and productivity lost by patients
infected with filariasis is greater than previously perceived. Lymphatic filariasis is a disease of poverty that is prevalent in remote rural areas and semi-urban and urban areas (WHO, 2000). According to a study conducted in India, Kumari et al., (2007) reported that LF is the cause of an estimated annual burden of 5.77 million DALYs. That is quite costly to already struggling and developing nations.

The disease exerts a heavy social burden that is quite severe of the specific attitude toward the disease (WHO, 2000). Those affected are both physically and emotionally incapacitated and are unable to go about their daily duties. According to a WHO report, the fight against LF is a fight against poverty (WHO, 2000).

A study carried out in the Philippines in 2003 showed that the elimination of LF would reduce poverty and increase the quality of health (Tan, 2003). Other studies carried out by the WHO have indicated that the economic returns from LF treatment outweighs the investment made towards LF elimination (WHO, 2000). The sacrifices made, especially by the governments of poor endemic countries, may seem draining now, but the prospect of an LF-free future and a generation of more productive citizens is worth more than the money spent to take care of the problem now. One of the sustainable development goals (SDGs) is to improve the health of the world’s citizens, provide better health care and management to all and give everyone the right to be able to live a healthy and productive life. In LF elimination, improvement of the quality of life is an important primary outcome of the therapeutic benefit and can be used as an indicator to assess the impact of morbidity management and disability prevention in elimination programs (Kumari et al., 2007).

**Integration of Lymphatic Filariasis Elimination with Other Disease Control Programs**

Many parasitic and infectious diseases have overlapping spatial distribution, with similar vectors and environmental determinants and particularly common in the tropics and subtropics, home to the world’s least developed countries, where these overlapping,
pervasive infections play an essential role in perpetuating the vicious cycle of poverty (Malecela – Lazaro et al., 2004). In most of these countries, disease specific control programs have been set up, operating within the national health system, thereby utilizing the same resources and personnel (GAELF, 2017; WHO, 2017). There is an opportunity now to integrate these programs under the Global Fund programs at minimal extra cost through community-directed systems, which have proven sustainability (Molyneux, 2008).

There have been successes in integrated disease and vector control (Gunn et al., 2018). One study shows that parasite control (‘de-worming’ or treating) could reduce the morbidity and mortality of at-risk populations by avoiding permanent disability, improved nutritional status, reducing morbidity and children afford school attendance. LF, as an NTD, can be controlled or eliminated through biannual or drug interventions (Kastner et al., 2017). One study documented that the control of parasitic infections through yearly treatment improves health status and reduces the burden of disease and low economic productivity of affected individuals and communities (Gedge et al., 2018). Malaria treatment and bed net distribution could also be enhanced through established NTD distribution channels (Stone et al., 2014).

Programs to integrate disease surveillance and vector management aim at controlling vector-borne diseases by combining approaches that are sustainable, cost-effective and have an impact on the transmission of diseases, along with the WHO target on NTDs in neglected communities need to work together and come up with an integrated solutions to disease-control. A number of national programs are in the stages of integrating control of diseases such as LF, onchocerciasis, soil transmitted-helminths, schistosomiasis, trachoma, and others (Malecela – Lazaro et al., 2004).

In LF endemic communities, the objective of control and eventual elimination is to reduce transmission and morbidity (WHO, 2018). Successful programs have been based on a complete understanding of the disease distribution dynamics (Simonsen, 2003). The
reduction of transmission through mass chemotherapy may be supplemented by vector control strategies (Bockarie et al., 2008; Stone et al., 2014).

Additional measures may be needed to disrupt LF transmission to ensure the success of the GPELF (Burkot et al., 2006). MDA alone can achieve great success, but to be more effective and easier to handle, integration of MDA and vector control ensure increased sustainability of transmission suppression (Burkot et al., 2006). Mosquito control program in many tropical nations to control the vectors of disease can be an important collaborator of the elimination programs (Cho et al., 2012). Malaria control programs that have been around for a long time can be incorporated as part of the vector control. Vector control should be used to only supplement, and not replace, MDA. Similarly, there are programs for soil transmitted helminthes (STH) control targeting schools and institutions. These programs can also be included and used to increase drug distribution networks.

**Operational Research**

Problem-solving research is needed to increase the effectiveness of LF elimination globally (Lammie et al., 2017). Problems encountered by national NPELF programs need scientific-based and practical solutions. An active research community linked closely with country programs responds to current problems and anticipated barriers. Currently, operational research efforts focus on the outcomes of research in clinical management especially in handling SAEs by working closely with national pharmacovigilence authorities in order to better monitor and investigate incidences (WHO, 2005a).

Although GPELF efforts to date have focused principally on the initiation or up-scaling of programs, some countries/regions will be nearing the end of their projected 4–6 annual rounds of MDA (Shamsuzzaman et al., 2017). Assessment of the LF situation at that point might identify residual pockets of infection and lead to activities that might be termed mopping up, consolidation, termination of residual foci, or downscaling.
Operational research should be undertaken in programs that have achieved 6 – 7 yearly cycles of treatment. (Malecela – Lazaro et al., 2004).

The study on trends in transmission after MDA in the eight communities in Ghana indicates that some of the vectors (An. gambiae s. s.) are able to pick up the infection and transmit infective larvae at very low levels of microfilaremia in humans (Gyapong, 2005). Mathematical models suggest that transmission characteristics vary considerably from one endemic area to another with different vector species and endemicity levels prevailing, which may affect the intensity and duration of MDAs required (Michael, 2002). A deeper understanding of how chemotherapy affects infection and transmission patterns in various endemic settings is important for making qualified decisions on the most appropriate control strategy. In a study conducted in a highly endemic area, results suggest that elimination would most likely require additional years of annual treatment (Simonsen et al., 2004).

Behavioral research to ensure community compliance, both systematic compliance and systematic non-compliance, is also needed to ensure increased treatment coverage of the populations at risk. Scientists in endemic countries need to look into essential diagnostic tool, drug development and looking into alternative techniques for monitoring and evaluating programs that are specifically tailored to address national programs (Plichart and Lemoine, 2013). Coverage and compliance with MDA in many endemic areas are not at the desired levels (Simonsen et al., 2010; Hussain et al., 2014). The reasons for this are behavioral, and could be due to poor knowledge of the disease (Talbot et al., 2008; Abd Elaziz et al., 2013; Hussain et al., 2014). These are issues that can be redressed by providing communities with correct and adequate information. In African countries, community-directed treatment is in wide use (Amazigo et al., 2007; Duamor et al., 2017). This method is feasible and can achieve higher compliance (Wijers and Kaleli, 1984) unlike other countries, like India, where the government health system is capable of operating MDA (Babu, 2005).
Monitoring and Evaluation of MDA Programs

After the recommended rounds of MDA have been completed and transmission interrupted, caution should be exercised on deciding when to stop chemotherapy. Some campaigns often, but not always, succeed in achieving significant reductions in mf rates and intensities and LF associated morbidity (Laigret et al., 1980; Esterre et al., 2001; Ichimori et al., 2001). Others, however, may take longer and untreated cases may be reservoirs of reemerging infection (Mallawaeachchi et al., 2018). Plans should be put in place to monitor the success of the program. Lymphatic filariasis elimination programs focuses particularly on monitoring the program outcomes and on pursuing research needed to ensure that the monitoring approach has a sound scientific basis (Gyapong, 2004).

Monitoring is important in the management of any program to enable the success and assist program managers to achieve the project objectives (WHO, 2005). One study indicated that the first round of mass treatment results in a drastic decrease in levels of microfilaremia and a slight decrease in parasite antigenemia, further rounds of MDA may be necessary to achieve a sustained reduction (Njenga et al., 2008).

Selective monitoring on two aspects, first, the number of people being targeted for MDA and second, the impact of MDA on the targeted population, are the two main issues that need to be monitored and evaluated (Lemoine et al., 2016). Specific indicators for monitoring should be identified so that they can be compared over time and between different implantation units or countries (WHO, 2005).

The main process indicator relating to transmission interruption for LF programs is MDA coverage, which can be operationally defined as reported, surveyed, or geographic coverage, each determined differently and each with a specific program implications (WHO, 1998). The principal impact indicator relating to transmission interruption is the prevalence of infection in humans as defined by microfilaremia; serum antigen (ICT) positivity and incidence of infection (antibody positivity) are also assessed (WHO,
Relative to determination of mf by microscopic inspection of blood, the traditional gold standard used to evaluate the mf reservoir, IgG4 antibody to Bm14, is better suited to monitor progress and possibly detect recrudescent or persisting transmission of *W. bancrofti* after MDA has ceased (Tisch *et al.*, 2008).

Monitoring and evaluation by measuring the prevalence of *W. bancrofti* infection in mosquitoes has proven to be useful for monitoring LF transmission during MDAs in other elimination programs (Bockarie *et al.*, 1998 and Goodman *et al.*, 2003). Compared to mf detection, mosquito dissection is more acceptable because it is a minimally invasive method. The limitation of this method, however, is that there are reports that when mf prevalence and density are low, the sensitivity of the dissection technique decreases. Polymerase chain reaction (PCR) is a more sensitive method than dissection, and it has the practical advantage of being useful for testing pools of mosquitoes in areas of low transmission.

The decline in sensitivity of the immunological, parasitological and entomological testing after several rounds of MDA raises the concern about the reliability of these testing methods in the long–term epidemiological monitoring of infection and making programmatic decisions about when to stop MDAs. Immunochromatographic card testing in the long-term should be supplemented with methods that are more sensitive before program end-points are determined (Njenga *et al.*, 2008). One such method of monitoring is molecular xeno-monitoring (MX) using PCR for filarial detection in mosquitoes that complements the traditional diagnostic methods (WHO, 2005). Xenomonitoring refers to the detection of parasite DNA/RNA in mosquitoes using molecular techniques.

Monitoring infection in the vector population can be an essential tool for surveillance of infection and for measuring control program success (Weil, 2005). This method involves the testing of filarial DNA in wild caught mosquitoes. Molecular xeno-monitoring is used for identifying endemic areas and as a surveillance tool for early detection of
resurgent transmission (Weil, 2005). When transmission is low, monitoring requires both large numbers of mosquito vectors, and a sensitive detection method like PCR.

Vector monitoring is ideal because mosquitoes may offer a real time estimate of transmission (Goodman et al., 2003; Plichart et al., 2006; Hoda et al., 2007). It is convenient and less invasive. Studies in Egypt and Papua New Guinea utilizing MX as a monitoring tool suggests that MX provides information on the changing rates to filarial transmission and the potential risk of transmission either during or after therapy (Weil, 2005). Molecular xeno-monitoring is based on the ability of mosquitoes to pick mf from a blood meal providing point prevalence estimates of filarial parasites in the mosquitoes in the area of interest and it should be used as a means of efficiently sampling endemic populations for the presence of microfilaria (Weil, 2005).

When the infection prevalence in the vector population is low after treatment, the transmission of the infection can be measured by pool-screening (group testing) so that infection prevalence estimates can be calculated from certain assumption (Weil, 2005). Pool-screening is challenging because it is difficult to quantify the positive pools as containing a single infected insect or more (Pilotte et al., 2016; Okorie and de Souza, 2017). An important development which favors PCR-pool-screening methodology is the algorithm for estimating the infection rate in the *Simulium damnosum* complex which can also be applied to LF vectors (Boakye et al., 2007).

However, parasite DNA can be detected in both vector and non-vector mosquitoes for two weeks or longer after they ingest mf-positive blood (Fisher et al., 2007). Thus, although MX with vector and non-vector mosquito species may be a sensitive method for indirectly detecting filarial parasites in human populations, positive test results for parasite DNA in mosquitoes do not necessarily prove that transmission is ongoing in the study area (Schmaedick et al., 2014).
Kenya’s National Program to Eliminate Lymphatic Filariasis Program

In 2001, a baseline survey was carried out to determine prevalence and intensities of the LF burden in the selected study area in Malindi sub-county. Kenya’s NPELF was initiated in 2002 with support from the GPELF. The drugs used for mass chemotherapy are DEC and albendazole. Albendazole was donated by the GSK. DEC on the other hand is not free so the Ministry of Health (MOH) has to fund for its supply. Mass chemotherapy and the associated IEC materials and methods are accompanied by significant costs for the MOH. This becomes challenging because LF is not a priority disease for the MOH meaning that at the time the study was being done there are no funding and no budget line for the NPELF.

The communities in Malindi district have previously received three rounds of MDA; in 2002, 2003 and 2005 respectively. Due to financial constraints, the MOH was unable to administer the necessary drugs in 2006 and 2007. Figure 4 below provides a graphical description of the treatment line. The proposed study was conducted in 2009, after the fourth round of MDA that was administered in 2008 to determine the impact of the missed MDAs in 2004, 2006 and 2007.

Pre-MDA baseline antigenemia and microfilaremia data were collected for each of the consenting participants recruited in 2002. MDA was administered to the study communities in April, 2002 by the research team assisted by the health staff of Malindi District Hospital in collaboration with the local dispensaries located in the various study communities. The first Post-MDA data were collected in 2003 to assess the impact of mass treatment.
Figure 2.4: Treatment line for MDA that was done in Malindi Sub-County between 2002 and 2009
The second round of MDA was administered by Kenya’s NPELF, with the help of Community Drug Distributors (CDDs) using the more effective community directed treatment (COM-DT) strategy (Wamae, 2006), after it scaled up its activities to include the entire district of Malindi in September, 2003. The second Post-MDA data were collected in 2004 to assess the impact of that treatment.

The third round of MDA was delayed until March, 2005 due to budgetary constraints. In the same year, because of high loss of the follow-up participants, additional participants from the respective communities were recruited to join in the study. The third Post-MDA data in the first four study communities were collected in November 2006 (Fig 2.3). Data collection for the remaining four study communities was suspended temporarily and resumed in April 2007, following flooding during the short rains in the district.

In 2006 and 2007, again owing to budgetary constraints, MDA was conducted in the whole district. In December 2008, the fourth round of MDA was conducted and assessment data collected in March and May, 2009 (fourth post-MDA data).
CHAPTER THREE
MATERIALS AND METHODS

3.1 Study Site

The study area is located in Malindi subCounty, in the Coastal of Kenya, covering an area of 7,605 km\(^2\) with a total population of approximately 80,000 people in 2002 and approximately 281,552 people by 2009 (Figure 5). The district borders Kilifi County to the south, Tana River County to the north and northwest and the Indian Ocean to the east. Malindi subCounty has four major topographical features, the Coastal Plains, the Foot Plateau, the Coastal Range and the Nyika Plateau (50 Treasures of Kenya, 2013). The climate is generally hot and humid near the ocean and hot and dry further inland.

![Figure 3.1: A map of the study location in Malindi subCounty](image-url)

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The present study (KEMRI SSC No. 1481) was conducted in a previously identified \textit{W. bancrofti} endemic area along River Sabaki in Malindi district with eight sentinel communities, these are; Burangi, Chakama, Jilore, Magongoloni, Marikano, Mkondoni, Mwangatini, and Shakahola. They were selected for the collection of detailed baseline and epidemiological data of bancroftian filariasis and for monitoring the impact of mass drug treatment by the NPELF. This study was linked to other studies on LF that carried out the baseline studies and data on treatment coverage, and prevalence and intensity studies being conducted in the same area since 2002 (KEMRI SSC Nos. 597, 658, 1116).

\textbf{3.2 Study Design}

The study design was a mixed method operational research study of participants who have been on annual MDA since 2002 (Njenga \textit{et al.}, 2001, Njenga \textit{et al.}, 2007). The study aimed to assess the microfilaremia and antigenemia since the beginning of the mass treatment from 2002 to 2009. The retrospective follow-up was possible through examination of previous field and laboratory records. The primary outcome was to assess changes in yearly mf and CFA status of the study population.

\textbf{3.3 Study Population}

The main group of people inhabiting Malindi District is the Giriama, a major sub-group of the Miji Kenda who occupy most of the Coast Province (Trip down Memory Lane, 2013). In urban areas, there are small groups of people of Arabic descent with are large portion of urban inhabitants being immigrants from other parts of Kenya (Bresnahan, 2010). The Giriama usually live in homesteads widely dispersed in the countryside and practice small-scale farming. Their houses are mainly made of mud walls and thatched with coconut leaves or grass with open eaves that allow entry to mosquitoes.
3.4 Inclusion Criteria

All individuals/mature minors and minors whose parents/guardians gave consent and assent were included in the blood collection and their selected households chosen for mosquito collection.

3.5 Community Mobilization

Mobilization of the communities was done through public meetings (barazas). Each community is headed by a Village Chairman/Chairwoman who is usually appointed by the local government administrator, (Chief or Assistant Chief). This organization is essential in mobilizing the communities during different community activities. Informed consent was obtained from prospective volunteers. The objectives and procedures were explained to them in Swahili language. The study participants were required to sign or thumb print the consent forms to show that they understood the statements in the documents and that they are satisfied with the explanations provided for the consent process. Names and other personal records remained confidential.

3.6 Exclusion Criteria

Reluctant residents and their households were not sampled. Severely ill persons for any reason were not included in the study.

3.7 Selection of the Study Households

The houses in eight study communities were stratified into blocks containing 5 homesteads that are all easily accessible within one hour walking time. In each block, 10 houses were selected. All individuals and parents/guardians for minors who gave informed consent were recruited for the study. Those living in the houses selected for mosquito collection were requested to provide blood samples for mf detection and filarial antigen testing. The target study population was a convenience sample of 160 persons in each community, assuming that an average of 4 consenting individuals would be found in each household. A total of 1280 individuals were enrolled for the study.
3.8 Blood Collection

In 2002, 2003 and 2005, blood samples were collected from the follow-up group between 2030hrs and 2400hrs due to microfilaria periodicity (Gatika et al., 1994). Finger prick blood samples for mf enumeration and Immunochromatographic Card Test (ICT) testing were collected for post MDA assessment. In 2009, blood samples for CFA testing were collected during the day only. The blood samples that were positive for CFA provided an additional blood sample for mf enumeration. A finger prick blood sample was obtained by cleaning the tip of the middle finger, sterilized with a cotton swab soaked in 70% isopropyl alcohol, and pricked with a sterile needle. The blood sample was then collected in a heparinized capillary tube and a drop of the blood sample put on the ICT Card or in a tube containing 0.9 ml of 3% acetic acid for mf enumeration. After application of a whole blood sample to the ICT, (Binax Inc., USA) the ICT card test results were recorded 10 minutes later and disseminated to the participants.

3.9 Immunochromatographic Card Testing

For CFA testing a finger prick blood sample was added to the sample pad on the open ICT test card. The pad contains dried colloidal gold-labeled polyclonal anti-filarial antibodies that bind to W. bancrofti adult worm antigens circulating in the blood. The card was then closed and antibody-antigen complexes, along with unbound antigen, flowed across a nitrocellulose strip and were trapped by a monoclonal antibody (AD12.1) in the strips’ coating. The participants’ results were ready after 10 minutes. Each card contained a control line (pink in color) and a test (pink in color). Blood samples for antigen negative persons displayed only one pink line (control line) whereas the card of a person who is antigen positive exhibited two pink lines (control and test lines).

Any tested card that did not display the control line was discarded. ICT cards that were used at pre-treatment (2002) were from ICT Diagnostics/AMRAD ICT (New South Wales, Australia) and in 2003. Because of the change in the location of the card
manufacturer and the ownership of the company, since 2004 the cards were from Binax Inc (Portland, USA). There were no notable variations in the two types of card tests (Njenga et al., 2011).

3.10 Enumeration of Microfilaria in Blood

The counting chamber method (McMahon et al., 1979a) was used for enumerating W. bancrofti microfilaria in blood specimens. A capillary blood sample of 100μl was added into a tube containing 0.9 ml of 3% acetic acid which served as a fixative and preservative as well as a red blood cell lysing solution and stored at room temperature until later. In the laboratory, each specimen was transferred to a clean counting chamber and examined under the microscope. The microfilariae were counted and expressed as mf/ml of blood.

3.11 Microfilarial Density (MFD)

The microfilarial density (MFD) is the average number (arithmetic mean) of microfilaria in individuals who are positive for microfilaria. It was calculated as the total count (sum) of microfilaria in positive specimens divided by the total number of individuals found to be microfilaria positive: \([\frac{\sum x}{n}]\) where \(x\) was the number of microfilariae counted, \(n\) was the number of individuals positive for microfilariae. (Njenga et al., 2008).

3.12 Geometric Mean Intensity (GMI)

The Geometric Mean Intensity was used as an indicator of microfilarial intensity. The GMI is used to explain data that is highly skewed with extreme observations that have a large influence on the arithmetic mean, which make the corresponding confidence intervals wider. To decrease skewness the data was first transformed logarithmically to make the distribution as close to normal as possible. The GMI was calculated as the \(\{\text{antilog} \left[\frac{\sum \log(x + 1)}{n}\right]\} - 1\), where \(x\) was the number of microfilariae counted, \(n\) was the number of individuals positive for microfilariae (Njenga et al., 2008).
3.13 Community Microfilarial Load (CMFL)

The Community Microfilarial Load is an indicator of the intensity of microfilaremia in a community. The CMFL was calculated as the geometric mean of the number of microfilaria per ml of blood in all individuals examined for mf. Because this indicator included those persons with mf counts of zero, the mean was calculated after a log (x + 1) transformation. The CMFL was calculated as the \( \text{antilog} \left\{ \frac{\sum \log (x + 1)}{N} \right\} - 1; \) where \( x \) was the number of microfilariae counted, \( N \) was the number of people tested for microfilaremia. (Formula adapted from Njenga et al., 2008)

3.14 Mosquito Collection

There was a long dry spell between 2002 and 2004 that caused crop and livestock failure. The rains returned in the rainy season of 2005/2006 resulting in flooding in some areas in 2006 resulting in the suspension of data collection during that period. Unpredictable weather patterns resulted in another dry spell by the time this study was being done (2009), the expected rains had failed and thus there were no mosquitoes to collect for dissection and PCR testing.

3.15 Timing of Data Collection

The communities enlisted in the study have previously received 4 rounds of MDA in 2002, 2003, 2005 and 2008. The main studies to which the proposed study was linked to have been ongoing since 2001 and baseline data on microfilaremia, antigenemia (by ICT), antifilarial antibodies, and entomological indicators had been previously collected. Data were available from baseline 2002 (prior to the first MDA), and post-MDA data collected in 2003, 2005 and 2008.
3.16 Data Management and Analysis

Data collection forms (Appendix 6) were used for recording of data in the field. Statistical analysis were done using SPSS software version 15.0 for Windows Evaluation Version. The Students t–test and the Mann–Whitney rank–sum test (nonparametric tests were used to compare the differences in group where data was not normally distributed) were used to determine mean differences between two independent groups. One-way analysis of variance (ANOVA) or Kruskal–Wallis tests (in non-normal distributions) were employed to determine quantitative differences in more than two groups.

Associations of the overall prevalence were measured using the Pearson Chi-Square test. Paired comparisons of data collected at baseline and after MDA were used to test for change. McNemars test was used to test for change in paired data with non-normal distribution. In normal distributions, the T-test was used to test for change.

3.17 Ethical Considerations

Ethical approval was obtained from the KEMRI/National Ethics Review Committee for the protocol: SSC Protocol No. 1481. Only persons (parents and guardians for minors) who gave informed consent were recruited for the study. Finger pricking causes minute laceration of the fingertip and may also cause minor tenderness or soreness of the fingertip for a few hours. To minimize the risk of injury, qualified laboratory technicians were responsible for bleeding.

Acquisition of filarial infections requires repeated and lengthy exposure to infected mosquitoes, presumably due to the low pathogen load per bite, however, to minimize the risk of becoming infected with *W. bancrofti*, project staff were provided with single dose annual treatment consisting of DEC (6mg/kg) and albendazole (400mg), which was freely available at the NPELF.
### 3.18 Expected Application of the Research Results

This study, KEMRI SSC 1481 is part of ongoing studies, KEMRI SSC Nos. 597, 658, 1116, which have been approved by the KEMRI SSC and Ethical Review Committee (Appendix 1).

The data obtained from the study:

i. Showed the impact of missed MDA in an ongoing elimination program.

ii. Provided information on the current state of LF elimination in River Sabaki area in Malindi district.

iii. Provided useful information to the GPELF on the effect of missed MDA during elimination programs.

iv. Publication of the research findings in a peer-reviewed journal
CHAPTER FOUR

RESULTS

The results presented in this section include a description of the demographic characteristics of the study participants, their treatment, and their microfilaremia and antigenemia status to determine the effect of treatment on the at-risk population. Microfilaria prevalence data were further analyzed to identify the Microfilaria Density (MFD), the Geometric Mean Intensity (GMI), and the Community Microfilaria Load (CMFL) by community, gender and age.

4.1 Demographic Characteristics of Study Participants

The total number of people who were enrolled in the study from the eight selected study communities in 2002 was 1447. For the collection of baseline antigenemia and microfilaremia data in 2002, a total of 198, 148, 172, 198, 196, 182, 195 and 157 persons over 2 years of age were registered in Burangi, Chakama, Jilore, Magongoloni, Marikano, Mkondoni, Mwangatini, and Shakahola respectively. Of the number of participants tested, 643 were males and 803 were females. The number of females was higher than that of males but this was not statistically significant (p = 0.922).

The mean age of the participants at the beginning of the study was 20.9 years. The overall mean age between male and female participants was 20.1 and 21.5 years respectively and when compared, this difference was not statistically significant (p = 0.220).

The ages of the participants in the eight communities ranged between 17.6 – 26.6 years. Shakahola village had the lowest mean age (17.6 years) where as Marikano village had the highest mean age (26.6 years).

Within the villages, there was no significant difference in the ages of the participants between Burangi and Chakama (p = 0.163), Jilore and Magongoloni (p = 0.520), Magongoloni and Marikano (p = 0.153), Mkondoni and Mwangatini (p = 0.516) and
Mwangatini and Shakahola (p = 0.217). There was however statistical significance between the means of the ages in Chakama and Jilore (p < 0.001) and Marikano and Mkondoni (p < 0.001).

The community of Marikano had the highest mean age of 26.6 years and the community of Shakahola had the lowest mean age of 17.6 years. There was a statistical difference between the highest and lowest mean age (p < 0.001).

4.2 Treatment Coverage

Information on compliance to treatment was obtained from oral interviews of the study participants as to whether they received treatment or not. Pregnancy, refusal, and being away at the time that drugs were distributed were the principal reasons given for noncompliance among persons not treated.

Among all the interviewed participants, 81.2% (1278) confirmed to have received treatment in 2002. In 2003, 79.3% (1248) of the participants confirmed to have received treatment. In 2005, 94.0% of the participants (1542) received treatment. The number of participants who received treatment in 2008 was 75.5% (827).

The observed distribution of treatment among the study participants is summarized in Table 4.1. In 2002, 2003, 2005 and 2008, of the participants who were interviewed and the number of doses missed by individuals varied during the four annual MDAs. The treatment information of 6 participants was missing from the system.

Overall, 9.5% (240 participants) of the participants either missed all four treatments or information about their treatment status was not available. From the data set, 27.5% (694 persons) of the participants received one MDA. 33.8% (852) of the participants received 2 rounds of MDA.

From the treatment administered in 2002, 2003, 2005 and 2008, 18.0% (455) participants received three treatments. Over 11.2% (283) participants received all 4 rounds of treatment administered in 2002, 2003, 2005 and 2009 respectively.
4.2.1 Treatment Coverage by Community

The overall treatment coverage in 2002 was over 80% in five of the eight communities. Six out of eight study communities recorded treatment coverage of over 80% of the population at risk in 2003. In 2005, all eight communities had covered over 80% of the population. In 2008 only 3 of the 8 study communities recorded less than 80% treatment coverage. Table 4.1 summarizes the percentages of those who received treatment in each study community in the years that treatment was administered. In 2002, of the 1278 (81.2%) participants who receive treatment 221, 121, 159, 133, 179, 153 and 122 were from Burangi, Chakama, Jilore, Magongo loni, Marikano, Mkondoni, Mwangatini and Shakahola respectively. Treatment percentages ranged from 67.2% - 96.8% in that year. There was a significant difference between the study communities in regard to treatment coverage (p < 0.001).

In 2003, 1248 (79.3%) of the participants received treatment with 226, 132, 161, 181, 133, 161, 119 and 135 participants being from communities of Burangi, Chakama, Jilore, Magongoloni, Marikano, Mkondoni, Mwangatini and Shakahola respectively. There was a significant difference between the groups (p < 0.001). Treatment coverage percentages in that year ranged from 53.8% in Mwangatini to 88.0% in Magongoloni.

In 2005, 1542 participants received treatment and of these, 224, 184, 131, 130, 234, 230, 209 and 200 participants were from the communities of Burangi, Chakama, Jilore, Magongoloni, Marikano, Mkondoni, Mwangatini and Shakahola respectively with a significant difference between the groups (p < 0.001). The percentage of treatment coverage was over 80% and ranged from 84.0% to 99.5%. Of the 827 participants interviewed 132, 138, 61, 91, 91, 108, 138 and 68 participants received annual MDA from the communities of Burangi, Chakama, Jilore, Magongoloni, Marikano, Mkondoni, Mwangatini and Shakahola respectively. The percentage range in the eight communities was 42.5% coverage in Shakahola and 97.2% coverage in Mkondoni. There was a significant difference between the groups (p < 0.001).
Table 4.1: Treatment coverage among study participants in all eight communities in the years that treatment was administered

<table>
<thead>
<tr>
<th>Community</th>
<th>2002</th>
<th>2003</th>
<th>2005</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants Treated/Participants Interviewed</td>
<td>Participants Treated/Participants Interviewed</td>
<td>Participants Treated/Participants Interviewed</td>
<td>Participants Treated/Participants Interviewed</td>
</tr>
<tr>
<td>Burangi</td>
<td>221/265 (83.4)</td>
<td>226/266 (85.0)</td>
<td>224/229 (97.8)</td>
<td>132/160 (82.5)</td>
</tr>
<tr>
<td>Chakama</td>
<td>121/155 (78.1)</td>
<td>132/155 (85.2)</td>
<td>184/185 (99.5)</td>
<td>138/142 (97.2)</td>
</tr>
<tr>
<td>Jilore</td>
<td>159/186 (85.5)</td>
<td>161/186 (86.6)</td>
<td>131/156 (84.0)</td>
<td>61/89 (68.5)</td>
</tr>
<tr>
<td>Magongoloni</td>
<td>190/207 (91.8)</td>
<td>181/207 (87.4)</td>
<td>130/140 (92.9)</td>
<td>91/138 (65.9)</td>
</tr>
<tr>
<td>Marikano</td>
<td>133/198 (67.2)</td>
<td>133/198 (67.2)</td>
<td>234/256 (91.4)</td>
<td>91/108 (84.3)</td>
</tr>
<tr>
<td>Mkondoni</td>
<td>179/185 (96.8)</td>
<td>161/183 (88.0)</td>
<td>230/244 (94.3)</td>
<td>108/126 (85.7)</td>
</tr>
<tr>
<td>Mwangatini</td>
<td>153/221 (69.2)</td>
<td>119/221 (53.8)</td>
<td>209/219 (95.4)</td>
<td>138/173 (79.8)</td>
</tr>
<tr>
<td>Shakahola</td>
<td>122/156 (78.2)</td>
<td>135/157 (86.0)</td>
<td>200/212 (94.3)</td>
<td>68/160 (42.5)</td>
</tr>
<tr>
<td>All</td>
<td>1278/1573 (81.2)</td>
<td>1248/1573 (79.3)</td>
<td>1542/1641 (94.0)</td>
<td>827/1096 (72.2)</td>
</tr>
</tbody>
</table>
4.2.2 Treatment Coverage by Gender

In the years that treatment was administered 1278, 1248, 1542 and 827 males and females from the study communities received treatment. Treatment coverage among the males and females reflected that there were a higher number of female participants who received treatment compared to the number of male participants. The treatment coverage by among the male and female participants in the study communities is summarized in Table 4.2. The treatment data were collected from individual verbal confirmation of participation in the treatment exercise.

Of the 1573 persons who were interviewed in 2002, 586 (82.2%) males and 692 (80.4%) females received treatment. There was no statistical significance between the groups (p = 0.190). 562 males (78.8%) and 686 females (79.8%) received treatment of the 1573 persons interviewed in 2003, with the differences between the two genders not statistically significant (p = 0.967).

In 2005, 703 males (92.6%) and 839 females (95.2%) of the 1640 persons interviewed received treatment. The difference in the number of male participants compared to the female participants was not statistically significant (p = 0.036). Of the participants who received treatment in 2008, 384 were male (76.5%) and 443 were female (74.6%) of the 827 persons who were interviewed. There was no significant difference between the groups (p = 0.349).
Table 4.2: Treatment status among the male and female participants in 2002, 2003, 2004 and 2007.

<table>
<thead>
<tr>
<th>Year</th>
<th>Participants Treated /Participants Interviewed (%)</th>
<th>All Treated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>586/713 (82.2)</td>
<td>1278/1573 (81.2)</td>
</tr>
<tr>
<td>2003</td>
<td>562/713 (78.8)</td>
<td>1248/1573 (79.3)</td>
</tr>
<tr>
<td>2004</td>
<td>703/759 (92.6)</td>
<td>1542/1640 (94.0)</td>
</tr>
<tr>
<td>2007</td>
<td>384/502 (76.5)</td>
<td>827/1096 (75.5)</td>
</tr>
</tbody>
</table>

4.2.3 Treatment Coverage by Age

The treatment by age among the study participants is summarized in Table 4.3. The age of the participants who received treatment ranged from between 2 years to over 50 years of age. From the 81.2% of the participants who received treatment in 2002, the majority (88.9%) of participants who participated were within the 2 – 10 year age group. In 2003, the highest number of participants (88.5%) were between the 2 – 10 year ages group. In 2005, the majority (96.7%) of the participants were between the 21 – 30 age group and in 2008, the most (78.0%) of the study participants were also between the age of 21 – 30 year age group.

Those participants between the age group of 2 – over 50 year age group who received treatment ranged from 72.7% – 88.9%. In 2002, 409 participants were between 2 – 10 years, 343 participants were between the age of 11 – 20 years, 173 were between the age of 21 – 30 years, 127 participants were between the age of 31 – 40 years, 106 participants between the age of 41 – 50 years and 120 participants over the age of 50
years.

In 2003, of the 408 participants were between 2 – 10 years or age. 347 participants were between 11 – 30 years, 171 participants were between the age of 21 – 30 years, 117 participants were between 31 – 40 years, 101 participants were between 41 – 50 years and 104 participants were over the age of 50. The age group percentages ranged between 71.1% for participants over the age of 50 to 88.5% for the participants between the age of 2 – 10 years.

Of the participants interviewed in 2005, 669 participants were between 2 – 10 years, 330 participants were between the age of 11 – 20 years, 204 were between the age of 21 – 30 years, 126 participants were between the age of 31 – 40 years, 105 participants between the age of 41 – 50 years and 107 participants over the age of 50 years. The age group percentages of the participants ranged between 90.0% - 96.7% with the lowest percentage being between the 31 – 40 years of age and highest percentage being participants between the age of 21 – 30 years.

Those age group of the participants ranged between 2 to over 50 years age group and the percentage of those who received treatment ranged from 70.0% – 78.0% during the follow-up MDAs. In 2002, 371 participants were between 2 – 10 years, 143 participants were between the age of 11 – 20 years, 113 were between the age of 21 – 30 years, 73 participants were between the age of 31 – 40 years, 70 participants between the age of 41 – 50 years and 56 participants over the age of 50 years.
Table 4.3: Treatment coverage by age group (yr) from 2002, 2003, 2005 and 2008 when treatment was administered.

<table>
<thead>
<tr>
<th>Year</th>
<th>Participants Treated/ Total Number of Participants (%)</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 - 10 Yrs (%)</td>
<td>11 - 20 Yrs (%)</td>
</tr>
<tr>
<td>2002</td>
<td>409/460 (88.9)</td>
<td>343/446 (76.9)</td>
</tr>
<tr>
<td>2003</td>
<td>408/461 (88.5)</td>
<td>347/447 (77.6)</td>
</tr>
<tr>
<td>2005</td>
<td>669/709 (94.3)</td>
<td>330/447 (93.0)</td>
</tr>
<tr>
<td>2008</td>
<td>371/491 (75.6)</td>
<td>143/187 (76.5)</td>
</tr>
</tbody>
</table>

*The age specifics of one participant were not available
4.3 Microfilaremia and CFA Prevalence and Intensity

Microfilaria prevalence was determined by the examination of 100 μL of finger prick blood collected between 20:30hrs and 24:00hrs and examined under a microscope using the counting chamber technique. Microfilariae status was designated as negative or positive without regard to the absolute level of microfilariae. Circulating filarial antigen was determined by the ICT card test using a random 100μl finger prick blood sample.

Table 4.4 indicates the distribution of the participants from each community who took part in antigenemia and microfilaremia testing. In 2002, 2003, 2004 and 2007, most participants were tested for both antigenemia and microfilaremia but there were a few participants who did not provide an adequate blood sample for both tests. In 2009, only those who tested ICT positive were required to provide a blood sample for microfilaria examination. In both cases, where the blood sample was not adequate, the more sensitive ICT test was given priority.


Of the 1447 people who were eligible for testing, a total of 1417 participants were tested for microfilaremia and antigenemia in 2002. In 2003, of the 915 eligible participants, 913 were tested for both antigenemia and microfilaremia. In 2004, of the 1016 participants, 1018 provided for both antigenemia and microfilaremia testing. Of the 1304 participants in 2007, 1289 were tested for antigenemia and microfilaremia. In 2009, 1096 participants were tested for antigenemia and only the 153 participants who tested antigen positive were tested for microfilariae.
Table 4.4: The distribution of individuals who participated in blood examination for immunochromatographic tests and microfilariae detection.

<table>
<thead>
<tr>
<th>Community</th>
<th>Participants Examined for ICT</th>
<th>Participants Examined for Microfilariae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2002</td>
<td>2003</td>
</tr>
<tr>
<td>Burangi</td>
<td>199/193*</td>
<td>150/150</td>
</tr>
<tr>
<td>Chakama</td>
<td>148/148</td>
<td>58/58</td>
</tr>
<tr>
<td>Jilore</td>
<td>172/172</td>
<td>100/99*</td>
</tr>
<tr>
<td>Magongoloni</td>
<td>198/194*</td>
<td>154/154</td>
</tr>
<tr>
<td>Marikano</td>
<td>196/192*</td>
<td>105/105</td>
</tr>
<tr>
<td>Mkondoni</td>
<td>182/181*</td>
<td>110/110</td>
</tr>
<tr>
<td>Mwangatini</td>
<td>195/180*</td>
<td>131/130*</td>
</tr>
<tr>
<td>Shakahola</td>
<td>157/157</td>
<td>107/107</td>
</tr>
<tr>
<td>All</td>
<td>1447/1417*</td>
<td>915/913*</td>
</tr>
</tbody>
</table>

* Some study participants did not provide an adequate blood sample for microfilariae enumeration.
In 2002, 1447 participants were involved in the study. Of these, 804 were female and 643 were male. There was a statistical significance between the female and the male participants (p < 0.001). In 2003, 797 participants were tested for antigenemia. 380 were female and 417 were male, with females being slightly more than the males however, there was a significant difference between the males and the females (p < 0.001). Of the 1016 participants tested for antigenemia in 2004, there were 556 female participants and 460 males. There was significant difference in the means (p < 0.001) of the two genders.

From those 1304 participants who participated in 2007, 618 were male and 686 were female with a statistically significant difference between the genders, (p < 0.001). Of the 1096 participants tested in 2008, there were 502 males and 594 females. Like the previous years, there was a significant difference (p = 0.005) between the two sexes.

Figure 4.1 summarizes the gender distribution of the participants who were tested for antigenemia using the ICT card in 2002, 2003, 2004, 2007 and 2009.

![Figure 4.1](image-url)

**Figure 4.1** Gender distribution of study participants tested for antigenemia. The number of females who participated was significantly higher in 2002, 2004, 2007 and 2009.
When comparing the distribution of the gender of the participants in the years of testing, there were slightly more females than males who participated in all the years except for 2003 where the number of males was slightly more than that of females.

4.3.1 Treatment Status and Microfilaremia

Table 4.5 represents the participants in the study communities who were mf positive in the years that testing was done. Of the 773 participants who took treatment in 2002, 69 (8.9%) participants were found to be microfilaria positive. Participants with a count of more than one microfilaria ranged from 4 – 20 participants from the eight communities with the highest number (20 participants) being from Mwangatini and the fewest (4 participants) being from Shakahola.

In 2003, 49 (5.9%) participants of the 827 who received treatment were microfilaria positive whose who were positive ranged from 3 -10 participants with Mwangatini having the least number of positives (3 participants) and Jilore having the most positive persons in that year (10 participants).

From the MDA administered in 2005, 1218 participants received treatment. Out of these, 23 (1.9%) participants were microfilaria positive. Results in the various communities ranged from 0 – 6 persons who were found to be microfilaria positive. The community of Chakama recorded no positive person while the community of Mwangatini had 6 positive participants.

Of the 814 persons who received treatment in 2008, 6 (0.7%) were found to be microfilaria positive. Five of the communities (Burangi, Chakama, Magongoloni, Mwangatini and Shakahola) recorded no participant with microfilaria. Jilore recorded 3 participants who were microfilaria positive, Marikano recorded 2 positive participants and Mwangatini recorded 1 microfilaria positive participant.
Table 4.5: Treatment results for the participants who were mf positive from the eight study communities in all the years that testing was done.

<table>
<thead>
<tr>
<th>Community</th>
<th>2002</th>
<th>2003</th>
<th>2005</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants’ mf positive</td>
<td>Participants treated (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burangi</td>
<td>8/221  (3.6)</td>
<td>7/226  (3.1)</td>
<td>2/224  (0.9)</td>
<td>0/132  (0.0)</td>
</tr>
<tr>
<td>Chakama</td>
<td>6/121  (5.0)</td>
<td>6/132  (4.5)</td>
<td>0/184  (0.0)</td>
<td>0/138  (0.0)</td>
</tr>
<tr>
<td>Jilore</td>
<td>7/159  (4.4)</td>
<td>10/161 (6.2)</td>
<td>4/131  (0.7)</td>
<td>3/61   (1.6)</td>
</tr>
<tr>
<td>Magongoloni</td>
<td>20/190 (10.5)</td>
<td>4/181  (2.2)</td>
<td>1/130  (0.8)</td>
<td>0/91   (0.0)</td>
</tr>
<tr>
<td>Marikano</td>
<td>5/133  (3.8)</td>
<td>5/133  (3.8)</td>
<td>3/234  (1.3)</td>
<td>2/91   (2.1)</td>
</tr>
<tr>
<td>Mkondoni</td>
<td>11/179 (6.1)</td>
<td>7/161  (4.3)</td>
<td>3/230  (1.3)</td>
<td>1/108  (0.9)</td>
</tr>
<tr>
<td>Mwangatini</td>
<td>8/153  (5.2)</td>
<td>3/119  (2.5)</td>
<td>6/209  (2.9)</td>
<td>0/138  (0.0)</td>
</tr>
<tr>
<td>Shakahola</td>
<td>4/122  (3.3)</td>
<td>7/135  (5.2)</td>
<td>4/200  (2.0)</td>
<td>0/68   (0.0)</td>
</tr>
<tr>
<td>All</td>
<td>69/1278 (41.9)</td>
<td>49/1248 (31.8)</td>
<td>23/1542 (9.9)</td>
<td>6/827  (4.6)</td>
</tr>
</tbody>
</table>
4.3.2 Microfilaremia by Community

Table 4.6 shows the mf prevalence in the study communities during the period of study. The number of microfilaria positive participants decreased in all the years of testing after subsequent MDA of the study communities in Malindi District, Kenya. Microfilaria prevalence ranged from 20.9% pre-treatment in 2002, 10.5% after the first mass drug treatment, 7.1% after the second MDA in 2004, 1.9% prevalence in 2007 after the third MDA, and 0.9% microfilaremia prevalence tested in 2009 after the fourth round of treatment. There was a general decrease in microfilaria prevalence with each treatment.

Among the participants from each community, the community of Marikano had the highest prevalence (22.9%) in 2002. There was however no statistical significance between the communities (p = 0.463) in 2002. Magongoloni had the highest prevalence (14.8%) in 2003 although the difference between the groups was not statistically significant (p = 0.069). Jilore had the highest prevalence in 2004, 2007 and 2009 of 9.0%, 6.8% and 3.5% respectively. The difference in the microfilaremia prevalence between the study communities was not statistically significant in 2004, 2007 and 2009 (P = 0.702, P = 0.135 and P = 0.240 respectively).

The decrease in the microfilaremia prevalence varied within the different communities. In Burangi, the number of participants positive for mf ranged from 44 (22.8%) – 0 (0%) participants in the years that testing was done. The percentage change in microfilaremia in Burangi ranged from 69% decrease in 2003 to 100% decrease in the community’s microfilaremia in 2009. In Chakama the number of participants positive for mf ranged from 32 (21.6%) – 0 (0%). The percentage of participant who were microfilaria positive from Jilore ranged from 44 (22.7%) – 3 (3.5%). Microfilariae prevalence in Marikano ranged between 44 (22.9%) – 2 (1.9%). In Mkondoni, the mf prevalence ranged from 32 (17.7%) – 1 (0.8%). The percentage decrease in the mf prevalence in Mwangatini was 95.12% with mf prevalence ranging between 41 (22.8%) – 2 (1.3%). Microfilaria prevalence among the participants in Shakahola ranged from 28 (17.8%) – 2 (1.3%) with a percentage decrease of 92.86%.

<table>
<thead>
<tr>
<th>Community</th>
<th>Participants positive for microfilaremia / Participants Tested (%)</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burangi</td>
<td></td>
<td>44/193</td>
<td>16/151</td>
<td>12/188</td>
<td>2/226</td>
<td>0/159</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(22.8)</td>
<td>(8.6)</td>
<td>(6.4)</td>
<td>(0.9)</td>
<td>(0.0)</td>
</tr>
<tr>
<td>Chakama</td>
<td></td>
<td>32/148</td>
<td>11/58</td>
<td>8/112</td>
<td>0/183</td>
<td>0/139</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(21.6)</td>
<td>(9.8)</td>
<td>(7.1)</td>
<td>(0.0)</td>
<td>(0.0)</td>
</tr>
<tr>
<td>Jilore</td>
<td></td>
<td>32/173</td>
<td>9/99</td>
<td>11/122</td>
<td>(5.0)</td>
<td>3/85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(18.5)</td>
<td>(7.4)</td>
<td>(9.0)</td>
<td>(6.8)</td>
<td>(3.5)</td>
</tr>
<tr>
<td>Magongoloni</td>
<td></td>
<td>44/194</td>
<td>21/154</td>
<td>6/142</td>
<td>1/140</td>
<td>0/138</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(22.7)</td>
<td>(14.8)</td>
<td>(4.2)</td>
<td>(0.7)</td>
<td>(0.0)</td>
</tr>
<tr>
<td>Marikano</td>
<td></td>
<td>44/192</td>
<td>9/105</td>
<td>9/111</td>
<td>3/111</td>
<td>2/106</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(22.9)</td>
<td>(8.1)</td>
<td>(8.1)</td>
<td>(2.8)</td>
<td>(1.9)</td>
</tr>
<tr>
<td>Mkondoni</td>
<td></td>
<td>32/181</td>
<td>14/110</td>
<td>9/118</td>
<td>3/127</td>
<td>1/125</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(17.7)</td>
<td>(11.9)</td>
<td>(7.6)</td>
<td>(2.4)</td>
<td>(0.8)</td>
</tr>
<tr>
<td>Mwangatini</td>
<td></td>
<td>41/180</td>
<td>11/130</td>
<td>9/123</td>
<td>6/216</td>
<td>2/171</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(22.8)</td>
<td>(8.3)</td>
<td>(7.3)</td>
<td>(2.9)</td>
<td>(1.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(17.8)</td>
<td>(4.8)</td>
<td>(7.7)</td>
<td>(2.0)</td>
<td>(1.3)</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td></td>
<td>297/1418</td>
<td>96/914</td>
<td>72/1020</td>
<td>24/1290</td>
<td>10/1079</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(20.9)</td>
<td>(10.5)</td>
<td>(7.1)</td>
<td>(1.9)</td>
<td>(0.9)</td>
</tr>
</tbody>
</table>
Figure 4.2 gives a graphical presentation of microfilaria prevalence in the study communities. The microfilaria prevalence decreased by about 96% from 2002 to 2009.

4.3.4 Microfilaremia by Gender

Table 4.7 presents the microfilaria prevalence in the male and the female participants. According to the results, there was no significant difference in the prevalence of microfilaremia between the males and the females. Figure 4.3 gives a graphical presentation of this data. The percentage prevalence of those who were microfilaria positive was highest in 2002 (22.6% in the males and 19.6% in the females) and lowest in 2009 (0.6%) in the males and (1.2%) among females. 297 of the 1419 participants (mf prevalence of 20.9%) tested mf positive with 156 being female and 141 being male. There was no significant difference between the males who were positive and the females who were positive (p = 0.007).
Table 4.7: Microfilaria prevalence in males and females in the eight study communities from baseline (2002) to the last testing (2009).

<table>
<thead>
<tr>
<th>Year</th>
<th>Males</th>
<th>Females</th>
<th>Both</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants Tested (%)</td>
<td>Participants Microfilariae Positive / Participants Tested (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>141/624 (22.6)</td>
<td>156/795 (19.6)</td>
<td>297/1419 (20.9)</td>
<td>0.007</td>
</tr>
<tr>
<td>2003</td>
<td>50/416 (12.0)</td>
<td>46/498 (9.2)</td>
<td>96/914 (10.5)</td>
<td>0.006</td>
</tr>
<tr>
<td>2004</td>
<td>36/461 (7.8)</td>
<td>36/559 (6.4)</td>
<td>72/1020 (7.1)</td>
<td>0.090</td>
</tr>
<tr>
<td>2007</td>
<td>11/610 (1.8)</td>
<td>13/680 (1.9)</td>
<td>24/1290 (1.9)</td>
<td>0.771</td>
</tr>
<tr>
<td>2009</td>
<td>3/494 (0.6)</td>
<td>7/585 (1.2)</td>
<td>10/1079 (0.9)</td>
<td>0.044</td>
</tr>
<tr>
<td>All</td>
<td>241/2605 (9.3)</td>
<td>258/3117 (8.3)</td>
<td>499/5722 (8.7)</td>
<td></td>
</tr>
</tbody>
</table>
In 2003, of the 914 participants tested, 50 male and 46 female participants (with a prevalence of 10.5%) were found to be microfilaremia positive. The number of participants found positive was higher in females than in males although this difference was not found to be statistically significant ($p = 0.006$). Of the 1020 participants who were tested in 2004, 36 male and 36 female participants (7.1%) were found to be microfilaria positive. There was no significant difference between the males and the females ($p = 0.090$).

1290 participants were tested in 2007 and 11 male and 24 female participants (1.9%) were found to be microfilaremic. The difference between the males and females was not significant ($p = 0.774$). Data collected post-MDA 4 in 2009 showed that of the 1079 participants tested 3 males and 7 females were having detectible microfilaria. The percentage prevalence in 2009 was 0.9 %. With a $p$-value of 0.044, there was no statistical difference between the male and the female participants.

Figure 4.3 Microfilaria prevalence among the study participants by gender.
4.3.5 Microfilaremia by Age Distribution

Changes in microfilaria prevalence in different age groups are illustrated in Table 4.8. Microfilaria prevalence decreased significantly in all the age groups after four rounds of mass treatment. In 2002, those between the age of 2 – 10 years had the lowest prevalence (8.6%) while those >50 years had the highest prevalence (37.5%). In 2003, those over the age of 31 – 40 years and those over 50 years both had a prevalence of 19.4% while those aged 2 – 10 years had the lowest prevalence (3.8%). In 2004, those over 50 years had the highest prevalence (12.3%) and those between the ages of 2 – 10 years had the lowest mf prevalence (1.8%). In 2007, those between the ages of 31 – 40 had the highest microfilaria prevalence (5.0%) and those between the ages of 2 – 10 years had a prevalence of 0.8%. After four rounds of treatment, the lowest mf prevalence in 2009 was between the age of 11 – 20 years (0.0%) and the highest prevalence was between the ages of 41 – 50 years (3.4%).
Table 4.8: The microfilaria prevalence by age distribution.

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 - 10</td>
<td>30/348 (8.6)</td>
<td>11/289 (3.8)</td>
<td>6/336 (1.8)</td>
<td>5/619 (0.8)</td>
<td>1/486 (0.2)</td>
</tr>
<tr>
<td>11 - 20</td>
<td>76/418 (18.2)</td>
<td>25/265 (9.4)</td>
<td>16/256 (6.3)</td>
<td>4/252 (1.6)</td>
<td>0/183 (0.0)</td>
</tr>
<tr>
<td>21 - 30</td>
<td>55/225 (24.4)</td>
<td>18/120 (15.0)</td>
<td>14/142 (9.8)</td>
<td>5/164 (3.0)</td>
<td>2/141 (1.4)</td>
</tr>
<tr>
<td>31 - 40</td>
<td>44/154 (28.6)</td>
<td>19/98 (19.4)</td>
<td>15/106 (14.1)</td>
<td>5/100 (5.0)</td>
<td>2/103 (1.9)</td>
</tr>
<tr>
<td>41 - 50</td>
<td>39/132 (29.5)</td>
<td>10/75 (13.3)</td>
<td>11/99 (11.1)</td>
<td>2/80 (2.5)</td>
<td>3/88 (3.4)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>53/142 (37.3)</td>
<td>13/67 (19.4)</td>
<td>10/81 (12.3)</td>
<td>3/74 (4.1)</td>
<td>2/78 (2.6)</td>
</tr>
<tr>
<td>All</td>
<td>297/1419 (20.9)</td>
<td>96/914 (10.5)</td>
<td>72/1020 (7.1)</td>
<td>24/1289 (1.9)</td>
<td>10/1079 (0.9)</td>
</tr>
</tbody>
</table>
The prevalence of microfilaremia among those aged between 2 – 10 years decreased significantly from 8.6% in 2002 to 0.2% in 2009 (p < 0.001), with a percentage decrease of 70%. For those between the age of 11 – 20 years, microfilaria prevalence decreased with statistical significance from 18.2% in 2002 to 0.0% in 2009 (p < 0.001) with a percentage decrease of 100%. There was a significant decrease (p < 0.001) in microfilaria prevalence for those participants between the ages of 21 – 30 years, from a prevalence of 24.4% in 2002 to 1.4% in 2009 with a decrease of 94%.

The decrease in microfilaria prevalence for participants between the age of 31 – 40 was statistically significant from 24.6% in 2002 to 1.9% in 2009 (p < 0.001) with a percentage decrease of 92%. For participants between the ages of 41 – 50 years, there was a significant difference (p < 0.001) from 29.5% in 2002 to 3.4% with a percentage decrease of 88% in 2009. For those >50 years of age, there was a significant decrease (p < 0.001) of microfilaria prevalence after four MDA treatments from an initial prevalence of 37.3% in 2002 down to a prevalence of 2.6% with a percentage decrease of 93% in 2009.

**4.4 Geometric Mean Intensity**

The GMI is an indicator of the intensity of infection and transmission in the community. Microfilaremia intensity was not directly proportional to microfilaria prevalence. Figure 4.4, Table 4.9, and Table 4.10 summarize the prevalence and geometric mean intensity (GMI) of microfilaria for the eight study communities.

**4.4.1 Geometric Mean Intensity by Community**

The overall GMI decreased from 559.4mf/ml in 2002 to 78.6mf/ml in 2009. Table 4.9 summarizes the overall intensity of microfilaria in the eight study communities. Microfilaria intensity decreased by 70.9% in 2003, by 80.7% in 2004, by 81.8% in 2007 and by 86.1% in 2009. The participants from the community of Shakahola had a higher (1281.8 mf/ml) than all the other communities in 2002. Chakama had the highest GMI (361.8 mf/ml) in 2003, Marikano had the highest GMI both in 2004 (183.5 mf/ml) and
in 2007 (387.6 mf/ml). In 2009, the community with the highest GMI was Shakahola with a GMI of 190.9mf/ml. There was no statistical significance in 2002 (p = 0.172), 2003 (p = 0.172), 2004 (p = 0.396), 2007 (p = 0.886) and 2009 (p = 0.315) among the communities respectively.

![Geometric Mean Intensity of Communities](image)

**Figure 4.4: Geometric mean intensity of the eight study communities in 2002, 2003, 2004, 2007 and 2009.**

The overall GMI in the 297 microfilaremic persons at baseline (2002) was 559.4mf/ml. The intensity among the eight communities ranged from 234.7mf/ml to a high of 1281.7mf/ml. This difference was no significant difference within the communities (p = 0.327). In 2003, the overall GMI of the 96 microfilaria positive participants was 163.3mf/ml. The GMI ranged from 107.2mf/ml to 361.8mf/ml. With a P = 0.068, the difference was not significant within the study communities. The overall GMI in 2004 for the 72 participants who were tested was 108.5mf/ml. The GMI ranged from 56.9mf/ml to 183.5mf/ml. The P < 0.001 was statistically significant. The overall GMI
in the 24 microfilaric persons in 2007 was 102.7 mf/ml. The intensity among the eight communities ranged from a low of 0.0 mf/ml to a high of 387.6 mf/ml. This difference within the communities was not significant by village (p = 0.519). There was an increase in GMI in some of the communities. In 2009, the overall GMI of the 10 microfilaria positive participants was 78.6 mf/ml. The GMI ranged from 0.0 mf/ml to 190.9 mf/ml in three of the study communities. With a P = 0.683, the difference was not significant within the communities.


<table>
<thead>
<tr>
<th>Community</th>
<th>GMI† (Participants microfilaria positive)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2002</td>
</tr>
<tr>
<td>Burangi</td>
<td>522.3 (44)</td>
</tr>
<tr>
<td>Chakama</td>
<td>913.0 (32)</td>
</tr>
<tr>
<td>Jilore</td>
<td>554.6 (32)</td>
</tr>
<tr>
<td>Magongoloni</td>
<td>685.9 (44)</td>
</tr>
<tr>
<td>Marikano</td>
<td>234.7 (44)</td>
</tr>
<tr>
<td>Mkondoni</td>
<td>694.5 (32)</td>
</tr>
<tr>
<td>Mwangatini</td>
<td>398.7 (41)</td>
</tr>
<tr>
<td>Shakahola</td>
<td>1281.8 (28)</td>
</tr>
<tr>
<td>Total</td>
<td>559.4 (297)</td>
</tr>
</tbody>
</table>
Table 4.10: The percentage change in the geometric mean intensity for all eight study communities in 2002, 2003, 2005 and 2008.

<table>
<thead>
<tr>
<th>Year</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Microfilaria Positive Participants (n)</td>
<td>297</td>
<td>96</td>
<td>72</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>GMI†</td>
<td>559.9</td>
<td>163.3</td>
<td>108.5</td>
<td>102.7</td>
<td>78.6</td>
</tr>
<tr>
<td>Percent Change of Baseline (2002)</td>
<td>100.0%</td>
<td>71%</td>
<td>81%</td>
<td>82%</td>
<td>86%</td>
</tr>
</tbody>
</table>

†The Geometric Mean Intensity is measured by mf/ml
4.4.2 Geometric Mean Intensities by Gender

The GMI for the positive 141 males and the 156 females that were microfilaria positive was 618.9 mf/ml and 508.8 mf/ml respectively in 2002. As a general rule, microfilaremia prevalence increased with age for both sexes with a marked increase in males. However, the differences were not significantly different.

Table 4.11 illustrates the GMI by gender in 2002, 2003, 2004, 2007 and 2009. There were no statistically significant differences between the male and female participants (p = 0.883 in 2002, P = 0.952 in 2003, P = 0.974 in 2004, P = 0.565 in 2007 and P = 0.474 in 2009). The GMI for the male participants ranged from 618.9 mf/ml in 2002 to 67.9 mf/ml in 2009. From baseline (2002), the GMI percent change was 74% in 2003. In 2004, the change in the GMI was 84%. The change in the GMI among the male participants in 2007 was 88%. By 2009, the change in the GMI among the male participants was up to 89%.

The GMI for the female participants ranged from 508.8 mf/ml in 2002 to 82.1 mf/ml in 2009. In 2003, the GMI among the female participants had changed by 67.79% from 508.8 mf/ml to 163.9 mf/ml. The change in the GMI in 2004 was 76.61% when compared to the baseline GMI for the female participants. The GMI decreased by 76.61% in 2004 from the baseline to 119.0 mf/ml. In 2007, the GMI for the female participants had reduced by 74.27% which was a slight increase when compared with the GMI from the previous year. By 2009, the percentage decrease in the female participants GMI was at 83.86% when compared to the baseline GMI values.

| Year | Male |  | Female |  |  |  |  |  |
|------|------|  |------|----|  |----|----|---|
|      | Participants | microfilaria | positive | GMI† |  | Participants | microfilaria | positive | GMI† | All | P - value |
| 2002 | 141  |  | 618.9 |      |  | 156 | 508.8 |          | 559.4 | 0.883 |
| 2003 | 50   |  | 160.9 |      |  | 46 | 163.9 |          | 163.3 | 0.952 |
| 2004 | 36   |  | 97.0 |      |  | 36 | 119.0 |          | 108.5 | 0.974 |
| 2007 | 11   |  | 75.4 |      |  | 13 | 130.9 |          | 102.7 | 0.565 |
| 2009 | 3    |  | 67.9 |      |  | 7 | 82.1 |          | 78.6 | 0.474 |

†The Geometric Mean Intensity is measured by mf/ml
4.4.3 Geometric Mean Intensities by Age

Table 4.12 summarizes the GMIs within the different age groups. The overall GMIs from the year that treatment began to the years that the participants were treated were 559.4 mf/ml in 2002, 163.3mf/ml in 2003, 108.5mf/ml in 2004, 102.7mf/ml in 2007 and 78.6mf/ml in 2009.

The participants between the ages of 2 – 10 years had a mean GMI ranging from 432.6mf/ml in 2002 to 60.0mf/ml in 2009 with a percentage decrease of 59.74% in 2003, 64.33% in 2004, 85.51% in 2007 and 86.13% in 2009. The mean GMIs for those participants between the age of 11 – 20 years ranged from 586.1 mf/ml in 2002 to 0.0 mf/ml in 2009, representing a 100% change in the GMI.

Those participants between the age of 21 – 30 year, the GMI was 330.7 mf/ml in 2002 and dropped to 75.0 mf/ml in 2009. For the participants between the ages of 31 – 40 years, the mean GMIs ranged from 867.0mf/ml in 2002 to 95.4 mf/ml in 2009. The mean GMI ranged from 987.7mf/ml in 2002 to 50.5mf/ml in 2009 for those participants between the ages of 41 – 50 years. Participants over the age of 50 years had a mean GMI of 472.7mf/ml in 2002 to 140.2mf/ml in 2009.

<table>
<thead>
<tr>
<th>Age Group (Yrs)</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 - 10</td>
<td>30/432.6</td>
<td>11/174.1</td>
<td>6/154.3</td>
<td>5/62.7</td>
<td>1/60.0</td>
</tr>
<tr>
<td>11 - 20</td>
<td>76/586.1</td>
<td>25/247.4</td>
<td>16/122.0</td>
<td>4/196.1</td>
<td>0/0</td>
</tr>
<tr>
<td>21 - 30</td>
<td>55/330.7</td>
<td>18/144.7</td>
<td>14/107.5</td>
<td>5/101.0</td>
<td>2/75.0</td>
</tr>
<tr>
<td>31 - 40</td>
<td>44/867.0</td>
<td>19/123.7</td>
<td>15/118.2</td>
<td>5/106.3</td>
<td>2/95.4</td>
</tr>
<tr>
<td>41 - 50</td>
<td>39/987.7</td>
<td>10/183.8</td>
<td>11/123.3</td>
<td>2/119.5</td>
<td>3/50.5</td>
</tr>
<tr>
<td>&gt;50</td>
<td>53/472.7</td>
<td>13/107.6</td>
<td>10/52.4</td>
<td>3/79.6</td>
<td>2/140.2</td>
</tr>
<tr>
<td>All</td>
<td>297/558.4</td>
<td>96/162.3</td>
<td>72/107.5</td>
<td>24/101.7</td>
<td>10/77.6</td>
</tr>
</tbody>
</table>
4.5 Microfilaria Density

Microfilarial Density (MFD) describes the intensities of microfilaria based on the positive mf test results. There was a significant decrease in the density of microfilaria in the community from the data collected from the first treatment in 2002 until the fourth treatment in 2008 (Figure 4.5).

In 2002, 2003, 2004, 2007 and 2009, the microfilaria density was 208.5mf/ml in 2002, 66.9mf/ml in 2003, 42.4mf/ml in 2004, 29.5mf/ml in 2007 and 12.3mf/ml in 2009. The percentage change MFD in 2003, 2004, 2007 and 2009 was 67.9% after one mass treatment, 79.7% after two MDAs, 55.8% after three MDAs and 71.0% after four rounds of MDA respectively compared to the baseline density in 2002. Figure 10 and Table 4.13 illustrate the overall MFD in the communities in all the years of testing. According to Table 4.13, There as a significant difference in the MFD of all the years.

![Graph showing Microfilaria Density]

Figure 4.5: The microfilaria density in the community in the years 2002, 2003, 2004, 2007 and 2009.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Microfilaria Positive Participants (n)</th>
<th>MFD</th>
<th>P – value</th>
<th>Percent change from baseline (2002)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2002</td>
<td>2003</td>
<td>2004</td>
<td>2007</td>
</tr>
<tr>
<td>2002</td>
<td>297</td>
<td>96</td>
<td>72</td>
<td>24</td>
</tr>
<tr>
<td>2003</td>
<td>66.9</td>
<td></td>
<td>42.4</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2007</td>
<td>100%</td>
<td>86%</td>
<td>94%</td>
<td></td>
</tr>
</tbody>
</table>

Note: MFD = Microfilaria Density.
4.5.1 Microfilaria Density by Community

The difference in the MFD between the communities was not significantly different (p = 0.327) in 2002. In 2003, the difference between the communities was not significantly different (p = 0.068). In 2004, the difference between the MFD was no statistically significant (p = 0.794). The difference in the MFD between the study communities in 2007 was not statically different (p = 0.519). In 2009, the MFD between the communities was not significant (p = 0.683).

Between the years that the MFD was derived, there was a significant difference in 2002 (p < 0.001) (Table 4.14). In 2003, there was a significant difference in the MFD from the previous year (p < 0.001). In 2004, with a P = 0.007, there was no significant difference in the MFD when compared to the previous year. In 2007, there was no difference in the MFD of the community (p = 0.346). The difference in the overall MFD in the communities in 2009 was significantly different. The general trend was a significant decrease in the community load of microfilaria after mass treatment (Table 4.14).
Table 4.14: Community microfilaria density.

<table>
<thead>
<tr>
<th>Community</th>
<th>Mean</th>
<th>Year</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burangi</td>
<td>Mean</td>
<td>34.4</td>
<td>5.5</td>
<td>3.9</td>
<td>0.3</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>194</td>
<td>151</td>
<td>188</td>
<td>226</td>
<td>159</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chakama</td>
<td>Mean</td>
<td>56.8</td>
<td>41.6</td>
<td>4.7</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>148</td>
<td>58</td>
<td>112</td>
<td>183</td>
<td>139</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jilore</td>
<td>Mean</td>
<td>32.7</td>
<td>2.5</td>
<td>2.1</td>
<td>0.3</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>173</td>
<td>99</td>
<td>122</td>
<td>79</td>
<td>85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magongoloni</td>
<td>Mean</td>
<td>64.7</td>
<td>3.8</td>
<td>3.3</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>194</td>
<td>154</td>
<td>142</td>
<td>140</td>
<td>138</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marikano</td>
<td>Mean</td>
<td>35.7</td>
<td>5.8</td>
<td>6.2</td>
<td>2.0</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>192</td>
<td>105</td>
<td>111</td>
<td>111</td>
<td>106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community</td>
<td>Mean</td>
<td>6.6</td>
<td>0.7</td>
<td>1.1</td>
<td>0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>-------</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mkondoni</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>181</td>
<td>110</td>
<td>118</td>
<td>127</td>
<td>125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mwangatini</td>
<td>Mean</td>
<td>34.8</td>
<td>6.1</td>
<td>1.3</td>
<td>0.5</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>180</td>
<td>130</td>
<td>123</td>
<td>216</td>
<td>171</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shakahola</td>
<td>Mean</td>
<td>47.9</td>
<td>1.9</td>
<td>1.2</td>
<td>0.8</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>157</td>
<td>107</td>
<td>104</td>
<td>209</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Mean</td>
<td>43.6</td>
<td>7.0</td>
<td>3.0</td>
<td>0.5</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Number of Participants (N)</td>
<td>1419</td>
<td>914</td>
<td>1020</td>
<td>1291</td>
<td>1079</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.5.2 Microfilaria Density by Gender

A graphical presentation of the Microfilaria Density (MFD) of the study participants by gender is shown in Figure 4.6. Between the male and female participants, there was no significant difference in 2002 between the MFD (p = 0.883). In 2003, the MFD between the male and female participants was also not significantly different (p = 0.952). There was no significant difference in the MFD between the male and female participants in 2004 (p = 0.974). In 2007, the MFD between the males and females was not significantly different (p = 0.565). In 2009, as with all the previous years, there was no significant difference between the MFD of the male and female participants (p = 0.474).

Among the male and female participants, there was a significant difference in the MFD in 2003, (p < 0.001). The difference in the overall MFD among the males and females in 2003 was significant (p < 0.001). In 2004, the difference in the MFD was significant (p < 0.003). The overall MFD in 2007 was not significantly different (p = 0.015) and this was similar to the difference in the MFD in 2009, which was not statistically significant (p = 0.231).

![MFD by Gender](image)

**Figure 4.6: Microfilaria density in the male and female participants in 2002, 2003,**
4.5.3 Microfilaria Density Age

In 2002, the MFD between the different age groups was not statically different (p = 0.064). The difference in the MFD between the age groups was not significant (p = 0.925) in 2003. In 2004, the MFD among the different age groups was not statistically significant (P 0.716). The difference in the MFD between the age groups was not significant (p = 0.680) in 2007. In 2009, the MFD between the age groups was not statistically significant (p = 0.959). The MFD summarized by age group are represented in Figure 13 – Figure 18 and Table 4.15.

The difference in the MFD of among the different ages in 2002 was significant (p < 0.001). In 2003, the difference in the study populations’ age grouping for the MFD was statistically significant (p < 0.001). The statistical significance in 2004 (p = 0.005) represented the significant difference in the MFD by age. In 2007 and 2009, there was no statistical significance in the difference in the MFD in the different age groups.

<table>
<thead>
<tr>
<th>Classified Age of Participants in 2002</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 - 10 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants with a Microfilaria Count (N)</td>
<td>348</td>
<td>289</td>
<td>336</td>
<td>619</td>
<td>486</td>
</tr>
<tr>
<td>Mean</td>
<td>12.8</td>
<td>1.9</td>
<td>0.3</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Std. Error of Mean</td>
<td>3.9</td>
<td>1.1</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>11 - 20 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants with a Microfilaria Count (N)</td>
<td>418</td>
<td>265</td>
<td>256</td>
<td>252</td>
<td>183</td>
</tr>
<tr>
<td>Mean</td>
<td>41.3</td>
<td>7.4</td>
<td>2.8</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Std. Error of Mean</td>
<td>7.9</td>
<td>3.0</td>
<td>1.8</td>
<td>0.3</td>
<td>0.0</td>
</tr>
<tr>
<td>21 - 30 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants with a Microfilaria Count (N)</td>
<td>225</td>
<td>120</td>
<td>142</td>
<td>165</td>
<td>141</td>
</tr>
<tr>
<td>Mean</td>
<td>24.68</td>
<td>12.41</td>
<td>7.77</td>
<td>1.34</td>
<td>0.13</td>
</tr>
<tr>
<td>Std. Error of Mean</td>
<td>5.63</td>
<td>6.84</td>
<td>4.93</td>
<td>1.07</td>
<td>0.10</td>
</tr>
<tr>
<td>31 - 40 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants with a Microfilaria Count (N)</td>
<td>154</td>
<td>98</td>
<td>106</td>
<td>100</td>
<td>103</td>
</tr>
<tr>
<td>Mean</td>
<td>84.1</td>
<td>15.4</td>
<td>7.3</td>
<td>0.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Std. Error of Mean</td>
<td>24.3</td>
<td>11.0</td>
<td>5.3</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>41 - 50 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participants with a Microfilaria Count</td>
<td>132</td>
<td>75</td>
<td>99</td>
<td>80</td>
<td>88</td>
</tr>
</tbody>
</table>

85
<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. Error of Mean</th>
<th>Participants with a Microfilaria Count</th>
<th>Std. Error of Mean</th>
<th>Participants with a Microfilaria Count</th>
<th>Total</th>
<th>Std. Error of Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50 years (N)</td>
<td>76.5</td>
<td>19.5</td>
<td>142</td>
<td>20.6</td>
<td>1419</td>
<td>1419</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>7.5</td>
<td>3.7</td>
<td>67</td>
<td>2.4</td>
<td>914</td>
<td>914</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>2.3</td>
<td>1.0</td>
<td>81</td>
<td>0.9</td>
<td>1020</td>
<td>1020</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>1.7</td>
<td>1.6</td>
<td>74</td>
<td>1.6</td>
<td>1290</td>
<td>1290</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>0.5</td>
<td>78</td>
<td>0.4</td>
<td>1079</td>
<td>1079</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>43.6</td>
<td>4.7</td>
<td>1419</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.0</td>
<td>1.8</td>
<td>914</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.0</td>
<td>1.0</td>
<td>1020</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>0.2</td>
<td>1290</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>0.0</td>
<td>1079</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.6 Community Microfilarial Load

The Community Microfilarial Load (CMFL) represents the relative intensity of the community (CMFL) changes from a high of 2.8mf/ml at baseline in 2002 to 0.0mf/ml in 2009. This represents a 100.0% change from the baseline. The details of the changes in the CMFL are presented in Figure 4.7 and Table 4.16.

Figure 4.7: Averages for the community microfilarial load (CMFL) in 2002, 2003, 2004, 2007 and 2009.

<table>
<thead>
<tr>
<th>Year</th>
<th>2002</th>
<th>2003</th>
<th>2005</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of participants in the community positive for microfilaria (N)</td>
<td>1078</td>
<td>1289</td>
<td>1019</td>
<td>913</td>
<td>1418</td>
</tr>
<tr>
<td>CMFL</td>
<td>2.8</td>
<td>0.7</td>
<td>0.4</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>P - value</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.007</td>
<td>0.346</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Percentage Change</td>
<td>100.0%</td>
<td>75.0%</td>
<td>85.7%</td>
<td>96.4%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

4.6.1 Community Microfilaria Load in the study communities

The overall CMFL in the communities ranged from 2.2mf/ml to 3.4mf/ml in 2002. The CMFL was significant with values <0.001 in 2002, 2003, and 2009. However, there was no significant difference between the community groups (p = 578). In 2003, the communities’ microfilariae intensity ranged from 0.3mf/ml to 3.1mf/ml. There was a significant difference between the community groups CMFL (p < 0.001). The CMFL in
2004 ranged between 0.2mf/ml to 0.5mf/ml. With a P = 0.889, there was no significant difference between the community groups. In 2007, the intensity of microfilariae in the communities ranged from 0.0mf/ml to 0.2mf/ml. There was no significant difference between the groups (p = 388). In 2009, the CMFL intensity ranged between 0.0 mf/ml to 0.2 mf/ml and with a P = 0.95, there was no significant difference between the community groups. This is summarized in Table 4.17 below.

There was a significant difference in the CMFL between the years that the communities were tested (p < 0.001)

<table>
<thead>
<tr>
<th>Community</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burangi</td>
<td>3.1</td>
<td>0.7</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Chakama</td>
<td>3.4</td>
<td>2.1</td>
<td>0.4</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Jilore</td>
<td>2.2</td>
<td>0.6</td>
<td>0.5</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Magongoloni</td>
<td>3.4</td>
<td>0.9</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Marikano</td>
<td>2.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Mkondoni</td>
<td>2.2</td>
<td>1.0</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Mwangatini</td>
<td>2.9</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Shakahola</td>
<td>2.6</td>
<td>0.3</td>
<td>0.4</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>All</td>
<td>2.8</td>
<td>0.7</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>
4.6.2 Community Microfilaria Load by Gender

Figure 4.8 and Table 4.18 both summarize the Community Microfilaria Load by gender. Between the male and female participants, the CMFL had a decreasing trend with the males having a slightly higher CMFL although this was not statistically significant in 2002 ($p = 0.567$). The difference between the CMFL between the male and female participants was not statistically significant ($p = 600$) in 2003. In 2004, the CMFL between the male and female participants was not significantly different ($p = 0.795$). The CMFL in 2007 was not significantly different between the males and the females ($p = 0.559$). There was no significant difference in the CMFL between the male and female participants in 2009.

![Community Microfilaria Load](image_url)

Table 4.18: Community Microfilaria Load by Gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>3.3</td>
<td>0.8</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Female</td>
<td>2.4</td>
<td>0.6</td>
<td>0.4</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>All</td>
<td>2.8</td>
<td>0.7</td>
<td>0.4</td>
<td>0.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

4.6.3 Community Microfilaria Load by Age

Between the different age groups, there was a significant difference in the CMFL in 2002, (p < 0.001). In 2003, there was no significant difference between the age groups CMFL (p = 0.402). The difference in the CMFL within the age groups was not statistically significant (p = 0.253) in 2004. In 2007, the difference in the CMFL within the different age groups was not statistically significant (p = 0.226). The difference in the age group CMFL was not significant in 2009 (p = 0.083). These results are shown in Table 4.19 below.

<table>
<thead>
<tr>
<th>Classified Age</th>
<th>Community Microfilaria Load (mf/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2002</td>
</tr>
<tr>
<td>2 - 10 years</td>
<td>0.7</td>
</tr>
<tr>
<td>11 - 20 years</td>
<td>2.2</td>
</tr>
<tr>
<td>21 - 30 years</td>
<td>3.1</td>
</tr>
<tr>
<td>31 - 40 years</td>
<td>5.9</td>
</tr>
<tr>
<td>41 - 50 years</td>
<td>6.7</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>9.0</td>
</tr>
<tr>
<td>All</td>
<td>2.8</td>
</tr>
</tbody>
</table>

### 4.7 Circulating Filarial Antigen

Table 4.20 shows the CFA prevalence using the ICT test in the eight study communities. 34.4% (501/1447), 26.6% (242/915), 18.7% (188/1016) and 14.0% (183/1305) were antigen positive in 2002, 2003, 2004 and 2007 respectively. In 2009, 11.4% (115/1041) were antigen positive. In the same year, for the first time, 3.6% (38/1041) were recorded as faint positives representing uncertain positive results.
Table 4.20: Circulating Filarial Antigen by Community and Gender in the years 2002, 2003, 2004, 2007 and 2009

<table>
<thead>
<tr>
<th>Community</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009</th>
<th>Faint Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. ICT Positive / No. Tested (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burangi</td>
<td>69/198 (34.8)</td>
<td>35/149 (23.5)</td>
<td>29/187 (15.5)</td>
<td>29/229 (12.7)</td>
<td>12/159 (7.5)</td>
<td>7/159 (4.4)</td>
</tr>
<tr>
<td>Chakama</td>
<td>44/148 (29.5)</td>
<td>19/58  (32.8)</td>
<td>20/113 (17.7)</td>
<td>26/185 (14.1)</td>
<td>16/142 (11.3)</td>
<td>8/142 (5.6)</td>
</tr>
<tr>
<td>Jilore</td>
<td>66/172 (38.4)</td>
<td>25/100 (25.0)</td>
<td>24/123 (19.5)</td>
<td>14/78  (17.9)</td>
<td>13/89  (14.6)</td>
<td>6/89 (6.7)</td>
</tr>
<tr>
<td>Magongoloni</td>
<td>85/198 (42.9)</td>
<td>49/154 (31.8)</td>
<td>31/143 (21.7)</td>
<td>12/140 (8.6)</td>
<td>20/138 (14.5)</td>
<td>0/138 (0.0)</td>
</tr>
<tr>
<td>Marikano</td>
<td>65/196 (33.2)</td>
<td>27/105 (25.7)</td>
<td>24/111 (21.6)</td>
<td>20/113 (17.7)</td>
<td>15/108 (13.9)</td>
<td>2/108 (1.9)</td>
</tr>
<tr>
<td>Mkondoni</td>
<td>50/182 (27.5)</td>
<td>28/110 (25.5)</td>
<td>20/118 (16.9)</td>
<td>15/127 (3.9)</td>
<td>11/126 (8.7)</td>
<td>2/126 (1.6)</td>
</tr>
<tr>
<td>Mwangatini</td>
<td>71/195 (36.4)</td>
<td>38/131 (29.0)</td>
<td>21/122 (17.2)</td>
<td>29/219 (13.2)</td>
<td>15/173 (8.7)</td>
<td>9/173 (5.2)</td>
</tr>
<tr>
<td>Shakahola</td>
<td>51/157 (32.5)</td>
<td>21/107 (19.6)</td>
<td>19/98 (19.4)</td>
<td>18/212 (8.5)</td>
<td>13/106 (12.3)</td>
<td>4/106 (3.8)</td>
</tr>
<tr>
<td>Both Males</td>
<td>241 (16.7)</td>
<td>124 (13.6)</td>
<td>99 (9.8)</td>
<td>97 (7.4)</td>
<td>59 (5.7)</td>
<td>20 (1.9)</td>
</tr>
<tr>
<td>Females</td>
<td>260 (18.0)</td>
<td>118 (12.6)</td>
<td>89 (8.8)</td>
<td>76 (6.6)</td>
<td>56 (5.4)</td>
<td>18 (1.7)</td>
</tr>
<tr>
<td>All</td>
<td>501/1447 (34.6)</td>
<td>242/915 (26.5)</td>
<td>188/1016 (18.5)</td>
<td>173/1305 (13.3)</td>
<td>115/1041 (11.0)</td>
<td>38/1041 (3.7)</td>
</tr>
</tbody>
</table>
4.7.1 Circulating Filarial Antigen by Community

The prevalence of antigenemia in the eight communities ranged from 34.6% in 2002 to 3.7% in 2009 and the difference within the different communities was significant, with an overall significant difference within the years (p < 0.001) (Table 4.20).

In 2002, the community of Burangi had a prevalence of 34.8% which decreased significantly (p < 0.001) to 7.5% by 2009 with a percentage change of 21.5%. In Chakama, the prevalence decreased significantly (p < 0.001) from 29.5% in 2002 to 11.3% after four rounds of MDA with a percentage change of 38.3%.

The community of Jilore recorded a significant decrease in prevalence from 38.4% to 14.6% (p < 0.001) with a decrease in the percentage of 38.0%. The participants in Magongoloni had a CFA prevalence of 42.9% in 2002 which decreased to a prevalence of 14.5% by 2009 (p < 0.001) with a percentage change of 33.8%.

The community of Marikano recorded a significant decrease in prevalence from 33.2% in 2002 to 13.9% in 2009 (p < 0.001) with a decrease in the percentage of 41.9%. In 2002, the community of Mkondoni had a prevalence of 27.5% which decreased significantly (p < 0.001) to 8.7% by 2009 with a percentage change of 31.6%. The community of Mwangatini recorded a significant decrease in prevalence from 36.4% in 2002 to 8.7% in 2009 (p < 0.001) with a decrease in the percentage of 23.9%. The community of Shakahola recorded a significant decrease in prevalence from 32.5% pre-treatment to 12.3% post-MDA 4 (p < 0.001) with a decrease in the percentage of 37.8%.

Figure 4.9 below summarizes the prevalence of antigenemia in the eight study communities after MDA was administered. The percentage prevalence of ICT positive individuals in the study communities decreased significantly (p < 0.001) after four rounds of treatment from 34.6% prevalence to 11.0% prevalence.
4.7.2 Circulating Filarial Antigen Results by Gender

Of those tested using the ICT card, 501, 242, 188, 183 and 115 in total were antigen positive in 2002, 2003, 2004, 2007 and 2009 respectively. Table 4.20 describes the CFA data in all the communities. The general distribution of the gender of the participants in the years of testing shows that there were slightly more females than males who participated in all the years except for 2003 where the number of males was slightly more than that of females.

In 2002, 1447 participants were involved in the study. Of the 643 were male and 804 were female. There was no statistical difference between the two groups (p = 0.041). Of the 501 participants who were ICT positive, 241 (37.0%) males and 260 (32.2%) were females were found to be antigen positive.
In 2003, 915 participants were tested, 417 were male and 498 were female with the females being slightly more than the males however, there was no significant difference between the males and the females (p = 0.039). Of those found to be antigen positive, 124 (13.6%) participants were male and 118 (12.6%) participants were female. 

Of 1016 participants tested, there were 460 male and 556 female tested in 2004; there was no significant difference (p < 0.0241) between the two genders. Of the 188 participants who were antigen positive, 99 (9.8%) were male and 89 (8.8%) were female. 

From those 1305 persons who participated in 2007, between the 619 male and the 686 female, there was no significant difference (p = 0.011) between the two genders. Of the 173 antigen positive participants, 97 (7.4%) were male and 76 (6.6%) were female.

Of the 1096 persons who were tested in 2009, 502 were males and 594 were females. Similar to the previous years, there was a difference (p = 0.141) between the two sexes. Of the 115 (11.0%) antigen positive participants, 59 (5.7%) were male and 56 (5.4%) were female. In this same year, 38 (3.7%) uncertain positives, 20 (1.9%) being male and 18 (1.7%) being female participants were recorded.
Figure 4.10 and Figure 4.11 illustrate the gender distribution of the participants who were tested in 2002, 2003, 2004, 2007 and 2009.

Among those tested, a higher proportion of male participants tested positive compared to females in all the years except 2002. In 2002, the number of females who were antigen positive using the ICT was slightly higher than that of the males. Faint positive results were only recorded in 2009.

4.7.3 Circulating Filarial Antigen by Age

Table 4.21 summarizes the ICT results recorded in all the years of testing by age groups. There was a general decrease in antigenemia in the different age groups.

In 2002, the frequency of positive ICT results was highest among the ages 11 – 20 which was 131 (26.1%) and lowest among the participants between the ages of 41 – 50 years who had a total of 61 (12.2%). The difference between each age group was statistically significant (p < 0.001).

The number of those who were ICT positive in 2003 ranged from 9.9% – 28.5% with a significant difference (p < 0.001) between the different age groups. The participants between the ages of 41 – 50 years had the fewest ICT positive participants while those
between the ages of 11 – 20 years had the highest ICT positive participants. Both results were similar to the results in 2002.

In 2004, the frequency of positive ICT results ranged from 12.2% - 26.1% with the highest age range being those participants between the age of 11 – 20 years and the lowest range being those participants between the age of 2 – 10 years. The difference between each age group was statistically significant (p < 0.001).

The number of ICT positive participants in 2007 was highest among the ages 21 – 30 and lowest among those between the ages of 41 – 50 years. The prevalence ranged from 9.9% - 23.3%. The difference between each age group was statistically significant (p < 0.001).

In 2009, the participants between the ages of 21 - 30 years had the highest number of ICT positive participants. Those between the ages of 2 – 10 years had the lowest number of ICT positive participants. The differences between the groups were statistically significant (p < 0.001). The change in the antigenemia results by age in all the years of testing is illustrated in Figure 4.12. Antigenemia frequency decreased significantly in all the age groups.

While there was a significant difference in the overall ICT results between 2002 (p < 0.001), there was no statistical significance within the groups in 2003 (p = 0.143) and 2004 (p = 0.936).
Table 4.21: Immunochromatographic card test results defined by the classified age group in all the eight study communities in 2002, 2003, 2004, 2007 and 2009.

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2007</th>
<th>2009 Faint Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 – 10</td>
<td>72/501 (14.4%)</td>
<td>38/242 (15.7%)</td>
<td>23/288 (12.2%)</td>
<td>28/172 (16.3%)</td>
<td>10/114 (8.8%) 9/38 (23.7%)</td>
</tr>
<tr>
<td>11 – 20</td>
<td>131/501 (26.1%)</td>
<td>69/242 (28.5%)</td>
<td>49/188 (26.1%)</td>
<td>38/172 (22.1%)</td>
<td>21/114 (18.4%) 10/38 (26.3%)</td>
</tr>
<tr>
<td>21 – 30</td>
<td>82/501 (16.4%)</td>
<td>42/242 (17.4%)</td>
<td>33/188 (17.6%)</td>
<td>40/172 (23.3%)</td>
<td>24/114 (21.1%) 5/38 (13.2%)</td>
</tr>
<tr>
<td>31 – 40</td>
<td>73/501 (14.6%)</td>
<td>40/242 (16.5%)</td>
<td>29/188 (15.4%)</td>
<td>23/172 (13.4%)</td>
<td>19/114 (16.7%) 5/38 (13.2%)</td>
</tr>
<tr>
<td>41 – 50</td>
<td>61/501 (12.2%)</td>
<td>24/242 (9.9%)</td>
<td>26/188 (13.8%)</td>
<td>17/172 (9.9%)</td>
<td>17/114 (14.9%) 6/38 (15.8%)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>82/501 (16.4%)</td>
<td>29/242 (12.0%)</td>
<td>28/188 (14.9%)</td>
<td>26/172 (15.1%)</td>
<td>23/114 (20.2%) 3/38 (7.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>P - Value</th>
<th>(&lt; 0.001)</th>
<th>(0.142)</th>
<th>(0.936)</th>
<th>(&lt; 0.001)</th>
<th>(&lt; 0.001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>501</td>
<td>242</td>
<td>188</td>
<td>172*</td>
<td>114*</td>
</tr>
</tbody>
</table>

* Data on age incomplete for 5 participants.
4.8 Impact of MDA on Microfilaremia

The impact of MDA was assessed using the post MDA data collected about a year after each mass treatment. A total of 1447, 915, 1016, 1305 and 1041 participants were tested for microfilaremia in 2002 (baseline), were tested in 2003 (post MDA 1), were tested in
2004 (post MDA 2), were tested in 2007 (post MDA 3) and were tested in 2009 (post MDA 4) respectively.

The overall prevalence of microfilaremia in 2002, 2003, 2004, 2007 and 2009 was 20.9% (with a range of a prevalence of 22.9% - 17.7%), 10.5% (14.8% - 4.8%), 7.1% (range 9.0% - 4.2%), 1.9% (range 6.8% - 0.0%) and 0.9% (range 3.5% - 0.0%) respectively. The changes in the study communities are shown in Figure 4.13.

After the first MDA, microfilaremia prevalence decreased by 49.8% and was significantly lower than at baseline (p < 0.001). After the second MDA, in 2004, microfilaremia decreased significantly by 66.0% (p < 0.001). In 2007, after the third round of MDA, microfilaria prevalence decreased by 90.9% (p < 0.001) and after the fourth round of MDA in 2009, microfilaremia prevalence decreased by 95.7% (p < 0.001).

![Graph showing trends in antigen positive and microfilaria positive frequencies](image)

**Figure 4.13** Trends in antigen positive and microfilaria positive frequencies for all the eight communities in 2002, 2003, 2004, 2007 and 2009.
5.1 Discussion

5.1.1 Effect of the Elimination on Lymphatic Filariasis

The public health significance and socio-economic importance of LF in affected communities are overwhelming (Molyneux et al., 2003). Elephantiasis is one of the most disabling and disfiguring of diseases. It is a disease of poverty – affecting the "poorest of the poor" – preventing those afflicted from living a normal working and social life. Lymphatic filariasis is a disease that requires time to establish and children who acquire the disease early and are shattered for life.

The elimination of LF is of important significance because with it, those affected will be able to tackle the elimination of extreme poverty and hunger. Being a disease of poor, LF elimination reduces the cost of healthcare and increase individual productivity (Molyneux, 2003).

5.1.2 The role of WHO, the GPELF and the NPELF

The GPELF calls for the LF endemic countries under the WHO to round up efforts to eliminate the disease as a public health problem. The programs’ strategies are based on the control transmission, in collaboration with NPELF and different partners, to reduce LF infection using available cost effective drugs that are able to reduce microfilaria loads significantly along with the integration of STH control and various other vector control measures (Molyneux, 2008). The drugs that are used are: (i) albendazole and ivermectin in countries co-endemic for onchocerciasis and LF; and (ii) DEC and albendazole in areas where LF alone is endemic (W. bancrofti, B. malayi and B. timori). A combined regimen of DEC and Albendazole is currently the recommended MDA regimen of annual treatment in Kenya. This annual dose may have a greater effect on eliminating W. bancrofti adult worms than DEC alone or DEC combined with
ivermectin (Tisch et al., 2005) however, one study suggests that there was no difference in the impact of DEC alone to DEC plus albendazole on microfilaria status, with a modestly greater effect of the combination on lowering antigenemia (the proportion of antigen-positive individuals decreased by 10% for DEC alone versus 17% for the combination) (Bockarie et al., 2007). The results may be different if the MDA regimen is different. In a study in Papua New Guinea (Bockarie et al., 2002), the first round of mass treatment with a DEC/ivermectin combination decreased the level of microfilaremia by 91%, but a further decrease of only 4% to 95% was seen after four rounds of MDA. These results are similar to the results observed in the current study with a marked decrease of 95.6% from a prevalence of 20.9% in 2002 to a prevalence of 0.9% by 2009.

The elimination of LF also strongly relies on effective monitoring and evaluation to evaluate the outcome of the member states’ program successes. The strategies used to monitor and evaluate the impact of the elimination of LF are: (i) extensive mapping and collection of baseline data, which is essential for follow-up evaluation of progress in achievement of desired treatment, antigenemia and microfilaremia status, using both ICT and microfilariae detection, and (ii) the need for surveillance to carefully monitor the progress of treatment and the endpoints of disease transmission. Monitoring would eventually require the use of more W. bancrofti sensitive methods as the program is heading towards completion. Such methods could include molecular xenomonitoring and the use of Bm14 markers that are specific to bancroftian filariasis.

Detailed epidemiological data on prevalence and intensity of disease and other indicators (clinical presentation) of transmission and infection are important to help assess the impact of mass chemotherapy and enable those concerned to understand the progress of the elimination program. Microfilaria detection and Immunochromatographic card testing are the gold standard methods of evaluating and monitoring infection during mass chemotherapy and LF transmission; (ii) Post – MDA surveillance to monitor the
effect of treatment and evaluate the indicators of the interruption of transmission to be able to determine the end point in a program; and (iii) Post – endpoint surveillance to be able to stamp out the re-emergence of the disease in endemic areas.

There are four main LF foci in the Coastal Province of Kenya, an area west of Mombasa town, an area bordering Tanzania, an area in Kilifi town and the area along the River Sabaki in Malindi District (Njenga, 2005). The present study was conducted in the selected study communities along the River Sabaki. The present study was conducted in inland rural communities in the North Coast region. This site is the same site of other LF studies (KEMRI SSC Nos. 597, 658, 1116). This study site was identified as a high LF endemic area and was thus selected (Wijers & Kaleli, 1983; Njenga et al., 2007). The results of this study provide additional insight into the interpretation of the progress of LF elimination in Malindi district, Kenya.

The original sample drawn in 2002 for the baseline study was composed of 643 males and 803 females. This might be as a result of their ease of availability and willingness to participate in the program. It may be that women were less worried about the nature of the tests and are more concerned with health issues or probably because most of the adult males work in towns and cities outside the communities and were not available at the time of testing. A number of people refused to participate in the citing suspicions that the blood drawn from them was meant for testing their HIV/AIDS status. As a result, more females were consistently registered in greater numbers than their male counterparts.

Of the participants recruited in the study, 52.8% have been children under the age of 15. These children were volunteered with their parents’ consent. Given that most of these children are in the primary school going age and hence easily available at home at most times in the year might explain their high numbers among the participants. The number of participants reduces with increase in age which reflects normal demographic trends.

This trend was similar to another study conducted in Zanzibar where the age-
group of 10–19 years old was the most represented, in line with current demographic trends in Tanzania and most developing countries (Weil, et al., 2007) and the number of females was generally higher than that of males. (Table 1, Figure 6). This can be mainly explained by the fact that both Kinyasini and Mtambile are rural areas where young males are either farmers or have employment in town. Hence, they usually leave their houses early in the morning and return back late in the evening (Mohammed, 2008). A younger age set may however affect the outcome of the results because LF has been previously recorded as a disease that increases with age.

5.1.3 Impact of MDA on Parasitemia and Antigenemia

Microfilaria prevalence and circulating filarial antigen intensities decreased substantially from the first MDA administered in 2002 from a prevalence of 20.9% in 2002 to 0.9% in 2009 and a decrease in intensity from 34.8% in 2002 to 10.8% in 2009. There was a marked decline in prevalence and intensity values between the first MDA and the second MDA. Subsequent treatment (MDA-3 and MDA-4) seemed to sustain the already declined prevalence and intensity levels. Despite the missing of three rounds of treatment, the results obtained show that there was a steady decrease in prevalence and intensity of infection. These results are similar to findings by Njenga et al., 2011 in a similar study of the same endemic area.

Seven years after commencement of MDA and after four rounds of treatment, only 10 individuals out of 1078 were mf positive in 2009. Based on microfilaremia data collected over this period, there is an evident decrease in the proportion of mf positive results to total mf results. This corresponds with a decreasing trend of positive ICT results. The baseline records that 20.9 percent of study participants tested positive in 2002 compared to 0.9% in 2009. This happened with missed MDA’s in three years over this period notwithstanding.
After four rounds of MDA with DEC/albendazole there was a marked decrease in the prevalence of microfilarial density from 208.49 in 2002 to 12.3 in 2009. Another study indicated a similar decrease in levels of microfilaremia, while suggesting that further rounds of MDA may be necessary to achieve a sustained reduction (Njenga et al., 2008). The significant decrease in microfilaria prevalence after each round of mass treatment suggests that most of those who were microfilaria positive at baseline might become microfilaria negative after subsequent rounds of MDA (Njenga et al., 2008).

When compared to ICT results, mf positive results declined more rapidly. The risk of being mf positive decreased by approximately 40% per year and this was considered to be statistically significant (OR = 0.591; P < 0.001). Therefore, despite missing three treatments, the impact of the MDA’s is therefore considered as having been effective in reducing the mf load over time from among the study participants and the population.

Furthermore there was no statistically significant risk of being at risk of infection by being a member of one community in relation to another. All participants in the study therefore had equivalent risk of being infected with the parasites.

5.1.4 Impact of MDA in Antigenemia

ICT tests from 2002 to 2007 were either considered positive or negative. However, in 2009, a number of ICT results were considered faint positive (indeterminate results). Of the 153 individuals’ who tested positive in 2009, 38 had results that were inconclusive. These may be as a result of circulating filarial antigens in the blood even after the clearing of circulating microfilaria infection or the presence of sterile adult worms, which may be an indicator of the need to administer a drug that will target the adult worms.

In long-term follow-up studies, it is important to acknowledge that the temporal relationship between drug-mediated killing of adult *W. bancrofti* worms and antigen or antibody clearance from plasma is not known (Tisch et al., 2009). In the case of antigen, the lack of change in status likely reflects the slow clearance of the Og4C3 target antigen.
from the circulation, as reported by other studies, (Nicholas et al., 1997) and the failure to completely eliminate adult worms with five annual rounds of MDA. Compared to ICT results, mf frequencies decreased more rapidly than ICT results.

Overall, ICT results in the study consistently reported a decline in the level of antigenemia among the study participants beginning with a high of 34.6% at baseline in 2002 to a low of 14.7% in 2009.

This tends to support previous studies with respect to filarial antigen, where this variable decreased to a greater extent in Egypt than Papua New Guinea. In the highest transmission area of Egypt, pre-MDA and post-MDA antigen positive rates were 19.0% and 4.8%, whereas in Papua New Guinea, there was no significant change after the fourth round of MDA relative to the pre-MDA prevalence of 86.5% (Tisch et al., 2009). The decline in levels of antigenemia was reported in other studies (Njenga et al., 2008; Noroes et al., 1997; Ottesen, 1985). The trend indicates that in spite of the missed MDAs in 2004, 2006 and 2007, a general decrease in the level of antigenemia has been observed amongst the study participants.

It was observed that a higher proportion of male participants tested positive in all the years. Whereas the participation of females as study participants was consistently higher in all communities, it was revealed that their general level of antigenemia is less than that of their male counterparts. This might be explained by the fact that women are more cooperative than men in health initiatives affecting their communities and that many of them are likely to follow through on treatment regimes. This is corroborated by the fact that many more females than males reported to have received treatment in the years that MDA was administered. These results corroborate the previous findings above that a higher proportion of antigen positive males were consistently recorded compared to females (Njenga et al., 2007).

It appears that the reduction in the frequency of infection is higher among younger participants than older ones. The composition of the positive results by age of the initial
study group in 2002 recorded a high frequency of children below the age of 15. The highest frequencies were reported in the 11 - 20 year age group. However, a review of the same results by age in 2009 revealed that there were virtually no antigen positive cases among children in the 2 - 10 year age group while the highest frequencies were recorded among older people above the age of 50.

The reduction in the infection frequencies among younger participants is an indication of reduction in transmission of the parasites. Positive responses in young children are suggestive of either recent filarial exposure or infection (Mladonicky et al., 2009). Persistence of infections among older participants on the other hand is a reflection of the established status of the infection after many years of exposure of people in this age group. In principle, children born after the introduction of MDA represent the best population for detecting incident infections (Tisch et al., 2004).

In a similar study the 7- to 8-year-old children (the youngest group examined) living in the highest transmission site in Egypt, pre- and post-MDA antibody rates fell from 10.0% to 0.4% (mf rates were not described); in Papua New Guinea, where 1- to 6-year-old children were examined, antibody rates fell from 75.0% to 37.0% (P < 0.01) and mf rates fell from 26% to 0% (P < 0.001).

Logistic regression results revealed that duration, sex and age of study participants were important determinants of ICT status. The effect of time was found to be statistically significant at P < 0.001. It was observed that with every passing year, the average level of antigenemia decreased by an average of 17%. This is an indication that in spite of the missed MDA in the indicated years, the level of antigenemia has been decreasing over time among the study participants and by extension in Malindi District.

The estimated risk of antigenemia for males was 1.4 times compared to that of females and this was considered to be statistically significant. As discussed before, this may be a result of women’s response to treatment and greater likelihood to cooperate with both researchers and medical personnel on matters affecting their families.
In 2002, the frequency of positive ICT results was highest among the ages 11-20 and lowest among ages 2 - 10. In 2009, the 11-20 age group manifested the lowest ICT test results compared to age 50 and above which recorded the highest. It appears that the reduction in the frequency of infection is higher among younger patients compared to reduction amongst older participants.

5.1.5 Impact of Treatment Coverage

As stated earlier, MDA was administered in 2002, 2003, 2005 and 2008. Ideally the study should have been able to track exactly the same people recruited in 2002 throughout the period of the study. This however was not possible due to unavoidable demographic movements, refusal to participate, and pregnancy and for children below the age of 2.

It was observed that on average, more females than males were recorded as having received treatment consistently over the years. This might be explained by the general higher proportion of females to males in this region that could be as a result of urban migration of the males in search of employment.

Treatment coverage among the study participants was generally observed to be reasonably high among all the communities and throughout all the years. It might be argued that this coverage is higher than that of the general population due to greater exposure to information on the usefulness of MDA as a result of interaction with the research team. It might also be implied that the study participants are a generally more cooperative group that is therefore expected to take initiative to ensure participation in MDA treatment rounds.

Nevertheless, it was observed that respondents recorded the highest participation in the MDA in 2005 at 94.1% compared to a low of 72.2% in 2008. This was corroborated by a number of complaints from the 2008 participants indicating that drug distribution in 2008 was not comprehensively carried out in the study area.
Overall, a total of 63% of study participants interviewed indicated having participated in all MDA’s, with 0% having missed all. This means that everyone in the study area received at least one round of MDA and that more than half the population had received all the rounds of the treatment.

5.2 Conclusion

Since the inception of Kenya’s National Program to Eliminate Lymphatic Filariasis in 2002, four rounds of Mass Drug Administration have been administered in the endemic population of Malindi, Kenya, between 2002 and 2009. Within this same period the recommend annual treatment regimen was missed four times. Despite the missed rounds of MDA, the four rounds of MDA administered within the study period showed a dramatic decrease in the microfilaria prevalence and circulating filarial antigen intensities of the participants in the 8 study communities in Malindi district. These results from the study suggest that, in an LF elimination program using a combination of DEC and albendazole, staggering of treatment may not have a negative effect on microfilaremia and antigenemia of the participants at risk.

The reduction may be attributed to several things:

- The MDA treatment that was provided,
- The use of integrated vector management in the control of malaria thus reduced vector contact with individuals,
- Reduced parasite intensities in affect individuals thereby limiting increase of transmission, or
- Environmental factors affecting vector breeding.

Even with the reduced microfilaremia and antigenemia levels in the study participants, it is recommended that MDA should be continued as regularly as is available to avoid extending the recommended treatment period which would also have financial implications. As the NPELF program in Kenya is heading toward completion, it will be imperative that surveillance should be carried out in the areas where treatment is being administered. There will also be need to comprehensively monitor and evaluate the
progress of the program to determine the end-points.

It is also recommended that as the mf and CFA levels further decline, more sensitive methods of testing may be necessary to be able to detect infection. The use of *W. bancrofti* specific tests such as the use of Bm14 markers and molecular xenomonitoring would be more appropriate in areas where infection levels are down.
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World Health Organization. 2014. A Global Brief on Vector-Borne Diseases


APPENDICES

Appendix 1  Letter of Approval from KEMRI-ERC

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840 - 00206 NAIROBI, Kenya
Tel: (254) (020) 2722541, 2713349, 0722-205661, 0733-400003, Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website: www.kemri.org

KEMRI/RES/7/3/1

November 8, 2009

TO: MS. MERCY L MKANDAWIRE (PRINCIPAL INVESTIGATOR)

THROUGH: DR. SAMUEL KARIUKI,
THE ACTING DIRECTOR, CMR,
NAIROBI

RE: SSC PROTOCOL NO. 1481 (RE-SUBMISSION): EVALUATION OF THE EFFECT OF MISSED MASS DRUG ADMINISTRATION ON FILARIAL INFECTION IN MALINDI DISTRICT, KENYA

Make reference to your letter dated October 22, 2009. Thank you for your response to the issues raised by the Committee.

This is to inform you that the issues raised during the 167th meeting of KEMRI/National Ethics Review Committee held on Tuesday 16th June 2009, have been adequately addressed.

Due consideration has been given to ethical issues and the study is hereby granted approval for implementation effective this 8th day of November, 2009, for a period of twelve (12) months.

Please note that authorization to conduct this study will automatically expire on 7th November 2010. If you plan to continue with data collection or analysis beyond this date, please submit an application for continuing approval to the ERC Secretariat by 26th September 2010.

You are required to submit any amendments to this protocol and other information pertinent to human participation in this study to the ERC prior to initiation. You may embark on the study.

Yours sincerely,

R. C. KITHINJI,
FOR: SECRETARY,
KEMRI/NATIONAL ETHICS REVIEW COMMITTEE
Appendix 2  Consent forms for persons aged 18 years and above

Title of Study: Evaluation of the effect of missed mass drug administration on filarial infection in Malindi district, Kenya.

Sponsor: Institute of Tropical Medicine and Infectious Diseases - Kenya Medical Research Institute (ITROMID - KEMRI) Project.

Introduction

You are asked to participate in a medical research study on lymphatic filariasis. Lymphatic filariasis is a disease caused by parasites that are transmitted from one person to another by mosquitoes. When the parasites enter the body, they move into vessels called the lymphatic vessels, where they grow into thread-like adult worms. If not diagnosed and treated promptly, filariasis can lead to severe disability due to the resulting lymphedema and hydrocele. The international body called the World Health Organization (WHO) has decided to eliminate lymphatic filariasis as a public health problem by giving treatment to all persons living in the areas where the disease occurs. The purpose of this consent form is to give you information that might help you to decide whether to participate in the study or not. You are allowed to ask questions related to the study and implications on your part.

Purpose of the study

The recommended treatment in Kenya is a combination of two drugs namely, diethylcarbamazine (DEC) and albendazole given once a year to all individuals living in endemic areas. Many elimination programs are faced by difficulties in conducting MDAs mainly due to financial limitations. In Kenya the communities in endemic areas have received four rounds of mass treatment in 2002, 2003, 2005 and 2008 respectively. Because of financial constraints, the Ministry of Health was unable to administer the necessary drugs in 2004, 2006 and 2007. This study will attempt to find out what impact the missing of regular rounds of MDA has on the overall success on the interrupting transmission. The information of this study will provide the Ministry of Health with
information about what impact missing the annual rounds of treat have on the overall success of eliminating lymphatic filariasis from the country.

**Procedure to be followed**

The study nurse or technician will prick your figure for a drop of blood to find out if it has filariasis parasites. If the first test is positive, a second finger prick blood sample will be required from you microfilaria counting using the Counting Chamber technique with the aid of a microscope. This counting will be done at the Malindi District Hospital – KEMRI laboratory and at the Langobaya National Water Corporation (NAWACO) dispensary laboratory. The blood will not be tested for HIV and the results of the various tests will be returned to you.

**Risks**

The risk from participation in this study is minimal. Blood drawing may cause a slight pain and possibly a bruise where the blood is drawn.

**Benefits**

Your blood will be checked for filariasis parasites. You and the rest of the community will be given mass treatment free of charge. The treatment also has benefits for removing intestinal worms.

**Assurance of confidentiality**

Your name and other records will remain confidential and will not appear when we present this study or publish its results. You will receive a copy of the consent form.

**Right to refuse or withdraw**

It is important that you understand the following general principles that will apply to all participants in the study:

1. Your participation is entirely voluntary

2. You may withdraw from this study any time without penalty or loss of benefits.
Please feel free to ask any questions that you may have.

Do you agree to participate?

I acknowledge that this consent for has been fully explained to me in a language that I understand and I agree to participate in the study.

Participant’s name: _________________________________________

Participant’s signature or thumb print: ______________________ Date: ___/___/09

Study Number: ____________________

Name of Witness: ____________________________

Signature of Witness: ______________________________ Date: ___/___/09

Investigator’s signature: ______________________________ Date: ___/___/09

Contact: If you have questions in the future, please contact the Principle Investigator, thru’ Dr. Sammy Njenga, Kenya Medical Research Institute (KEMRI), Center for Microbiology Research (CMR), P.O. Box 19464-00200, Nairobi. Telephone 020-2720794 or The Secretary, KEMRI ERC, P.O. Box 54840-00200, Nairobi. Tel 0722-205901/0733-400003
Appendix 3 Consent forms for persons below 8 years

Title of Study: Evaluation of the effect of missed mass drug administration on filarial infection in Malindi district, Kenya.

Sponsor: Institute of Tropical Medicine and Infectious Diseases - Kenya Medical Research Institute (ITROMID - KEMRI) Project.

Introduction

Your child/dependant is asked to participate in a medical research study on lymphatic filariasis. Lymphatic filariasis is a disease caused by parasites that are transmitted from one person to another by mosquitoes. When the parasites enter the body, they move into vessels called the lymphatic vessels, where they grow into thread-like adult worms. If not diagnosed and treated promptly, filariasis can lead to severe disability due to the resulting lymphedema and hydrocele. The international body called the World Health Organization (WHO) has decided to eliminate lymphatic filariasis as a public health problem by giving treatment to all persons living in the areas where the disease occurs.

The purpose of this consent form is to give you information that might help you to decide whether to allow your child/dependant to participate in the study or not. You are allowed to ask questions related to the study and implications on his/her part.

Purpose of the study

The recommended treatment in Kenya is a combination of two drugs namely, diethylcarbamazine (DEC) and albendazole given once a year to all individuals living in endemic areas. Many elimination programs are faced by difficulties in conducting MDAs mainly due to financial limitations. In Kenya the communities in endemic areas have received four rounds of mass treatment in 2002, 2003, 2005 and 2008 respectively. Because of financial constraints, the Ministry of Health was unable to administer the necessary drugs in 2004, 2006 and 2007. This study will attempt to find out what impact the missing of regular rounds of MDA has on the overall success on the interrupting transmission. The information of this study will provide the Ministry of Health with
information about what impact missing the annual rounds of treat have on the overall success of eliminating lymphatic filariasis from the country.

**Procedure to be followed**

The study nurse or technician will prick your child’s/dependant’s finger for a drop of blood to find out if it has filariasis parasites. If the first test is positive, a second finger prick blood sample will be required from your child/dependant for microfilaria counting using the Counting Chamber technique with the aid of a microscope. This counting will be done at the Malindi District Hospital – KEMRI laboratory and at the Langobaya National Water Corporation (NAWACO) dispensary laboratory. The blood will not be tested for HIV and the results of the various tests will be returned to you.

**Risks**

The risk from participation in this study is minimal. Blood drawing may cause a slight pain and possibly a bruise where the blood is drawn.

**Benefits**

Your child/dependant’s blood will be checked for filariasis parasites. The child/dependant and the rest of the community will be given mass treatment free of charge. The treatment also has benefits for removing intestinal worms.

**Assurance of confidentiality**

Your child/dependant’s name and other records will remain confidential and will not appear when we present this study or publish its results. You will receive a copy of the consent form.

**Right to refuse or withdraw**

It is important that you understand the following general principles that will apply to all participants in the study:

1. Your participation is entirely voluntary
2. You may withdraw your child/dependant from this study any time without penalty or
loss of benefits.

Please feel free to ask any questions that you may have.

Do you agree to let your child/dependant participate in the study?

I acknowledge that this consent for has been fully explained to me in a language that I understand and I agree to let my child/dependant participate in the study.

Parents/Guardian’s name: _________________________________________

Parents/Guardian’s signature or thumb print: ______________________ Date: ___/___/09

Study Number: ______________

Name of Child (Participant): ___________________________________________

Name of Witness: ___________________________________________________

Signature of Witness: ______________________ Date: ___/___/09

Investigator’s signature: __________________________ Date: ___/___/09

Contact: If you have questions in the future, please contact the Principle Investigator, thru’ Dr. Sammy Njenga, Kenya Medical Research Institute (KEMRI), Center for Microbiology Research (CMR), P.O. Box 19464-00200, Nairobi. Telephone 020-2720794 or The Secretary, KEMRI ERC, P.O. Box 54840-00200, Nairobi. Tel 0722-205901/0733-40003
Appendix 4  Kiswahili version of the consent form for persons aged 18 years and above

Utangulizi

Unaulizwa kujihusisha kwenye uchunguzi wa ugonjwa wa matende na mshipa. Ugonjwa wa matende na mshipa husababishwa na aina ya viini wanaenezwa kutoka kwa mtu mmoja hadi mwingine na mbu. Wanapoingia katika mwili wa binadamu, wakati mbu anapoumu, viini hao huwingia kwenye mshipa ya maji ambapo hukuwa minyoo wanaofanana na uzi wa kushonea nguo. Ugonjwa wa matende na mshipa usipo pimwa na kutibiwa ifaavyo unaweza kusabisha madhara mwili. Shirika la afya ulimwenguni (WHO) limeamua kuangamiza ugonjwa wa matende na mshipa kwa kuwatibu watu wote wanaishi katika maeneo yote unapatikana. Sabau ya fomu hii ya makubaliano nikukupa wewe ufahamisho ambapo ugonjwa huu unapatikana. Unaweza kuulizwa maswali yanayohusiana na uchunguzi huu.

Shabaha ya uchunguzi

Hapa inchini Kenya, matibabu ambayo yameidhinishwa kwa kuangamiza ugonjwa wa matende na mshipa ni dawa aina mbili, diethylcarbamazine (DEC) na albendazole, ambayo hupewa watu wote wanaishi katika maeneo yote ambapo ugonjwa huu unapatikana. Madawa haya yanatakiwa kumezwa mara moja kila mwaka. Mbinu za kuchunguza vile madawa haya yanavyo angamiza ugonjwa baada ya kugawanyiwa watu zinahitaji upimaji wa damu. Uchunguzi ambao tunakuelezea leo unakusudia kulinganisha mbinu zinazotumia mbu na zile zinazotumia damu ili kuchunguza vile madawa ya matende na mshipa yanavyo angamiza ugonjwa baada ya madawa hayo kumezwa na watu wanoishi maeneo yenye ugonjwa. Matokeo ya uchunguzi huu yataiwezesha wizara ya afya kufanya uamuzi wakati unaofaa kusimamisha ugawanyaji wa madawa kila mwaka bila kuogopa kuwa ugonjwa unaweza kutokea tena siku za usoni.
Yatakatayofanyika

Mfanyi kazi wa afya atachukua tine la damu kutoka kidole chako ili kupima ugonjwa wa matende na mshipa. Damu yako ama sehemu ya damu hiyo itapimwa mara ya kwanza. Kama ugonjwa wa mshipa na matende upo, damu nyingine kutoka kwenya kidole chako kita hitajika kuhesabu wadudu waliowndani ya damu na usaidizi wa darubini katika maaraba ya Malindi District Hospital au Langobaya National Water Corporation (NAWACO) dispensary laboratory. Damu yako haitapimwa ugonjwa wa ukimwi na utajulishwa matokeo ya upimaji ya ugonjwa wa matende na mshipa.

Madhara yanayoweza kutokea ukihusishwa

Madhara ambayo yanaweza kukubali wakati wa kujihusisha na uchunguzi huu ni kiwango kikubali unatesha uchunguzi huu na uchungu kidogo. Unaweza kuja mto wengine kusaidia kuwa kuzungumizwa matokeo ya ugonjwa wa matende na mshipa. Pia jeraha dogo laweza kutokea kwenye sehemu ambapo damu itatolewa.

Manufaa utakayopata ukihusishwa

Manufaa kwako ni kuwa damu yako itapimwa ili kujue kama una viini vinavyosababisha ugonjwa wa matende na mshipa, na ukipenda waweza kujulishwa matokeo ya upimaji. Wewe na watu wengine katika eneo lako hatari wana watapata madawa bila malipo yoyote. Madawa utakayopatiwa pia yana famida ya kuangamiza minyoo wengine tumboni.

Siri

Jina lako na stakabadhi zingine zinazokuhusu zitahifadhiwa kama siri na haziwezi kuonyeshwa wakati wa kutangaza matokeo ya uchunguzi huu ama tutakapo andika nakala. Utakatiwa kopi ya fomu hii ili ukiwesha mwenyewe.

Haki ya kukataa au kujiondoa

Nimuhimu ulewe yafuatayo:

1. Kujihusisha kwenye uchunguzi huu ni kwa hiari yako.

2. Unaweza kujiondoa wakati wowote bila kuadhibiwa au kupoteza manufaa.
Sasa unaweza kuuliza maswali yoyote yanayohusiana na uchunguzi huu. Unakubali kuhushishwa katika uchunguzi.

Nakubali kuwa hii fomu imeelezwa vyema kwa lugha ninayoielewa na nimekubali kuhushishwa katika uchunguzi.

**Jina:** ____________________________________________

**Sahihi au alama ya kidole:** __________________________ Tarehe: ___/___/09

**Nambari ya mhusika:** ______________________________

**Jina la shahidi:** ____________________________________

**Sahihi ya shahidi:** _________________________________ Tarehe: ___/___/09

**Sahihi ya mchunguzi:** __________________________________ Tarehe: ___/___/09

**Maelezo au maswali zaidi**

Ukiwa na maswali baadaye, unaweza kuwasiliana na mkuu wa uchunguzi huu kupitia Dkt Sammy M. Njenga, Kenya Medical Research Institute (KEMRI), Center for Microbiology Research (CMR). P.O. Box 19464-00200, Nairobi; Telephone 020-2720794 au Secretary, KEMRI - ERC. P.O. Box 54840-00200. Tel# 0722-205901/0733-400003.
Appendix 5  Kiswahili version of the consent form for persons below 8 years

Utangulizi

Mtoto wako anaulizwa kujihusisha kwene ya uchunguzi wa ugonjwa wa matende na mshipa. Ugonjwa wa matende na mshipa husababishwa na aina ya viini wanaonezwa kutoka kwa mtu mmoja hadi mwingine na mbu. Wanapoingia katika mwili wa binadamu, wakati mbu anapouma, viini hao huwingia kwene ya mshipa ya maji ambapo hukuwa minyoo wanaofanana na uzi wa kushonea nguo. Ugonjwa wa matende na mshipa usipo pimwa na kutibiwa ifaavyo unaweza kusabisha madhara mwilini. Shirika la afya ulimwenguni (WHO) limeamua kuangamiza ugonjwa wa matende na mshipa kwa kuwatibu watu wote wanaoishi katika maeneo yote amapo ugonjwa huu unapatikana. Sabau ya fomu hii ya makubaliani nikukupa wewe ufahamisho ambacho unaokusudia ama la. Unaweza kuulizwa maswali yanayohusiana na uchunguzi huu.

Shabaha ya uchunguzi

Hapa inchini Kenya, matibabu ambayo yameidhinishwa kwa kuangamiza ugonjwa wa matende na mshipa ni dawa aina mbili, diethylcarbamazine (DEC) na albendazole, ambayo hupewa watu wote wanaoishi katika maeneo yote ambapo ugonjwa huu unapatikana. Madawa haya yanatikia kuzingatia kwa moja kila mwaka. Mbinu za kuchunguza vile madawa haya yanavyo angamiza ugonjwa baada ya kugawanyiwa watu na zinaatikia upimaji wa damu. Uchunguzi ambao tunakuelezea leo unakusudia kulinganisha mbili za zile zinaatikia damu ili kuchunguza vile madawa ya matende na mshipa yanavyo angamiza ugonjwa baada ya madawa hayo kumezwa na watu wanaishi maeneo yenye ugonjwa. Matokeo ya uchunguzi huu yataiwezesha wizara ya afya kufanya uamuzi wakati unaofaa kusimamisha uguwa na ugonjwa wa matende na mshipa yanavyo angamiza ugonjwa baada ya madawa hayo kumezwa na watu wanaishi maeneo yenye ugonjwa. Matokeo ya uchunguzi huu yataiwezesha wizara ya afya kufanya uamuzi wa madawa kila mwaka bila kuogopa kuwa ugonjwa unaweza kutokea tena siku za usoni.
Yatakayofanyika

Mfanyi kazi wa afya atachukua tine la damu kutoka kidole cha mtotoko ili kupima ugonjwa wa matende na mshipa. Damu ya mtotoko itapimwa mara ya kwanza. Kama ugonjwa wa mshipa na matende upo, damu nyingine kutoka kwenya kidole chako kita hitajika kuhesabu wadudu walio ndani ya damu na usaidizi wa darubini katika maaraba ya Malindi District Hospital au Langobaya National Water Corporation (NAWACO) dispensary laboratory. Damu ya mtotoko haitapimwa ugonjwa wa ukimwi na utajulishwa matokeo ya upimaji ya ugonjwa wa matende na mshipa.

Madhara yanayoweza kutokea motto wako akihusishwa

Madhara ambayo yanaweza kumkakabali mtoto wako wakati wa kujihusisha na uchunguzi huu huu ni kidogo sana. Unaweza kuhisi uchungu wakati wa kutolewa damu. Pia jeraha dogo la aweza kutokea kwenye sehemu ambapo damu itatolewa.

Manufaa utakayopata ukihusishwa

Manufaa kwa mtoto wako ni kuwa damu yako itapimwa ili kujua kama una viini vinavyosababisha ugonjwa wa matende na mshipa, na ukipenda waweza kujulishwa matokeo ya upimaji. Wewe na watu wengine katika eneo lako watapata madawa bila malipo yoyote. Madawa mtoto wako atakayopatiwa pia yana faida ya kuangamiza minyoo wengine tumboni.

Siri

Jina la mtoto wako na stakabadhi zingine zinazokuhusu zitahifadhiwa kama siri na haziwezi kuonyeshwa wakati wa kutangaza matokeo ya uchunguzi huu ama tutakapo andika nakala. Utakatiwa kopi ya fomu hii ili ujiweke mwenyewe.

Uhifadhi ya sehemu ya damu ya motto wako

Baada ya kukamilisha uchunguzi huu, sehemu ya damu itakayobakia itahifadhiwa katika maabara ya KEMRI. Nambari bila jina la mtoto wako itatumiwa kutambulisha damu. Damu iliyi hifadhiwa yaweza kutumika kwenye uchunguzi zaidi wa matende na mshipa hapa nchini au nchi zingine, ikiwa uchunguzi umeidhinishwa na KEMRI.
Haki ya kukataa au kujiondoa

Nimuhimu ulewe yafuatayo:

1. Kujihiushisha kwenye uchunguzi huu ni kwa hiari yako.
2. Unaweza kumondoa mtoto wako wakati wowote bila kuadhibiwa au kupoteza manufaa.

Sasa unaweza kuuliza maswali yoyote yanayohusiana na uchunguzi huu. Unakubali mtoto wako ahushishwa katika uchunguzi.

Nakubali kuwa hii fomu imeelezwa vyema kwa lugha ninayoielewa na nimekubali mtoto wangu ahushishwe katika uchunguzi.

Jina la mzazi: ___________________________________
Sahihi au alama ya kidole (mzazi): ___________________________ Tarehe: ___/___/09
Jina la mtoto: ________________________________
Nambari ya mhusika: ________________________________
Jina la shahidi: ________________________________
Sahihi ya shahidi: ________________________________ Tarehe: ___/___/09
Sahihi ya mchunguzi: ________________________________ Tarehe: ___/___/09

Maelezo au maswali zaidi

Ukiwa na maswali baadaye, unaweza kuwasiliana na mkuu wa uchunguzi huu kupitia Dkt Sammy M. Njenga, Kenya Medical Research Institute (KEMRI), Center for Microbiology Research (CMR). P.O. Box 19464-00200, Nairobi; Telephone 020-2720794 au Secretary, KEMRI - ERC. P.O. Box 54840-00200. Tel# 0722-205901/0733-400003.
Appendix 6 Assent forms for mature minors (8yrs – 17yrs)

Title of Study: Evaluation of the effect of missed mass drug administration on filarial infection in Malindi district, Kenya.

Sponsor: Institute of Tropical Medicine and Infectious Diseases - Kenya Medical Research Institute (ITROMID - KEMRI) Project.

Introduction

You are asked to participate in a medical research study on lymphatic filariasis. Lymphatic filariasis is a disease caused by parasites that are transmitted from one person to another by mosquitoes. When the parasites enter the body, they move into vessels called the lymphatic vessels, where they grow into thread-like adult worms. If not diagnosed and treated promptly, filariasis can lead to severe disability due to the resulting lymphedema and hydrocele. The international body called the World Health Organization (WHO) has decided to eliminate lymphatic filariasis as a public health problem by giving treatment to all persons living in the areas where the disease occurs. The purpose of this consent form is to give you information that might help you to decide whether to participate in the study or not. You are allowed to ask questions related to the study and implications on your part.

Purpose of the study

The recommended treatment in Kenya is a combination of two drugs namely, diethylcarbamazine (DEC) and albendazole given once a year to all individuals living in endemic areas. Many elimination programs are faced by difficulties in conducting MDAs mainly due to financial limitations. In Kenya the communities in endemic areas have received four rounds of mass treatment in 2002, 2003, 2005 and 2008 respectively. Because of financial constraints, the Ministry of Health was unable to administer the necessary drugs in 2004, 2006 and 2007. This study will attempt to find out what impact the missing of regular rounds of MDA has on the overall success on the interrupting transmission. The information of this study will provide the Ministry of Health with
information about what impact missing the annual rounds of treat have on the overall success of eliminating lymphatic filariasis from the country.

**Procedures to be followed**

The study nurse or technician will prick your child’s/dependent’s finger for a drop of blood to find out if it has filariasis parasites. If the first test is positive, a second finger prick blood sample will be required from your child/dependant for microfilaria counting using the Counting Chamber technique with the aid of a microscope. This counting will be done at the Malindi District Hospital – KEMRI laboratory and at the Langobaya National Water Corporation (NAWACO) dispensary laboratory. The blood will not be tested for HIV and the results of the various tests will be returned to you.

**Risks**

The risk from participation in this study is minimal. Blood drawing may cause a slight pain and possibly a bruise where the blood is drawn.

**Benefits**

Your blood will be checked for filariasis parasites. You and the rest of the community will be given mass treatment free of charge. The treatment also has benefits for removing intestinal worms.

**Assurance of confidentiality**

Your name and other records will remain confidential and will not appear when we present this study or publish its results. You will receive a copy of the consent form.

**Right to refuse or withdraw**

It is important that you understand the following general principles that will apply to all participants in the study:

1. Your participation is entirely voluntary
2. You may withdraw from this study any time without penalty or loss of benefits.
Please feel free to ask any questions that you may have.

Do you agree to participate?

I acknowledge that this consent for has been fully explained to me in a language that I understand and I agree to participate in the study.

Participant’s name: ______________________________

Participant’s signature or thumb print: __________________________ Date: ___/___/09

Study Number: __________________________

Name of Witness: __________________________________________

Signature of Witness: __________________________ Date: ___/___/09

Investigator’s signature: __________________________ Date: ___/___/09

Contact: If you have questions in the future, please contact the Principle Investigator, thru’ Dr. Sammy Njenga, Kenya Medical Research Institute (KEMRI), Center for Microbiology Research (CMR), P.O. Box 19464-00200, Nairobi. Telephone 020-2720794 or The Secretary, KEMRI ERC, P.O. Box 54840-00200, Nairobi. Tel 0722-205901/0733-400003
Appendix 7  Kiswahili version of the assent form for mature minors (8yrs – 17 yrs)

Utangulizi

Unaulizwa kujihusisha kwenye uchunguzi wa ugonjwa wa matende na mshipa. Ugonjwa wa matende na mshipa husababishwa na aina ya viini wanaenezwa kutoka kwa mtu mmoja hadi mwingine na mbu. Wanapoingia katika mwili wa binadamu, wakati mbu anapouma, viini hao huwingia kwenye mshipa ya maji ambapo hukuwa minyoo wanaofanana na uzi wa kushonea nguo. Ugonjwa wa matende na mshipa usipo pimwa na kutibiwa ifaavyo unaweza kusabisha madhara mwilini. Shirika la afya ulimwenguni (WHO) limeamua kuangamiza ugonjwa wa matende na mshipa kwa kuwatibu watu wote wanaishi katika maeneo yote ampapo ugonjwa huu unapatikana. Sabau ya fomu hii ya makubaliano nikupuka wewe ufahamisho ambapo ugonjwa huu unapatikana ya uchunguzi tunaokusudia ama la. Unaweza kuulizwa maswali yanayohusiana na uchunguzi huu.

Shabaha ya uchunguzi

Hapa inchini Kenya, matibabu ambayo yameidhinishwa kwa kuangamiza ugonjwa wa matende na mshipa ni dawa aina mbili, diethylcarbamazine (DEC) na albendazole, ambayo hupewa watu wote wanaoishi katika maeneo yote ambapo ugonjwa huu unapatikana. Madawa haya yanatakiwa kumezwa mara moja kila mwaka. Mbinu za kuchunguza vile madawa haya yanavyo angamiza ugonjwa baada ya kugawanyiwa watu zinahitaji upimaji wa damu. Uchunguzi ambao tunakuelezea leo unakusudia kulinganisha mbinu zinazotumia mbili na zile zinazotumia damu ili kuchunguza vile madawa ya matende na mshipa yanavyo angamiza ugonjwa baada ya madawa haya kumezwa na wanaoishi maeneo yenye ugonjwa. Matokeo ya uchunguzi huu yataiwezesha wizara ya afya kufanya uamuzi wakati unaofaa kusimamisha ugawanyaji wa madawa kila mwaka bila kuogopa kuwa ugonjwa unaweza kutokea tena siku za usoni.
Yatakayofanyika

Mfanyi kazi wa afya atachukua tine la damu kutoka kidole chako ili kupima ugonjwa wa matende na mshipa. Damu yako ama sehemu ya damu hiyo itapimwa mara ya kwanza. Kama ugonjwa wa mshipa na matende upo, damu nyingine kutoka kwenya kidole chako kita hitajika kuhesabu wadudu walio ndani ya damu na usaidizi wa darubini katika maaraba ya Malindi District Hospital au Langobaya National Water Corporation (NAWACO) dispensary laboratory. Damu yako ha itapimwa ugonjwa wa ukimwi na utajulishwa matokeo ya upimaji ya ugonjwa wa matende na mshipa.

Madhara yanayoweza kutokea ukihusishwa

Madhara ambayo yanaweza kukubali wakati wa kujihusisha na uchungu kidogo sana. Unaweza kuhisi uchungu kidogo wakati wa kutolewa damu. Pia jeraha dogo laweza kutokea kwenye sehemu ambapo damu itatolewa.

Manufaa utakayopata ukihusishwa

Manufaa kwako ni kuwa damu yako itapimwa ili kujua kama una viini vinavyosababisha ugonjwa wa matende na mshipa, na ukipenda waweza kujulishwa matokeo ya upimaji. Wewe na watu wengine katika eneo lako watapata madawa bila malipo yoyote. Madawa utakayopatiwa pia yana faida ya kuangamiza minyoo wengine tumboni.

Siri

Jina lako na stakabadhi zingine zinazokuhusu zitahifadhiwa kama siri na haziwezi kuonyeshwa wakati wa kutangaza matokeo ya uchunguzi huu ama tutakapo andika nakala. Utakatiwa kopi ya fomu hii ili ujiwekee mwenyewe.

Haki ya kukataa au kujiondoa

Nimuhimu uelewe yafuatayo:

1. Kujihusisha kwenye uchunguzi huu ni kwa hiari yako.
2. Unaweza kujiondoa wakati wowote bila kuadhibiwa au kupoteza manufaa.
Sasa unaweza kuuliza maswali yoyote yanayohusiana na uchunguзи huu. Unakubali kuhusishwa katika uchunguзи.

Nakubali kuwa hii fomu imeelezwa vyema kwa lugha ninayoielewa na nimekubali kuhusishwa katika uchunguзи.

Jina: ________________________________

Sahihi au alama ya kido: ____________________________ Tarehe: ___/___/09

Nambari ya mhusika: ____________________________

Jina la shahidi: ________________________________

Sahihi ya shahidi: ____________________________ Tarehe: ___/___/09

Sahihi ya mchunguzi: ____________________________ Tarehe: ___/___/09

Maelezo au maswali zaidi

Ukiwa na maswali baadaye, unaweza kuwasiliana na mkuu wa uchunguзи huu kupitia Dkt Sammy M. Njenga, Kenya Medical Research Institute (KEMRI), Center for Microbiology Research (CMR). P.O. Box 19464-00200, Nairobi; Telephone 020-2720794 au Secretary, KEMRI - ERC. P.O. Box 54840-00200. Tel# 0722-205901/0733-400003.
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Appendix 9 Letter of Approval for manuscript publication

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840 - 00200 NAIROBI - Kenya
Tel. (254) (020) 2722541, 254 (020) 27-3349, 0722-209801, 0733-400003 Fax (254) (020) 3720030
Email: director@kemri.org info@kemri.org Website: www.kemri.org

KEMRI/AJHS/2013-2016/Vol1

19th May 2016

Mercy Mkandawire-Omwanza,
JKUAT,
P.O BOX 1527-00100,
Nairobi

Dear Mercy Mkandawire-Omwanza,


We are pleased to inform you that your above titled manuscript was approved for publication in the African Journal of Health Sciences (AJHS).

Thank you for taking interest in the Journal.

Kind Regards,

Jane M. Rintari (Miss), B.A (Hons) Degree in Sociology & Gov’t (UON), MPSM (AU), Zimbabwe,
Principal Administrative Officer (AJHS),
For: Editor-in-Chief, AJHS,
KENYA MEDICAL RESEARCH INSTITUTE (KEMRI).

In Search of Better Health
Appendix 10: Manuscript for Publication