

**SCHOOL OF PUBLIC HEALTH  
COLLEGE OF HEALTH SCIENCES  
UNIVERSITY OF GHANA**

**FACTORS ASSOCIATED WITH NON-COMPLIANCE TO MASS DRUG  
ADMINISTRATION FOR LYMPHATIC FILARIASIS IN ANKOBRA**

**BY**

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REQUIREMENT FOR THE AWARD OF MASTER OF PUBLIC HEALTH  
(MPH) DEGREE**

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## DECLARATION

I, ILO DICKO, do hereby declare that this proposal is my own work and that the same work has not been submitted anywhere for the same purpose.



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## **DEDICATION**

This work is dedicated to the memory of my father (BIREMA DICKO), may his soul rest in peace! I also dedicate it to my mother (ADIA SOW) and all my family.



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I thank God for all the blessings in my life so far.

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To everyone who helped me to undertake this MPH Program, I say thank you. Even though it's my name that appears on the cover page of this work, keep in mind that this work is yours also!

## LIST OF ABBREVIATIONS

<b>CFA</b>	-	Circulating Filarial Antigen
<b>ELISA</b>	-	Enzyme-Linked Immunosorbent Assay
<b>EU</b>	-	Evaluation Unit
<b>FTS</b>	-	Filariasis Test Strip
<b>GPELF</b>	-	Global Program to Eliminate Lymphatic Filariasis
<b>ICT</b>	-	Immunochromatographic Card Test
<b>IU</b>	-	Implementation Unit
<b>LF</b>	-	Lymphatic Filariasis
<b>MDA</b>	-	Mass Drug Administration
<b>MEWG</b>	-	Monitoring and Evaluation Working Group
<b>MMDP</b>	-	Morbidity Management and Disability Prevention
<b>NTD</b>	-	Neglected Tropical Diseases
<b>NTDCP</b>	-	Neglected Tropical Diseases Control Program
<b>RPRG</b>	-	Regional Programme Review Group
<b>STAG-NTD</b>	-	Strategic and Technical Advisory Group on Neglected Tropical Diseases
<b>TAS</b>	-	Transmission Assessment Survey
<b><i>W. bancrofti</i></b>	-	<i>Wuchereria bancrofti</i>
<b>WHO</b>	-	World Health Organization

## **OPERATIONAL DEFINITIONS**

### **MDA drug coverage rate**

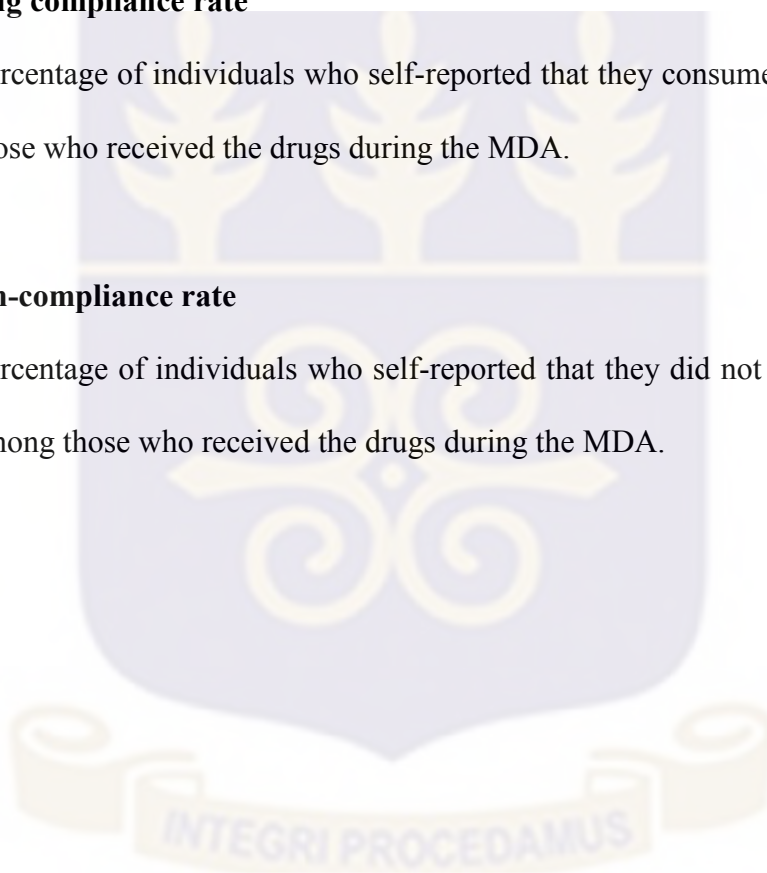
Percentage of people who reported that they received the drugs during the MDA among the interviewed community members.

### **MDA drug compliance rate**

Percentage of individuals who self-reported that they consumed the drugs, among those who received the drugs during the MDA.

### **MDA non-compliance rate**

Percentage of individuals who self-reported that they did not consume the drugs, among those who received the drugs during the MDA.



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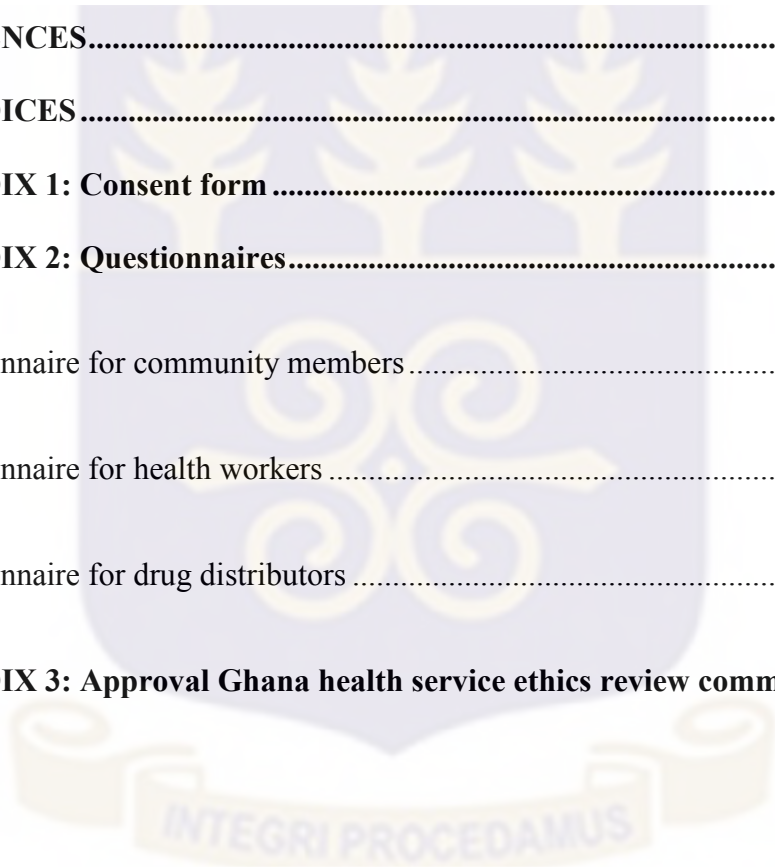
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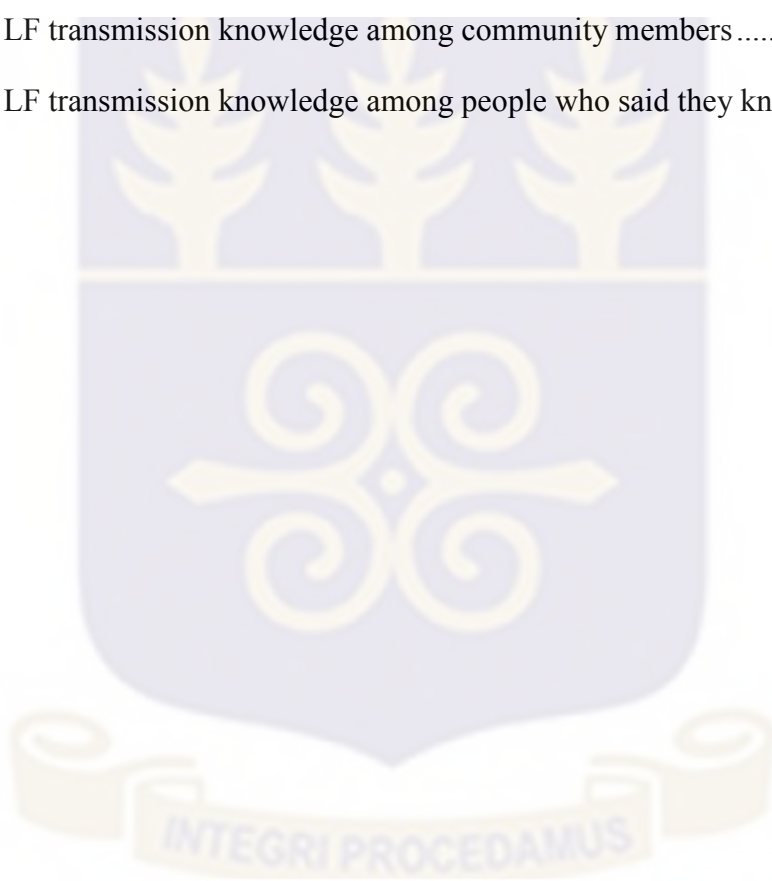
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## ABSTRACT

**Background:** Lymphatic filariasis (LF) is a parasitic disease that has been targeted for elimination since 2000. Mass drug administration (MDA) started in the Ankobra community in 2000. Nevertheless, the microfilaremia rate is still up to 4.5 % in 2016. Non-compliance to MDA is an important factor that can sustain the persistence of the disease after the required five to six MDA rounds. This study was aimed at determining the non-compliance level and the reasons as well as the factors associated with it in the Ankobra community, Ellebelle Health District in Ghana.

**Methods:** A cross-sectional study using a one-stage cluster sampling method was done between June and July 2017. A pre-tested questionnaire was used to collect information on sociodemographic characteristics, the latest MDA coverage, its non-compliance rate, reasons for and factors associated with it. In addition, two different types of questionnaire have been used to collect respectively information about the health workers and the drug distributors involved in the MDA process in the Ankobra community, Ellebelle Health District in Ghana.

**Results:** The MDA coverage and non-compliance rates among the community members in the Ankobra community were respectively 73.5 % (N= 200) and 33.33 % (N=147). The reasons reported for non-compliance were fear of adverse events (AE) (75.51 %), not willing to take the drugs (10.2 %), pregnancy (8.16 %), not suffering from LF (4.08 %) and taking other medications (2.04 %). Women, participants less than 30 years old, singles and educated people had increased odds of being non-compliant but the associations were not statistically significant (all p-values > 0.05). Thinking being not susceptible to LF was statistically associated with the non-compliance (OR= 2.47, [CI= 1.1-5.5]).

**Conclusion:** The present study reported MDA coverage and non-compliance rates of respectively 73.5 % and 33.33 % in 2016 in the Ankobra community. Fear of AE was the main reason reported for non-compliance. Health education strategies targeting the above identified non-compliant should be initiated in the Ankobra community to meet the GPELF elimination goal by 2020.

## CHAPTER ONE

### INTRODUCTION

#### 1.1 Background information

Lymphatic filariasis (LF) is a parasitic disease caused by three filarial species, *Wuchereria bancrofti* (*W. bancrofti*), *Brugia malayi* and *Brugia timori*. It is transmitted from person to person by mosquitoes (WHO, 2015; WHO, 2014; WHO, 2013). LF was endemic in 73 countries (Ottesen et al., 2008), 120 million people were infected in 2000. India and Africa were the most affected by the disease with respectively 49.2 % and 34.1 % as estimated infection burden (Molyneux, Hotez & Fenwick, 2005).

Since 2000, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) has been targeting LF for elimination by 2020 (Turner et al., 2016; Chu, Hooper, Bradley, Mcfarland & Ottesen, 2010; Ramaiah & Ottesen, 2014; Hooper, Chu, Mikhailov, Ottesen & Bradley, 2014). Its elimination requires at least five to six consecutive annual mass drug administration (MDA) rounds and a coverage rate of  $\geq 65\%$  in the at-risk population (Truscott, Turner & Anderson, 2015; Elaziz, El-setouhy, Bradley, Ramzy & Weil, 2013; Njomo, Amuyunzu-nyamongo, Magambo & Njenga, 2012; Krentel, Fischer & Weil, 2013; Shuford, Turner & Anderson, 2016).

Worldwide, LF is the second cause of permanent disability and the most common vector-borne parasitic disease after malaria (WHO, 2015; Ottesen, Hooper, Bradley & Biswas, 2008). Its chronic clinical manifestations are mainly hydrocele, lymphoedema and elephantiasis (WHO, 2010; WHO, 1994). Those suffering from these manifestations are

limited in their movements, and dependent on others financially (WHO, 2010; Ottesen et al., 2008; Ramaiah, Das, Michael & Guyatt, 2000); due to that, LF contributes to the aggravation of poverty (Tan, 2003; Huppertz, Capuano, Palmer, Kelly & Durrheim, 2009; Ruberanziza et al., 2009).

In some parts of Ghana, LF is endemic (Gyapong, Adjei & Gyapong, 1996; Souza, Yirenskyi, Otchere & Biritwum, 2016; Dzodzomenyo et al., 1999; Aboagye-antwi et al., 2015). In 2007, high microfilariae prevalence has been reported in five pilot districts in Ghana (Kanamitie, 2015). Currently, the number of MDA rounds undertaken across the country varies from nine to fifteen (Kanamitie, 2015). Kanamitie in 2015 reported that prevalence of antigenemia was 13 % in Agona Princess and Akonu (Western region) despite ten rounds of MDA with adequate coverage rates.

Compliance to the MDA, an essential component of the LF elimination process, is defined by the proportion of eligible individuals actually ingesting the drugs provided to them (Kyelem et al., 2008). Low level of compliance has already been reported worldwide (Senyonjo, Oye, Bakajika, Biholong & Tekle, 2016; Njomo et al., 2012). The untreated individuals constitute a potential parasite reservoir resulting in the recrudescence of the infection among those treated. Identifying the non-compliant and the possible factors contributing to the non-compliance in the endemic areas especially those still above the WHO elimination threshold (1% microfilaremia or 2% antigenemia) would be helpful in achieving the LF elimination goal by 2020.

## 1.2 Statement of the problem

The strategy adopted by the GPELF to eliminate LF is two-fold. One strategy is to treat the entire population at risk during MDA using albendazole plus either ivermectin where onchocerciasis endemic regions or diethylcarbamazine (DEC) elsewhere once a year. The second part is the management of the morbidity (elephantiasis, hydrocele) due to the disease (Stanton et al., 2016 ; WHO, 2010).

Success of MDA is reaching a microfilaremia level less than 1% or an antigenemia level less than 2 % in areas where *Anopheles* is the vector. It requires good coverage ( $\geq 65$  %) and good compliance level ( $\geq 80$  %) of the targeted population.

In Ghana, the Ankobra community in the Ellembelle health District started MDA in 2000 and has recorded quite good adequate coverage rates (63.4 %, 68.6 %, 87 %, and 92.2 % respectively for 2013, 2014, 2015 and 2016). Despite this fact, the microfilaremia rate in the Ankobra community during the latest assessment conducted in 2014 was still up to 4.5 % (Ghana Neglected Tropical Disease Control Program 2016, unpublished data).

If adequate measures are not taken to find out the causes of the persistent high microfilaremia level in the Ankobra community after the required 5 to 6 years of MDA, the LF elimination process in the entire country could be compromised. All the progress made so far could be threatened as a result of LF spreading since people harboring microfilaria constitute a reservoir of parasite for the disease.

### **1.3 Justification**

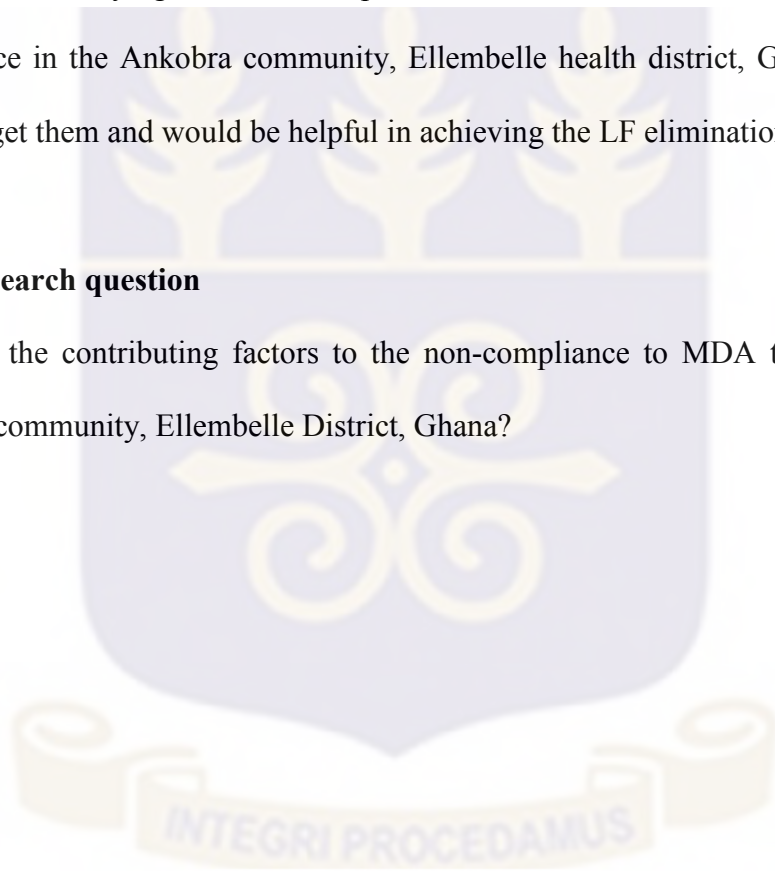
In many countries, there are issues to achieve a good compliance level to MDA, leading to persistence of parasite reservoirs that can sustain the reemergence of infection despite adequate reported coverage rates (Krentel et al., 2013).

A microfilaremia rate  $\geq 1\%$  after the required five to six MDA rounds could be linked to the non-compliance to MDA of the targeted populations (Krentel et al., 2013).

Therefore, identifying the non-compliant and the factors contributing to the non-compliance in the Ankobra community, Ellembelle health district, Ghana could help to better target them and would be helpful in achieving the LF elimination goal by 2020.

### **1.4 Research question**

What are the contributing factors to the non-compliance to MDA targeting LF in the Ankobra community, Ellembelle District, Ghana?



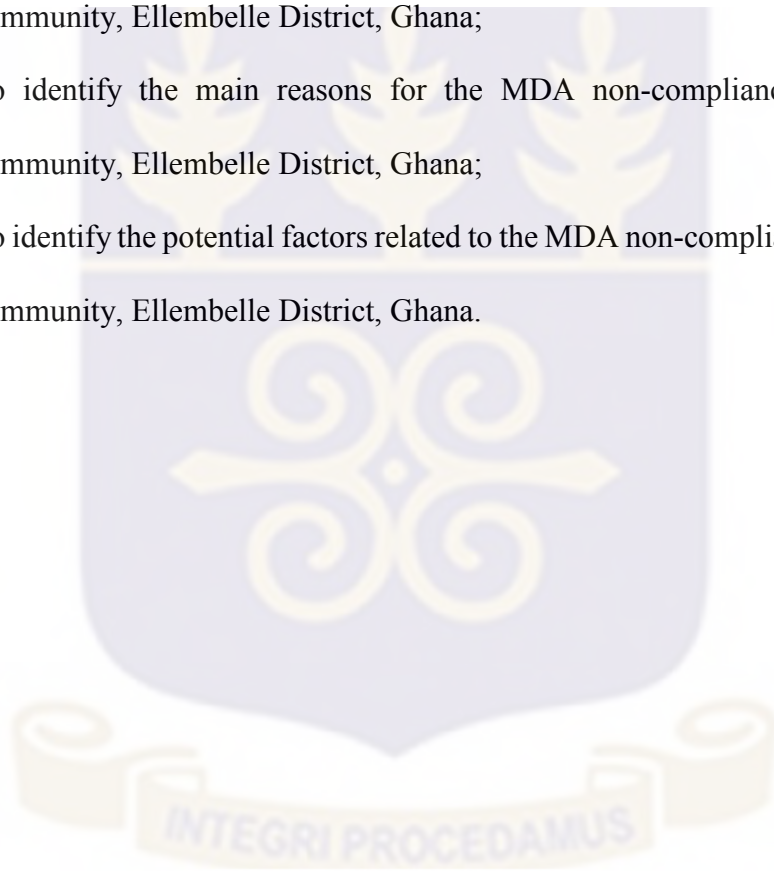
## **1.5 Study objectives**

### **1.5.1 General objective**

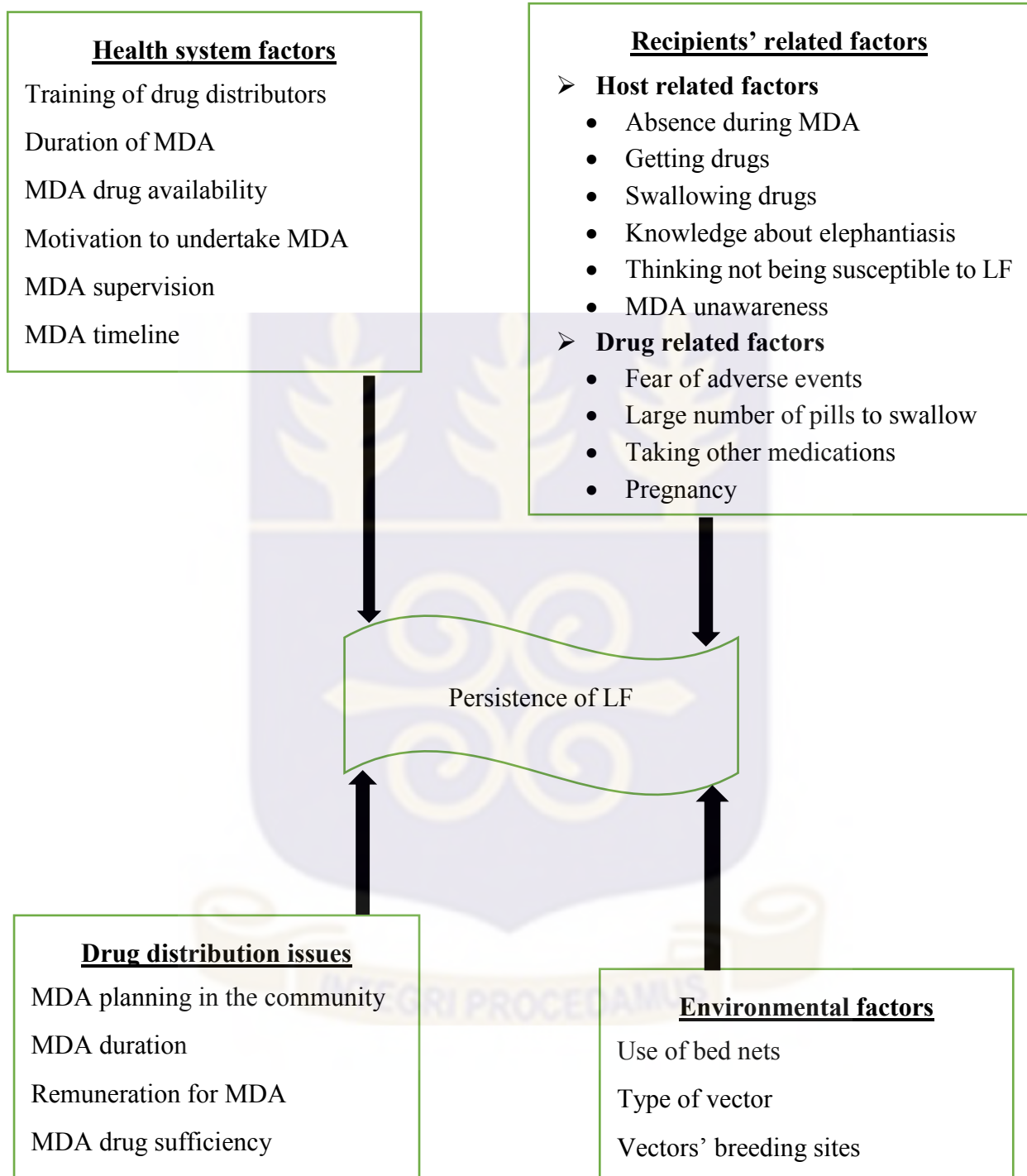
To determine the factors associated with the non-compliance to MDA targeting LF elimination in the Ankobra community, Ellembelle District, Ghana.

### **1.5.2 Specific objectives**

1. To determine the level of compliance to the MDA targeting LF in the Ankobra community, Ellembelle District, Ghana;
2. To identify the main reasons for the MDA non-compliance in the Ankobra community, Ellembelle District, Ghana;
3. To identify the potential factors related to the MDA non-compliance in the Ankobra community, Ellembelle District, Ghana.



### 1.6 Conceptual framework: Factors that may lead to LF persistence



## **Narrative**

Factors that may lead to the persistence of LF can be classified into four categories: drug distribution issues, health system factors, recipients' related factors, and environmental factors.

- Drug distribution issues refer to the knowledge that the drug distributors acquire when they are trained before MDA; to the duration of MDA is sufficient to allow the treatment of all the population at-risk and to the motivation of the drug distributors (will they be get paid for all the drug distribution days?).
- Health system factors look at whether MDA is implemented at the right period of time so as to reach most people at risk or not the amount of drugs provided to the drug distributors are sufficient to treat all eligible individuals in a well-supervised MDA round.
- Recipients' related factors seek to find out the factors mostly reported by the participants leading to LF persistence. They will look at mainly how the non-compliance to MDA, the awareness of the transmission mode of LF and its clinical manifestations like elephantiasis and hydrocele and knowledge of being susceptible to LF can impact LF persistence.
- Environmental factors can also be involved in the process leading to LF persistence, but this study will focus on the above cited factors.

Each of these four factors can have an impact on LF persistence in Ankobra community, Ellembele Health District in Ghana.

## CHAPTER TWO

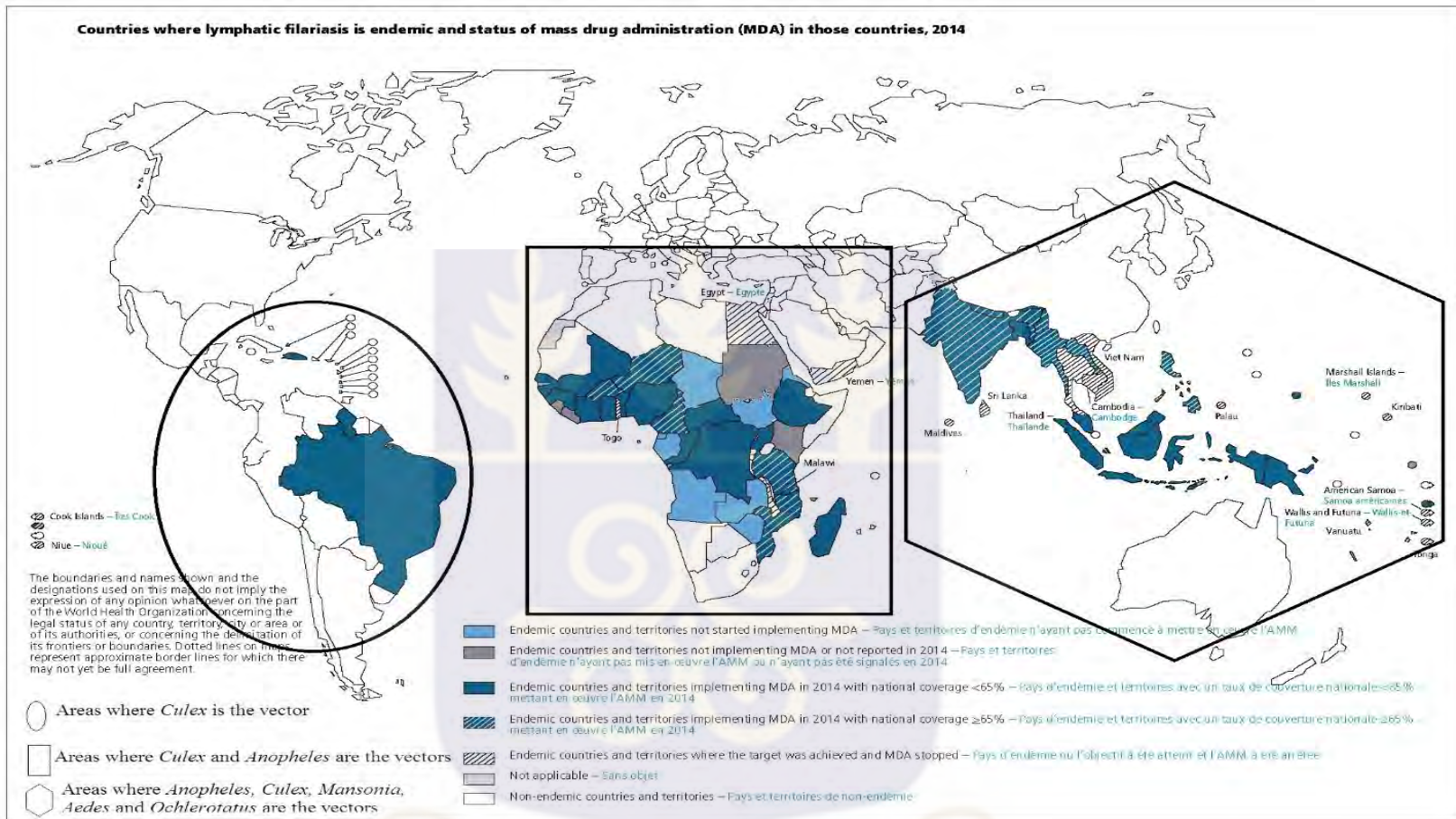
### LITERATURE REVIEW

#### 2.1 Burden and distribution of the disease

Globally, LF is the second most common vector-borne parasitic disease after malaria. It is seen in about 80 tropical and subtropical countries. Worldwide, WHO reported 120 million people infected and one billion at risk of the disease. LF is also recognized to be the second most common cause of long-term disability after mental illness (Ottesen, Duke, Karam & Behbehani, 1997). The Millennium Development Goals, stated that LF and other neglected tropical diseases contribute significantly to the overall African disease burden (Molyneux et al., 2005).

In 2014, 73 countries were endemic for LF and 36 million people were suffering from hydrocele and lymphedema. Among the endemic countries, 18 have already moved on to the surveillance phase but the remaining 55 require additional MDA rounds (WHO, 2015).

Togo and Malawi are in the post-MDA surveillance step (Figure 1) and are making considerable progress in term of Morbidity Management and Disability Prevention (MMDP). However, countries like Angola, Chad, Equatorial Guinea, Sao Tome and Principe and South Sudan need to start the MDA as soon as possible. In the meanwhile, countries like Benin, Burkina Faso, Ghana, Mali, Niger, Sierra Leone, Uganda and United Republic of Tanzania are expected to eliminate LF and stop MDA by 2020 (**Figure 1**).



**Figure 1:** Map of LF endemicity, elimination programme status worldwide

Source: WHO 2015

### **2.1.1 LF sociocultural burden**

People suffering from LF chronic manifestations are socially marginalized and neglected (Bandyopadhyay, 1996). It has been proven that a positive correlation between the severity of the visible disease and the degree of stigmatization (Evans, Hellen & Vlassotp, 1993).

Women suffering from LF have few chances to get married and to give birth making them a burden for their families. In Thailand and West Africa, this is sustained by the misconception that children born to a woman affected by LF will be similarly affected (Kumari, Harichandrakumar, Das & Krishnamoorthy, 2005).

### **2.1.2 LF economic burden**

As the disease progresses, the individual's capacity to work and be financially independent is increasingly troubled. Then, the affected individual becomes too severely disabled to contribute to create financial dependency regarding the family he/she is originating from.

## **2.2 LF transmission and GPELF strategy**

LF is a neglected tropical disease (NTD) caused by infection with the mosquito-borne, thread-like, parasitic filarial worms *W. bancrofti*, *Brugia malayi* and *Brugia timori* (WHO, 2013b). *W. bancrofti* is responsible for 90% of the morbidity due to LF and the remaining 10% are caused by *Brugia malayi* and *Brugia timori* (Bennuru & Nutman, 2009). LF is transmitted by many species of mosquitoes like *Anopheles*, *Culex*, *Aedes*, *Ochlerotatus* and *Mansonia*. The distribution of LF and its transmission vary according to the mosquito

species (WHO, 2013b). In West Africa, LF is transmitted by *Anopheles gambiae s.l.* and *Anopheles funestus* (WHO, 2011b; Appawu, Dadzie, Baffoe-Wilmot & Wilson, 2001).

LF is transmitted from human to human by female mosquitoes. During its blood meal on an infected human, the female takes up microfilariae and harbors it. Within the mosquito, microfilariae develop into the infective larval stage. When mosquito bites a healthy human, the infective larvae migrates into the skin and reach the lymphatic system where it becomes an adult worm. Adult male and female worms copulate to produce new microfilariae (**Figure 2**). Thus, transmission can be blocked by killing microfilariae. This procedure constitutes the backbone of the GPELF strategy to interrupt LF transmission by reducing the number of microfilariae in the blood of infected people in the communities to a level at which transmission to another person is not possible even in the presence of mosquito (WHO, 2013b).

The rationale supporting this strategy is based on the vectors' competence to transmit the infection at low microfilaremia levels. There are two main processes in the ability of vectors to pick up and transmit the infection: "facilitation" and "limitation" (Brenques, Subra, Mouchet, & Nelson, 1968). Facilitation is the transmission pattern of mosquitoes such as *Anopheles gambiae* complex that cannot transmit LF if the microfilariae load is very low (Pichon, Perrault, & Laigret, 1974). Mosquitoes that are more efficient to pick up and transmit LF when microfilariae loads are very low are said to exhibit limitation (Duerr, Dietz & Eichner, 2005).

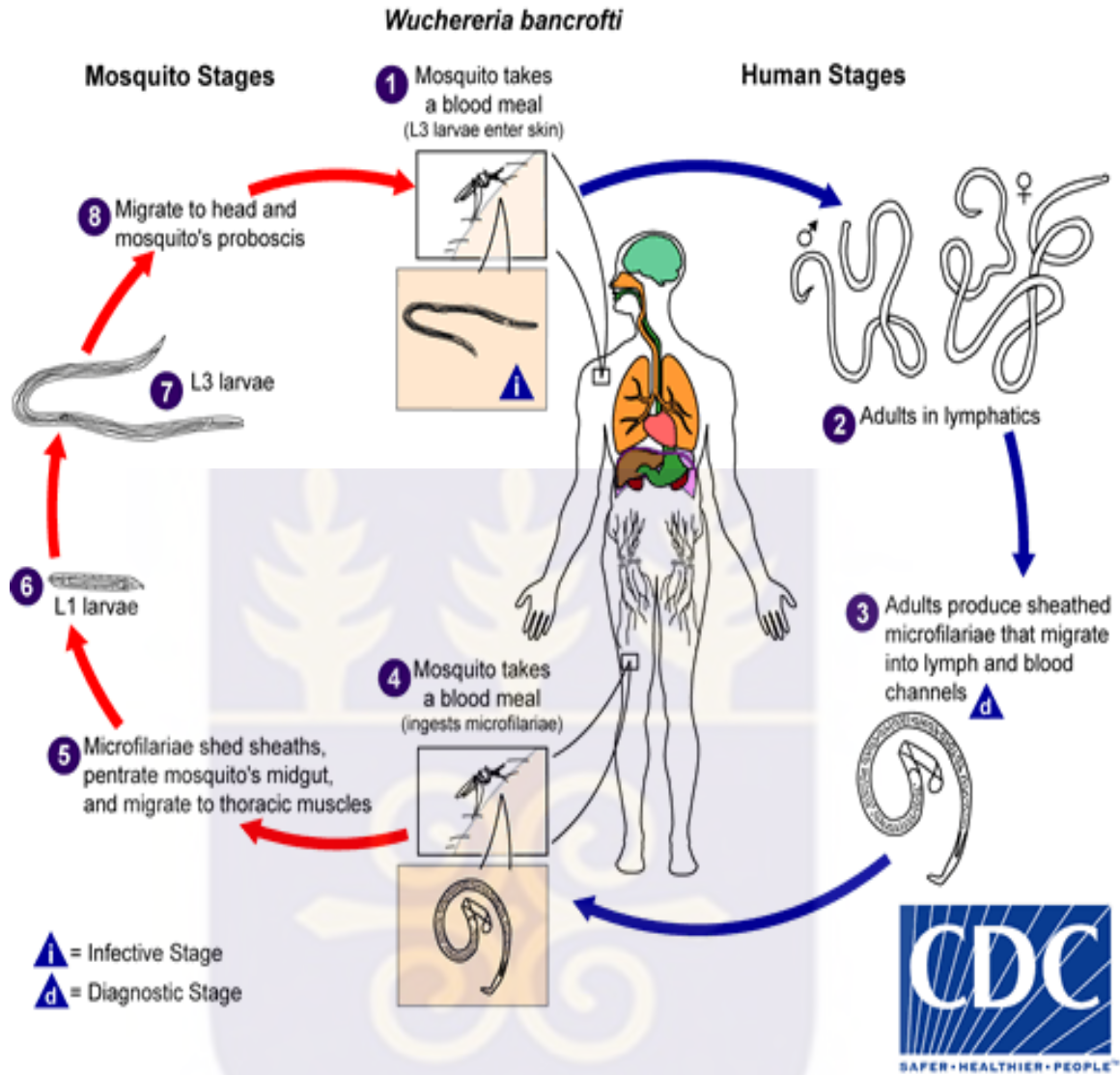


Figure 2: Life cycle of *W. bancrofti*

Source: ([http://www.cdc.gov/parasites/lymphaticfilariasis/biology\\_w\\_bancrofti.html](http://www.cdc.gov/parasites/lymphaticfilariasis/biology_w_bancrofti.html)).

## **2.3 Life cycle of mosquito**

Mosquitoes go throughout four different stages in their life cycle: egg, larva, pupa, and adult.

Generally, female mosquitoes lay their eggs in stagnant water; some do it near the water's edge and others attach their eggs to aquatic plants. Each mosquito species lays its eggs depending on its own ecological adaptations. According to their ecological preferences, mosquitoes can be either endophilic or exophilic, endophagic or exophagic and zoophagic or anthropophagic (WHO, 2013b).

### **2.3.1 Egg stage**

This is the first stage of mosquito life cycle. Eggs can be laid singly (*Anopheles*, *Ochlerotatus* and *Aedes*) or attached together making what is called "rafts" and float on the surface of the water (*Culex* and *Culiseta* species). Eggs usually hatch into larvae within 48 hours and water is a necessary part of this process (WHO, 2013b).

### **2.3.2 Larva stage**

The mosquito larva has a well-developed head with mouth brushes used for feeding, a large thorax with no legs, and a segmented abdomen.

The larva in the water needs to go to the surface for breathing. Larvae molt their skins four times and get larger after each molt. Most larvae have siphon tubes for breathing and hang upside down from the water surface. At this stage, some differences exist between species:

- *Anopheles* larvae do not have a siphon and lie parallel to the water surface to get a supply of oxygen through a breathing opening.
- *Coquillettidia* and *Mansonia* larvae attach to plants to obtain their air supply.

The larvae feed on microorganisms and organic matter in the water. During the fourth molt, the larva changes into a pupa (WHO, 2013b).

### **2.3.3 Pupa stage**

The mosquito pupa is comma-shaped. The head and thorax are merged into a cephalothorax, with the abdomen curving around underneath. The pupal stage is a resting, non-feeding stage of development. Pupae are mobile, responding to light changes and moving with a flip of their tails towards the bottom. This is the time the mosquito changes into an adult. In *Culex* species, this takes usually about two days. At the end of the development, the pupal skin splits and the adult mosquito (imago) emerges (WHO, 2013b).

### **2.3.4 Adult stage**

The period of development from egg to adult varies among species and is strongly influenced by ambient temperature. Some species of mosquitoes can develop from egg to adult in as few as five days, but a more typical period of development in tropical conditions would be some 40 days or more for most species. The variation of the body size in adult mosquitoes depends on the density of the larval population and food supply within the breeding water.

The newly emerged adult rests on the surface of the water for a short time to allow itself to dry and all its body parts to harden. The wings have to spread out and dry properly before it can fly. Blood feeding and mating will occur couple of days after the adults emerge (WHO, 2013b).

#### **2.4 Physiopathology of elephantiasis and hydrocele**

LF is a devastating disease involving the lymphatic system. The lymphatics play a crucial role in sustaining fluid homeostasis, and transportation of immune cells (Zawieja, 2005; Zawieja, 2009). Failing of the lymphatic system leads to lymphedema, which is a swelling due to accumulation of lymph in the tissues. It has the potential to progress into elephantiasis, a chronic manifestation of the disease, due to obstruction of the lymphatic drainage and the repetitive attacks by bacterial or fungal infections (Shenoy, 2008). Elephantiasis and hydrocele apparition and progression are associated with four factors (Bennuru & Nutman, 2009):

- the living adult worm,
- the inflammatory responses caused by death of the adult worm,
- the secondary bacterial or fungal infections and
- the microfilariae.

Lymphatics dilatation is due to the parasite and its degradation products whilst lymphatics obstruction is the consequence of immunological reactions caused by its presence into the system (Bennuru & Nutman, 2009).

## **2.5 Measures of human infection and LF transmission**

These measures can be classified into parasitological, immunological, medical imagery and molecular biology methods. Only the first two methods will be partly described in this thesis.

### **2.5.1 Parasitological methods**

Many epidemiological surveys and filariasis elimination programmes determine microfilaremia prevalence based on microfilariae detection methods to assess the effect of interventions.

The prevalence of LF based solely on microfilaraemia underestimates the real burden of the disease. However, it is inexpensive and can be used in laboratories with limited facilities.

Some additional microfilarial concentration techniques can also be used but only for research studies. They are:

- the membrane filtration technique;
- the modified Knott's concentration method; and
- the counting chamber technique.

## **2.5.2 Immunological methods**

### **2.5.2.1 Circulating filarial antigen (CFA) detection**

It is aimed at showing the presence of the CFA in the tested blood sample. It has the advantage of detecting infection in children (or adults) with LF who were tested negative for microfilaraemia (Steel, Ottesen, Weller & Nutman, 2001).

Enzyme-linked immunosorbent assay (ELISA) based on the detection of Og4C3 is another immunological method to detect filarial infection but it requires in addition to its operating cost, a well-trained technician and specialized equipment such as an ELISA reader, limiting its use on the field.

The ICT test was the preferred method for LF mapping. This test provides with result in 10 minutes and has sensitivity and specificity comparable to that of Og4C3. However, it has some backlogs such as the need of a cold chain (2-8 degrees Celsius), the necessity to read the card at exactly 10 minutes after blood application, a short shelf life (no more than nine months in suitable storage conditions) and the fact that one will remain positive several months after worms and Mf dying (Chesnais et al., 2013).

Recently, a new CFA test, the Alere Filariasis Test Strip (FTS) was produced. It uses similar reagents as those of the ICT, but on a different platform. The FTS is cheaper than the ICT and can be stored for a longer period of time. The two tests are comparable in terms of ease of use in the field. Additionally, laboratory studies demonstrated that the FTS could detect lower concentrations of CFA than ICT (Weil et al., 2013).

### 2.5.2.2 Filarial antibody detection

Many recombinant filarial antigens have been developed and used in filarial antibody assays with a presumably greater specificity for either the diagnostic or exposure assays. Bm14, WbSXP and BmR1 are three recombinant antigens commercially available that demonstrated a > 90% sensitivity in field studies without any cross-reactivity due to non-filarial helminth infections (Lammie et al., 2004).

More recently, Wb123 IgG4, an immunoassay based on detection of antibody to a *W. bancrofti* L3-specific antigen, was found very specific and sensitive (> 90%) in detecting *W. bancrofti* infection. It exists in a laboratory based ELISA format and in a field-friendly strips format with comparable performance (Steel et al., 2013). A biplex format of the strips exists for LF (Wb123) and onchocerciasis (Ov16) simultaneous diagnosis on the same test (Steel et al., 2013).

In sum, antifilarial antibody detection provides a good assessment tool of LF transmission after MDA cessation. This assertion is sustained by the fact that antibodies are detectable in infected humans before CFA or any other manifestation or sign associated with the infection. Antibody responses and their detection should be more sensitive than microfilaraemia or CFA detection (Lammie et al., 2004).

## 2.6 MDA and LF elimination

WHO recommends MDA using combinations of two drugs delivered to entire at risk populations; ivermectin plus albendazole in areas where onchocerciasis is co-endemic and DEC plus albendazole in other areas. These drugs reduce the number of microfilariae in the blood of infected people to levels where transmission is not possible by the vector (WHO, 2004). The effectiveness of MDA in reducing the prevalence and density of microfilaria in the blood is directly related to the proportion of the population that ingests the medicines every year (Michael et al., 2004). A minimum effective coverage of the total population is considered to be 65 % (Stolk, Swaminathan, Oortmarssen, Das & Habbema, 2003; Michael et al., 2004).

The factors that can affect LF program outcome are:

- a) the initial level of disease prevalence;
- b) the ability to the local vector to transmit the disease;
- c) the drug regimen used for the MDA; and
- d) the population coverage and population compliance (Kyelem et al., 2008; Michael et al., 2004; Boyd et al., 2010; Swaminathan, Subash, Rengachari, Kaliannagounder & Pradeep, 2008; Tisch, Michael & Kazura, 2005).

There are four steps in conducting LF elimination process:

- a) Step 1 (Mapping) is conducted at implementation unit (IU) level to determine whether active transmission is occurring and MDA is necessary. The process is

constituted with a mapping survey and review of existing data related to LF. The survey determines circulating filarial antigen (CFA) prevalence using immunochromatographic card test (ICT) or microfilaraemia prevalence using blood film in older school-aged or adult populations. If the prevalence is  $\geq 1\%$  (from the sample tested), the IU is considered endemic for LF;

- b) Step 2 (MDA) for the total population of the different implementation units (IU) considered endemic for LF.** The MDA recommended by the GPELF is based on co-administration of two of the three dedicated drugs. This is due to the fact that two drugs have been found to be more effective at clearing microfilaraemia than any single drug. Albendazole plus ivermectin is used in countries where onchocerciasis is co-endemic with LF, and DEC plus albendazole is used in countries free of onchocerciasis and where *Loa loa* is endemic. The whole process requires a well-organized and coordinated monitoring and evaluation at the local, regional and national levels. After three annual rounds of MDA, an optional mid-term assessment of the prevalence of microfilaraemia or CFA can be undertaken before the TAS eligibility assessment after the 5th MDA round. If the sentinel and spot-check sites are eligible for TAS, then a TAS can be undertaken followed by the 6th MDA round. That last round can be done even if the Evaluation Unit (EU) passes the TAS. The TAS is a standardized method to assess the impact of MDA and provide information that can help to decide whether to stop MDA in an EU. After five to six years of annual MDA rounds, LF elimination programmes' impact needs to be assessed to determine whether the programme has achieved its objective

of reducing levels of microfilariae in endemic areas to a level where transmission is unlikely to occur even if the MDA are stopped. TAS are designed to help programme managers determine whether areas have reached this critical threshold of infection. The targeted population for the TAS is the 6-7 years children that should be free of infection if the MDA was successful in stopping LF transmission. Antigenemia using Immunochromatographic card tests or Filaria Test Strips is usually determined within all the surveyed individuals in *W. bancrofti* endemic area. The survey is implemented in each EU that underwent at least 5 MDA rounds with a coverage rate of at least 65%.

- c) Step 3 (Surveillance) is used to monitor infection levels for approximately 5 years after stopping MDA. The surveillance period starts after the EU has passed the TAS. The TAS is also the recommended survey to detect any resurgence of LF transmission after MDA stopping. For post-MDA surveillance, the TAS should be conducted three times every 2-3 years to ensure that transmission is not re-emerging. The TAS planning and reports should be shared with WHO and the Regional Programme Review Group (RPRG) for advice.
- d) Step 4 (Verification) includes an assessment of detailed historical and epidemiological evidence of the absence of transmission (WHO, 2011a). It necessitates five main actions from the national programme managers, RPRG, WHO and the Strategic and Technical Advisory Group on Neglected Tropical Diseases (STAG-NTD):

- the compilation of all data related to LF before, during and after the national programme initiation from each IU;
- the national dossier preparation by the national programme for LF elimination after data analyses;
- the submission of the national dossier to the RPRG via WHO by the national programme;
- the dossier review by the RPRG that will stipulate recommendations to the Monitoring and Evaluation Working Group (MEWG) of the STAG-NTD via WHO headquarters;
- the review of the RPRG recommendations by the MEWG that will make their recommendations to the STAG-NTD.

China, with a total of 330 million people at-risk achieved in 2006 the elimination goal of LF by using MDA (De-Jian, Xu-Li & Ji-Hui, 2013). Other countries like Korea (Cheun et al., 2009), Egypt (Ramzy, Goldman & Kamal, 2005), Togo (Sodahlon et al., 2013) have eliminated LF.

## **2.7 Coverage rate and compliance rate during MDA**

According to Kyelem et al., (2008), *“population coverage is defined by the proportion of the population targeted by the program that was provided with the appropriate drugs”* and *“population compliance is defined by the proportion of eligible individuals actually ingesting the drugs provided to them”*.

Krentel et al. (2013) argues that differences between coverage rate and compliance rate may explain in some areas the persistence of LF transmission after multiple MDA rounds despite high reported coverage rates. They reported that training and motivation of drug distributors are crucial due to the fact that they interact directly with the population. Their capacity to convince people and to answer questions related to MDA can impact on the community compliance. They also reported that compliance decisions are also affected by perceptions of the potential benefits of participation compared to risk of adverse events (AE).

It has been reported after the tenth and the eleventh MDA rounds in three districts of Tamil Nadu, India, an overall coverage rate equal to 76.3 % and a compliance rate of 67.7 % which is below the required level to achieve LF elimination (Nandha, Krishnamoorthy & Jambulingam, 2013). They found a significant relationship between the number of visits of drug distributors and the coverage rate. In addition, they reported that the efforts made by drug distributors to prepare the community for an upcoming MDA were insufficient.

It has been reported in an Indian community that the fear of side effects, the lack of awareness of the benefits of MDA and the non-attendance of health staff in the villages are the causes of non-compliance. At the operational level, lack of adequate training of drug distributors, poor health communication activities before the MDA campaign and the absence of follow-up by health workers following MDA were reported (Hussain, Sitha, Swain, Kadam & Pati, 2014). In Burdwan district, West Bengal, India, it has been reported

after six MDA a coverage rate and a compliance rate respectively equal to 48.76 % and 70.07 %. This study highlighted the crucial need to improve compliance to MDA through strengthening of the awareness of both government health workers and community volunteers about the MDA program activities (Roy et al., 2013).

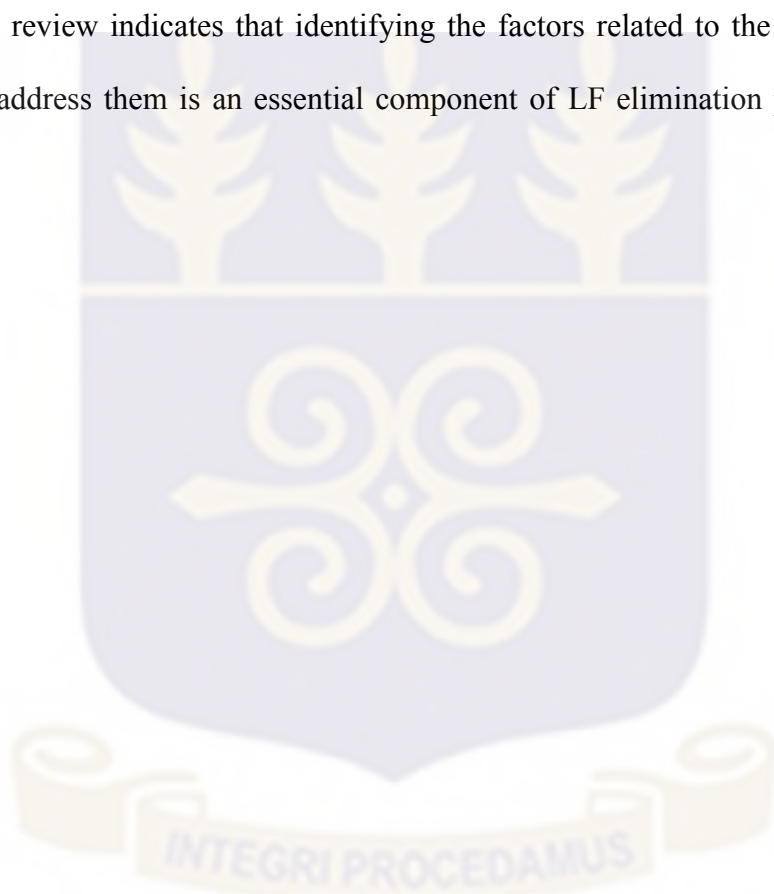
In Sri Lanka, it has been reported in eight districts designated as IU, a non-compliance rate equal to 28.6 % after sixty years of MDA (Weerasooriya et al., 2007). They showed a significant positive correlation between drug compliance and awareness.

In Kenya, a non-compliance rate of 27 % has been reported after six MDA rounds (Njomo et al., 2012). They reported that the house-to-house method of distribution influence positively compliance. The reasons associated with non-compliance were: feeling that the drugs were not necessary, drug distributor not visiting to issue the drugs, being absent and thinking that the drugs were meant for only the patients with LF clinical signs.

In the West region of Cameroon, a non-compliance rate of 28.2 % has been reported after the eleventh MDA round to ivermectin in Foubot and Massangam health districts (Senyonjo et al., 2016). They observed a strong association between non-compliance and an individual's experience of AE in the past. In addition, the systematic non-compliance was higher among females compared to males (OR = 1.7, Confidence interval = 1.1-2.6, p = 0.02).

Determining the compliance is the best indicator to know if MDA is well implemented. It has been estimated that a good compliance level is equal to 80 % or more of the targeted population (Nandha et al., 2013). When a proportion of the population fails to participate in MDA, a potential reservoir for the parasite is left untreated, opening the door to recrudescence of LF and reducing the probability of stopping its transmission (Talbot et al., 2008).

Literature review indicates that identifying the factors related to the non-compliance to MDA to address them is an essential component of LF elimination process in endemic countries.



## CHAPTER THREE

### METHODOLOGY

#### 3.1 Type and period of study

A cross-sectional study was conducted between June and July 2017. It was focused on the MDA targeting LF performed in 2016.

#### 3.2 Study location

The study was conducted at the Ankobra community in the Ellembelle health district.

##### 3.2.1 Ellembelle District

There are 98 districts endemic to LF out of a total number of 216 health districts in Ghana. Each LF endemic district is considered as an IU.

The Ellembelle District is one of the 22 districts in the Western Region of Ghana. According to 2010 Population and Housing Census, Ellembelle district is located between Longitude 2° 05" W and 2° 35" W, and Latitude 4° 40" N and 5° 20" N. Geographically, it is neighbored by the Jomoro District to the West, Wassa Amenfi West District to the North, Nzema East Municipal to the Southeast, Tarkwa-Nsuaem Municipal to the East, and a 70 km stretch of sandy beach along the Atlantic Ocean to the south. It covers 995.8 Km<sup>2</sup> about 9.8% of the landmass of the Western Region.

The Ellembelle District is 79.4 % rural and 21.6 % urban. An important in-migration and out-migration process exists in the District mainly due to mining activities and seasonal fishing. The district is irrigated by numerous rivers and streams, the most important being

the Ankobra River with its major tributaries called Ahama and Nwini rivers. In the southwestern part, the Amansure River and some other minor rivers and streams irrigate the district all year long. Together, these streams and rivers form the Ankobra Basin.

The district records an all-year round rainfall with the maximum monthly mean rainfall around May and June. Mean annual rainfall ranges from 26.8 to 46.6 mm (Population and Housing census, 2010).

The vegetation of the district is constituted by rain forest in the northern part of the district, while the Coastline, which is about 70 kilometers long, is mainly made of savanna vegetation.

### **3.2.2 Ankobra community**

The choice of the Ankobra community was based on the fact that the microfilaremia level is still up to 4.5 % after more than 10 rounds of MDA. In addition, there are no data available on the compliance to MDA in that area.

The study area is neighbored by Boblama to the West, by Nzema East district to the East and by the Gulf of Guinea to the South and North up to 30 m contour. Strand and mangrove make the dominant vegetation cover, with some rubber plantations. According to 2010 Population and Housing Census, Ankobra has a total of 158 houses with a population around 2,000 inhabitants. The main occupation of the in-habitants is fishing and its related businesses.

### **3.3 Variables**

#### **3.3.1 Dependent variable**

Not swallowing drugs during MDA in 2016 or non-compliance to MDA in 2016.

#### **3.3.2 Independent variables**

##### **3.3.2.1 Independent variables contributing to the non-compliance among the Ankobra community members**

They are mainly: sex, age, occupation, marital status, knowledge about LF.

For the details, see **APPENDIX 2**, Questionnaire for community members.

##### **3.3.2.2 Independent variables used in assessing the health system contribution to the non-compliance in the Ankobra community**

They are mainly training of drug distributors before MDA, drugs availability and sufficiency, supervision of MDA.

For the details, see **APPENDIX 2**, Questionnaire for health workers.

##### **3.3.2.3 Independent variables used in assessing the drug distribution system contribution to the non-compliance in the Ankobra community**

They are mainly MDA coverage, community members' compliance or not, reasons for non-compliance, MDA duration, drug distributors' motivation.

For the details, see **APPENDIX 2**, Questionnaire for drug distributors.

### **3.4 Study population**

There were three different study population

### **3.4.1 Community members**

To avoid situations where a community member wanted to be part of the study but was not major to decide himself (less than 18 years old), and his tutor didn't want him to participate, community members aged 18 years and older were included in this study.

#### **3.4.1.1 Inclusion criteria for community members**

- Being aged 18 years and older
- Being inhabitant of the Ankobra community for at least 2 years
- Being volunteer to participate to the study

#### **3.4.1.2 Exclusion criteria for community members**

Not being able to provide with an informed consent.

### **3.4.2 Drug distributors**

The drug distributors performing the MDA in the Ankobra community were enrolled in this study. No inclusion and exclusion criteria were used to select them since they were only five in the Ankobra community.

### **3.4.3 Health workers in the Ellembelle health district**

The Ellembelle health district workers were enrolled in this study.

#### **3.4.3.1 Inclusion criteria for health workers**

- Being health worker in the Ellembelle health district;
- Being involved in MDA supervision in the Ankobra community.

#### **3.4.3.2 Exclusion criteria for health workers**

Not being available to answer the study questionnaire during the study period.

### 3.5 Sampling

#### 3.5.1 Sample size calculation

##### 3.5.1.1 Required sample size for the Ankobra community members

The sample size was determined using the Cochran formula

$$N_0 = Z^2 pq / e^2 \text{ (Cochran WG, 1963),}$$

Where

- N<sub>0</sub>** is the required sample size,
- z** is the abscissa of the normal curve that cuts off an area  $\alpha$  at the tails,
- e** is the desired level of precision (set at 3% for this study because of the low prevalence of LF),
- p** is the estimated prevalence of LF in the population (equal to 4.5% according to the NTD control program 2016, unpublished data), and
- q** is 1-p (equal 1-0.045 for this study)

Thus

$$N_0 = (1.96)^2 \times (0.045) \times (1-0.045) / (0.03)^2 = 183$$

Using a 5 % markup for non-response, the final required sample size was 192 which has been rounded up to 200.

##### 3.5.1.2 Sample size for drug distributors

No sample size was determined for the drug distributors in the Ankobra community. Their number was five and all of them were enrolled and questioned;

### **3.5.1.3 Sample size for the Ellebelle health district health workers**

No sample size was determined for the Ellebelle health district health workers. Due to time constraints, the available health workers responding to the inclusion criteria were enrolled and questioned.

### **3.5.2 Sampling method**

Different sampling methods for the different study population were used

#### **3.5.2.1 Community members**

A one-stage cluster sampling method was used to select the community members.

The Ankobra community was divided in four clusters based on the distribution of the houses according to the main road crossing the community. Two clusters were randomly selected among them. All the houses in the selected clusters were eligible for the study. Then, a household survey was conducted. Two teams of 2 investigators used the door by door approach to administer the study questionnaire to the community members of all the houses in the selected clusters of the Ankobra community. All the community members eligible to participate to the study were enrolled till reaching the required sample size.

#### **3.5.2.2 Drug distributors**

Since the total number of drug distributors in the Ankobra community is five, they were all questioned to find out the issues related to the drug distribution during MDA campaigns.

### **3.5.2.3 Health workers involved in the supervision of MDA activities**

A convenient sample of thirty health workers involved in MDA supervision was questioned to find out the operational issues related to the MDA.

## **3.6 Data collection techniques / methods and tools**

Data were collected using a well-structured questionnaire containing both open- and closed-ended questions. Three different sets of questionnaires were used:

- A first one for the eligible representative sample of the Ankobra community,
- A second one for the drug distributors in the Ankobra community, and
- A third one for health workers involved in the MDA supervision in the Ellembelle district.

All questionnaires were administered with the assistance of two trained health workers, well versed in the local health system, as well as the local community members.

To reduce the risks of recall bias, all the questions about drug coverage and compliance during the present study were related to the MDA done in 2016 in the Ankobra community.

### **3.6.1 Training of interviewers**

Data collectors were recruited and trained to administer the study questionnaires in a friendly and professional manner. They were particularly coached on ways to conduct the interviews efficiently to ensure that good quality data are collected.

### **3.6.2 Pre-testing and review of instruments**

The study questionnaires were administered first to 20 people in the village of Oboom (Ga South) before their use in the Ankobra community. This village was selected with the agreement of the Neglected Tropical Diseases Control Program (NTDCP). The format, comprehension and completion of the questionnaires were assessed and revised accordingly.

### **3.6.3 Community entry**

After obtaining the approval from the Ellembelle District Health Directorate, a meeting with the Ankobra community chief and elders was done. We explained to them the objectives of the study to get their involvement and approval as well as the community engagement. Thereafter, we recruited the eligible community members.

### **3.6.4 Quality control**

To ensure the quality of the collected data, the principal investigator reviewed all filled questionnaires daily to correct or address any issue related to them. In addition, data were double-entered to minimize the errors.

### **3.7 Data processing and analysis**

Data were entered using Microsoft Excel version 2010. Data analysis was performed using STATA 14 (StataCorp LP, College Station, Texas, USA). Data have been presented using two-by-two tables for categorical variables; means and standard deviation (and/or median with minimum and maximum) for continuous variables. Tables, bar charts or pie charts

when appropriate were used to present simple frequencies. The Chi square and logistic regression have been used to compare and to measure the strength of the relationship between dependent and independent variables. The confidence interval was set at 95%.

When performing analysis to see whether there was association or not between the dependent variable (non-compliance) and the independent variables and estimating its strength, only the subjects who were covered by the MDA were considered out of the total Ankobra community members involved in the study.

The dependent variable, non-compliance to MDA is dichotomous. It has been used to perform a simple logistic regression with the independent variables to look for possible associations between them. After the simple logistic regression, the variables significantly associated with non-compliance to MDA and the ones known relevant according to the literature and having a p value less than 0.3 were used to perform the multiple logistic regression.

### **3.8 Data storage/ security and usage**

Hard and electronic copies data are stored in locked file cabinets, and access is limited to the principal investigator and the supervisors of the study.

### **3.9 Ethical considerations/ Issues**

Ethical clearance: the study protocol was approved by the Ethical Review Committee of the Ghana Health Service before the study initiation (see **APPENDIX 3**).

Approval from study area: permission was obtained from the District Director of Health Services, the administration of the Ellebelle District health facility and assembly and that of Ankobra community heads and opinion leaders.

Risks: The study didn't necessitate any invasive procedures to the study participants. However some participants might have felt uncomfortable to answer some questions. In such case, an answer was not mandatory for them.

Voluntary consent: All the study procedures were clearly explained to each study participant to be sure that they perfectly understood the topic and to obtain their individual informed consent. The content of the informed consent form was explained when necessary in the local language and then, written consent was obtained from each participant prior to performing any study related procedures. A copy of the informed consent sheet (see **APPENDIX 1**) was given to each participant for his personal records. The rights and welfare of the participants were protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Privacy and confidentiality: The name of the study participants as well as their personal information were kept confidential. Access to the research records is limited to the study principal investigator and the study supervisors.

Benefits to participants: Characteristics of the identified non-compliant (if they agree) will be communicated to the health facility to offer them the opportunity to be treated. The study provides information to understand factors associated with the non-compliance in the

Ankobra community. This information will be used by National LF Control Program to develop targeted interventions for LF elimination.

Compensation: Participants were not paid anything in the form of material or money for participating in this study. However, their participation was highly appreciated.

Declaration of conflict of interests: All investigators declared no competing interests.



## CHAPTER FOUR

### RESULTS

This study to determine the factors associated with non-compliance to MDA targeting LF in Ankobra was done between May and June 2017.

It took about 20, 25 and 30 minutes to question respectively a health worker involved in MDA supervision, a drug distributor and a community member.

#### **4.1 Sociodemographic characteristics of the study participants**

A total number of 200 community members were questioned between May and June 2017. Their main characteristics are detailed in Table 1. The mean age of the community respondents was 37.31 years with a standard deviation equal to 14.82. The median age was 34.5 years with extremes of 18 and 90 years. Most of the community respondents (62 %) are aged more than or equal to 30 years old. Women were more frequent (55 %) among the respondents. The sex ratio was 0.81. Most of the study participants were single (41 %), had a primary education level (49 %) and were fisherman (31 %) at the study moment.

In addition to the community members, a total number of 5 drug distributors, all living and performing MDA in the Ankobra community were enrolled and questioned.

Thirty Ellebelle health district workers involved in MDA supervision in the Ankobra community were also enrolled and questioned during this study.

**Table 1:** Sociodemographic characteristics of the Ankobra community members

<b>Characteristics</b>	<b>Frequency, N=200</b>	<b>Percentage (%)</b>
<b>Age in years</b>		
Mean ( $\pm$ standard deviation)	37.31 ( $\pm$ 14.82)	
Median (minimum-maximum)	34.5 (18-90)	
< 30 years old	76	38
$\geq$ 30 years old	124	62
<b>Sex</b>		
Female	110	55
Male	90	45
<b>Marital status</b>		
Single	82	41
Married	80	40
Divorced	22	11
Widowed	16	8
<b>Educational level</b>		
None	46	23
Primary	98	49
Secondary	46	23
Higher	10	5
<b>Occupation</b>		
Fisherman	62	31
Seller	59	29.5
Non worker	29	14.5
Farmer	25	12.5
Craftsman	17	8.5
Others*	8	4

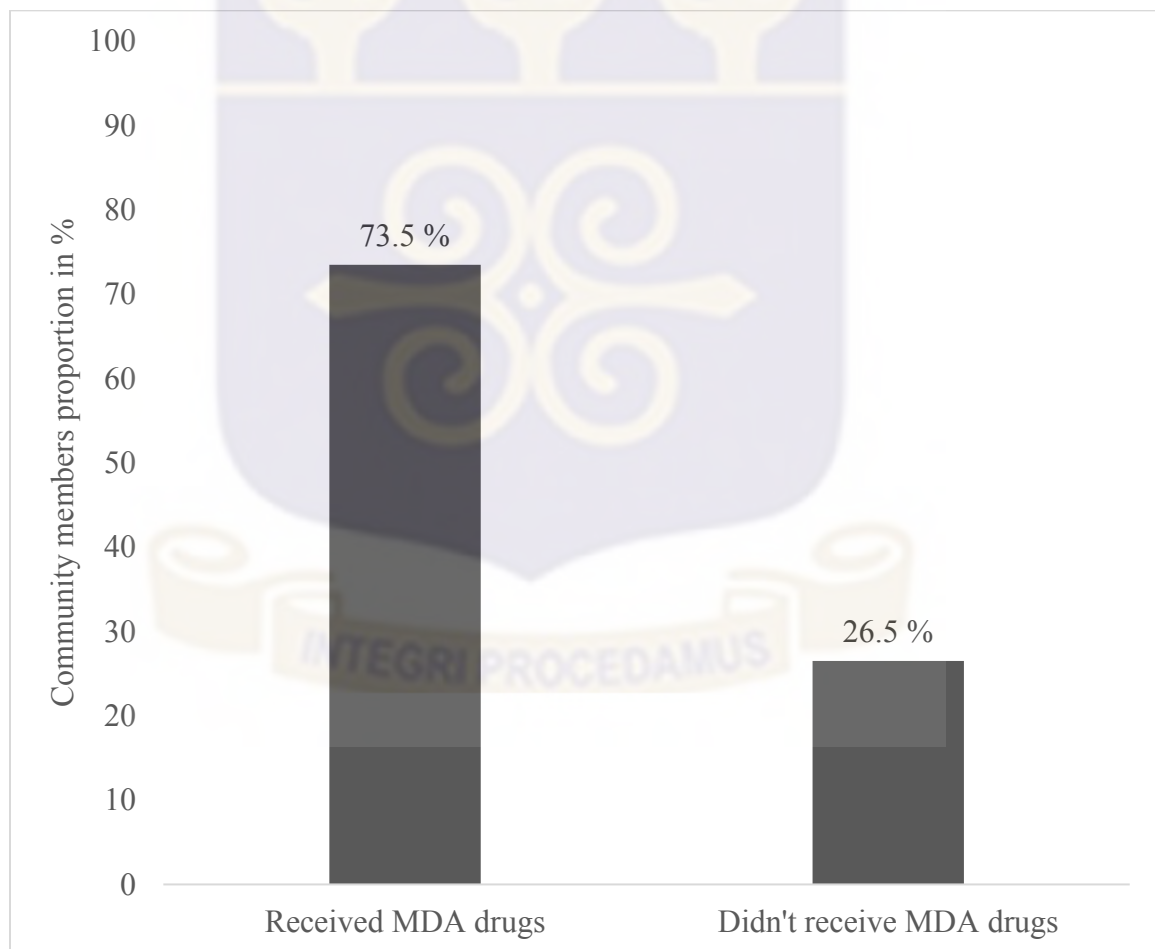
**Abbreviations:** \* = includes 2 teachers, 3 drivers, 1 nurse, 1 banker and 1 business man;

N = total number of community members.

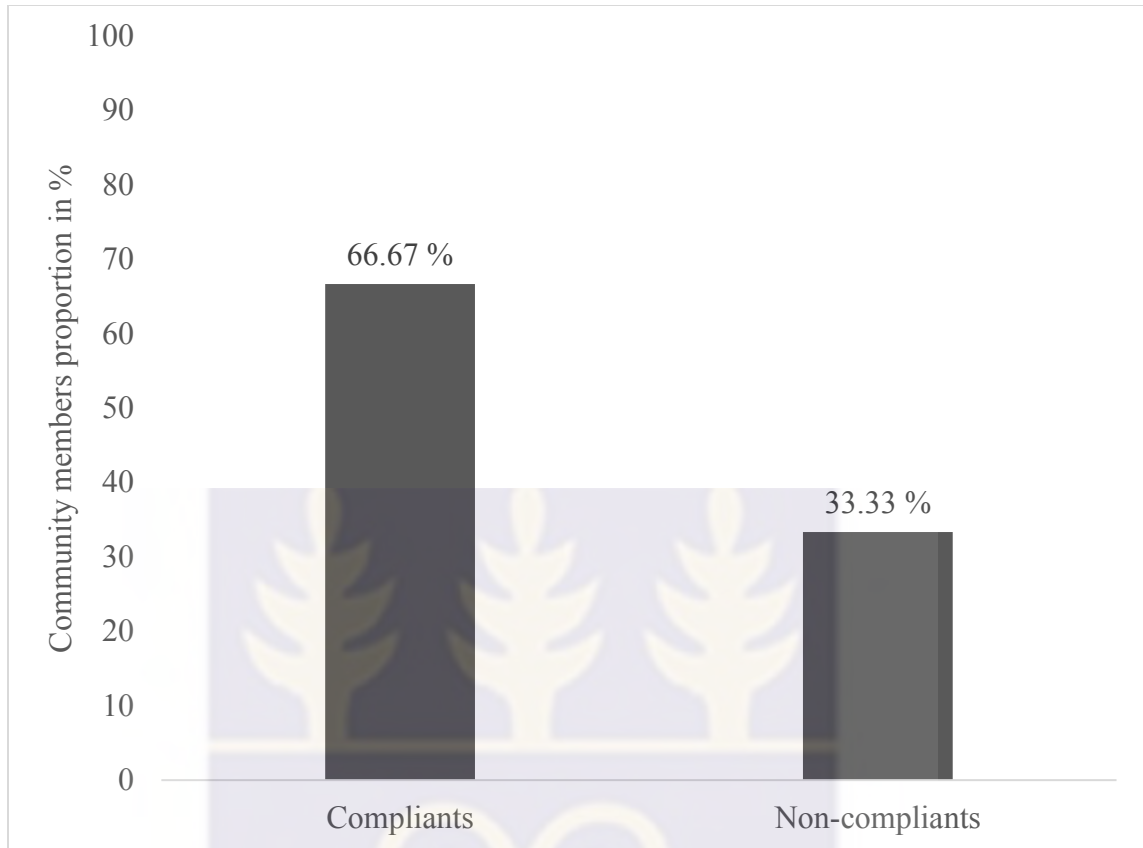
#### 4.2 Coverage rate and non-compliance level to the MDA in 2016

Among the 200 community respondents questioned in the Ankobra community, a proportion of 73.5 % received the MDA drugs in 2016 as depicted below in **Figure 3**.

The non-compliance rate was assessed among the community respondents who were covered during the drug distribution. Out of the total number of 200 respondents, 147 claimed that they received the MDA drugs in 2016. They were considered in the estimation of the non-compliance rate. Among them, 47 (33.33 %) reported to have not swallow the MDA drugs targeting LF in 2016. The results are depicted in **Figure 4**.



**Figure 3:** Coverage rate of the MDA targeting LF in 2016



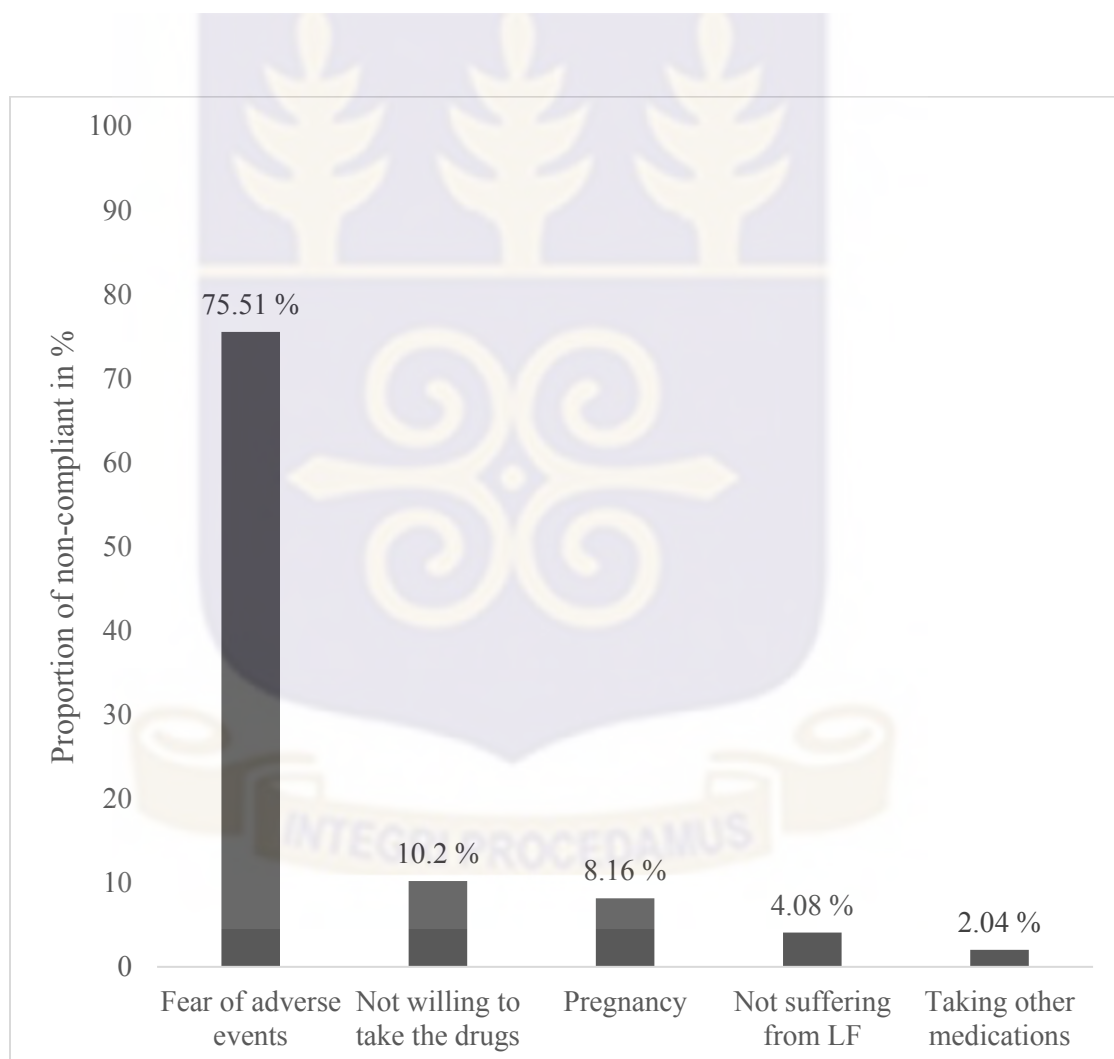
**Figure 4:** Compliance level to the MDA targeting LF in 2016



### 4.3 Reasons reported for non-compliance to the MDA in 2016

Out of the total number of 147 community respondents who claimed that they received the MDA drugs, 47 were non-compliant. The main reason they reported for non-compliance to the MDA was fear of AE (75.51%), followed by not willing to take the drugs (10.2%), pregnancy (8.16%), not suffering from LF (4.08%) and taking other medications (2.04%).

These results are depicted below in **Figure 5**.



**Figure 5:** Reasons reported for non-compliance to the MDA targeting LF in 2016

#### 4.4 Sociodemographic characteristics and non-compliance to the MDA in 2016

The 147 community respondents who claimed that they received the MDA drugs targeting LF in 2016 were concerned by this analysis. The respondents less than 30 years old (35.29 %), female (34.78 %), educated (35.51 %), single (34.88 %) were more likely to be non-compliant than respectively their counterparts aged more than 30 years old (32.29 %), male (30.91 %), uneducated (27.5 %) and married (31.15 %). However, none of the relationship between the variables age, sex, educational level, marital status and non-compliance were statistically significant (all p-values > 0.05). The results are depicted below in **Table 2**.

**Table 2:** Sociodemographic characteristics and non-compliance to the MDA in 2016

Characteristics	Non-compliant		Compliant		p-value
	N	%	N	%	
<b>Age groups</b>					0.71
< 30 years old	18	35.29	33	64.71	
≥ 30 years old	31	32.29	65	67.71	
<b>Sex</b>					0.63
Male	17	30.91	38	69.09	
Female	32	34.78	60	65.22	
<b>Education status</b>					0.36
Non educated	11	27.5	29	72.5	
Educated	38	35.51	69	64.49	
<b>Marital status</b>					0.57
Single	30	34.88	56	65.12	
Married	19	31.15	42	68.85	

**Abbreviations:** N = number of community members; < = less than; ≥ = more than or equal.

Community respondents who reported thinking being not susceptible to LF (39.39 %) were more likely to be non-compliant than their counterparts who think to be susceptible to the disease (20.83 %). This relationship was statistically significant ( $\text{Chi}^2= 5.01$ ,  $p = 0.03$ ). The results are shown in **Table 3**.

Respondents not suffering from lymphedema/hydrocele (34.78 %) and not knowing what is LF (45.45 %) were more likely to be non-compliant than respectively their counterparts suffering from lymphedema/hydrocele (11.11 %) and not knowing what is LF (32.35 %). However these relationships were not statistically significant (all p-values > 0.05). The results are shown in **Table 3**.

Study participants who knew how LF is transmitted (41.38 %) and have seen a case of the disease (35.61 %) were more likely to be non-compliant than their counterparts who didn't know it is transmitted (31.36 %) and didn't ever seen a case (13.33 %). However these relationships were not statistically significant (all p-values > 0.05). The results are shown in **Table 3**.



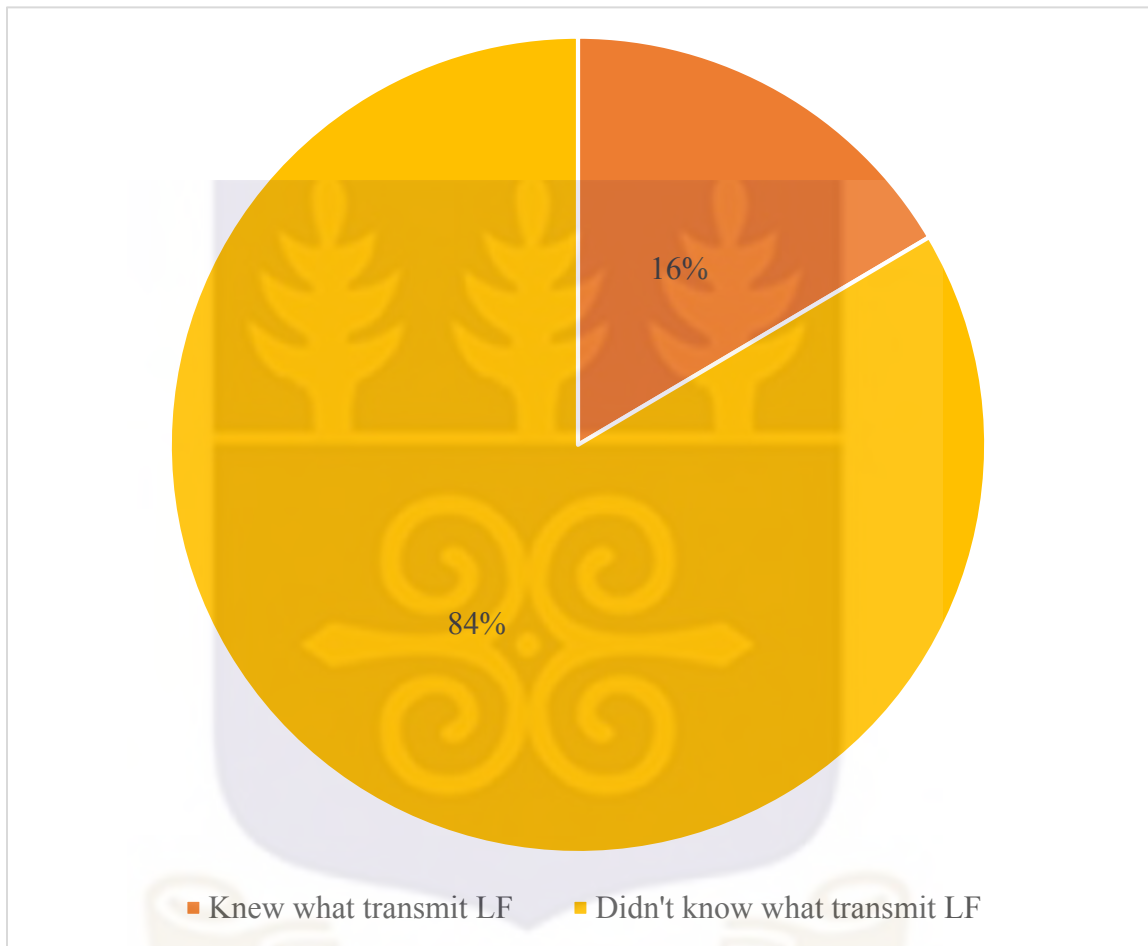
**Table 3:** LF knowledge factors and non-compliance to the MDA in 2016

Characteristics	Non-compliant		Compliant		p-value
	N	%	N	%	
<b>Lymphedema/hydrocele</b>					0.27*
Present	1	11.11	8	88.89	
Absent	48	34.78	90	65.22	
<b>Knowing what is LF</b>					0.51*
Yes	44	32.35	92	67.65	
No	5	45.45	6	54.55	
<b>Knowing what transmits LF</b>					0.31
Yes	12	41.38	17	58.62	
No	37	31.36	81	68.64	
<b>Previously viewing LF case</b>					0.08
Yes	47	35.61	85	64.39	
No	2	13.33	13	86.67	
<b>Thinking being susceptible to LF</b>					0.03**
Yes	10	20.83	38	79.17	
No	39	39.39	60	60.61	

**Abbreviations:** \* = Fisher's exact test, \*\* = statistically significant, N = number of community members.

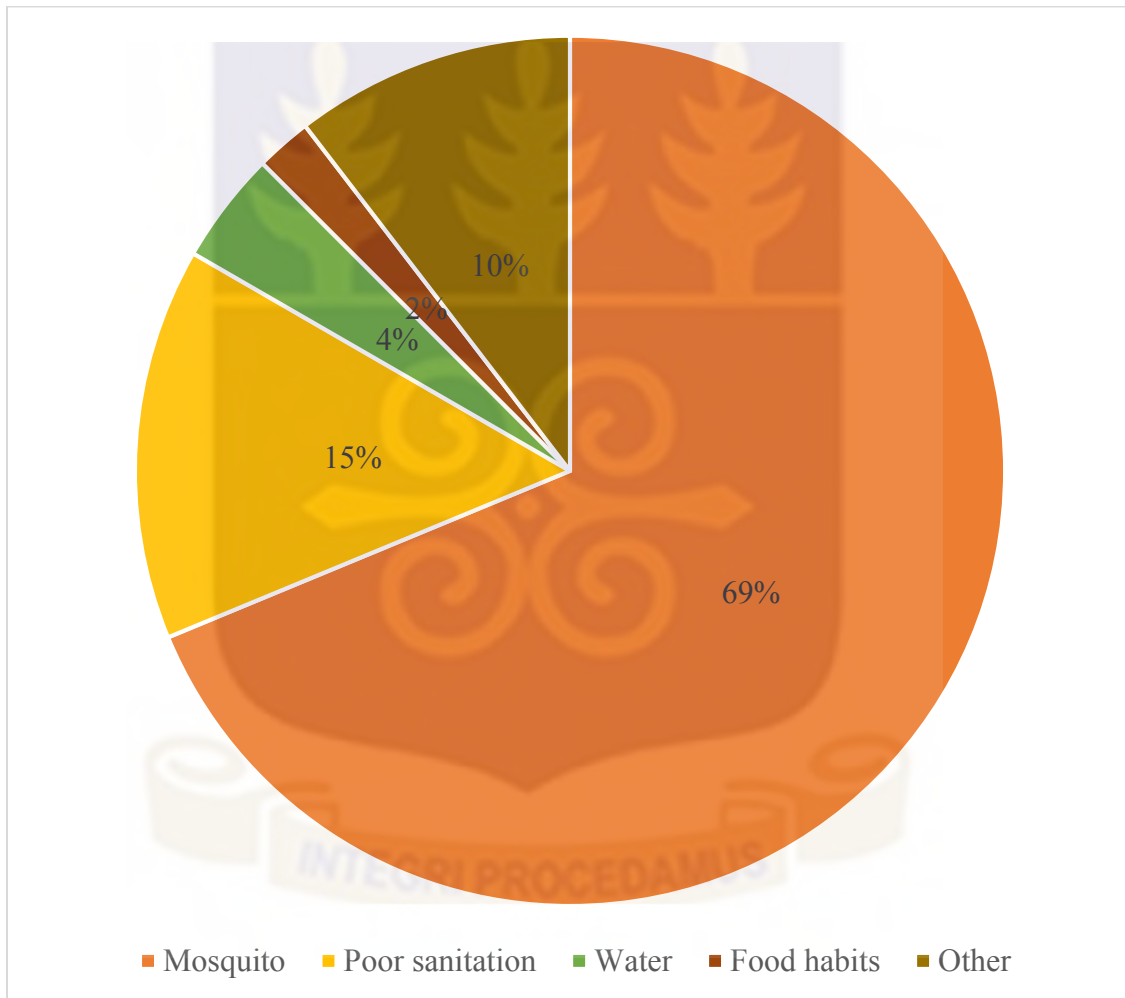
For the **Figure 6**, all the 200 community members were concerned by the analysis.

Most of the community members questioned (84 %, N= 200) didn't know how LF is transmitted. The results are depicted below in **Figure 6**.



**Figure 6:** LF transmission knowledge among community members

For the **Figure 7**, only the 48 community members who claimed they know how LF is transmitted were involved in the analysis. Among them, 69 % knew how it is transmitted (N= 48). The remaining community members thought that LF is transmitted via poor sanitation (15 %), water (4 %), food habits (2 %) and other ways (10 %). The results are depicted below in **Figure 7**.



**Figure 7:** LF transmission knowledge among people who said they know

#### **4.5 Factors associated with non-compliance to the MDA for logistic regression**

Logistic regression was performed to determine the strength of the association between the sociodemographic, LF knowledge factors and the non-compliance to MDA in 2016 in the Ankobra community. Data of the 147 community members who claimed that they received the MDA drugs in 2016 in the Ankobra community were used to perform this regression.

Presence of lymphedema/hydrocele, seeing a case of lymphedema/hydrocele before the study, knowing what is LF and how it is transmitted, and thinking being not susceptible to the disease were the LF knowledge factors used to perform a simple logistic regression. Thinking being susceptible to the disease was significantly associated with non-compliance to the MDA targeting LF in 2016 in the Ankobra community. Participants who reported thinking being not susceptible to the disease were 2.47 times more likely to be non-compliant than the ones who reported thinking being susceptible (Crude OR= 2.47, 95 % CI= [1.1, 5.52]). The results are shown in **Table 4**.

The other LF knowledge factors used were not significantly associated with non-compliance to the MDA targeting LF in 2016 in the Ankobra community (all the confidence intervals include 1 or all p-values > 0.05). The results are shown in **Table 4**.

Age, sex, educational level and marital status were the sociodemographic factors used to perform a simple logistic regression. None of them was significantly associated with non-compliance to the MDA targeting LF in 2016 in the Ankobra community (all confidence intervals include 1 or all p-values > 0.05). The results are shown in **Table 4**.

After the simple logistic regression, the variables known relevant and significantly associated with non-compliance to MDA according to the literature in addition to the ones with a p value less than 0.3 were used to perform the multiple logistic regression.

After adjusting for age, sex, presence of lymphedema/hydrocele, knowing what is LF and how it is transmitted, thinking being susceptible to the disease still remained significantly associated with non-compliance to MDA (Adjusted OR= 2.83, 95 % CI= [1.15, 6.98]). The results are shown in **Table 4**.



**Table 4:** Factors associated with non-compliance to the MDA for logistic regression

Characteristics	Non-compliant N (%)	Compliant N (%)	Crude OR		Adjusted OR	
			OR (95% CI)	p value	OR (95% CI)	p value
<b>Age groups</b>						
≥ 30 years old	31 (32.29)	65 (67.71)	1		1	
< 30 years old	18 (35.29)	33 (64.71)	1.14 (0.55, 2.34)	0.71	1.13 (0.53, 2.39)	0.74
<b>Sex</b>						
Male	17 (30.91)	38 (69.09)	1		1	
Female	32 (34.78)	60 (65.22)	1.19 (0.58, 2.43)	0.63	1.05 (0.49, 2.25)	0.71
<b>Education status</b>						
Educated	38 (35.51)	69 (64.49)	1			
Uneducated	11 (27.5)	29 (72.5)	0.68 (0.31, 1.53)	0.36	-	-
<b>Marital status</b>						
Married	19 (31.15)	42 (68.85)	1			
Single	30 (34.88)	56 (65.12)	1.18 (0.58, 2.38)	0.63	-	-
<b>Lymphedema / hydrocele</b>						
Present	1 (11.11)	8 (88.89)	1		1	
Absent	48 (34.78)	90 (65.22)	4.26 (0.51, 35.12)	0.17	2.98 (0.33, 26.55)	0.32
<b>Knowing what is LF</b>						
Knew	44 (32.35)	92 (67.65)	1		1	
Didn't know	5 (45.45)	6 (54.55)	1.74 (0.5, 6.02)	0.38	1.57 (0.43, 5.66)	0.48
<b>Knowing how LF is transmitted</b>						
Knew	12 (41.38)	17 (58.62)	1		1	
Didn't know	37 (31.36)	81 (68.64)	0.64 (0.28, 1.49)	0.3	0.42 (0.16, 1.09)	0.07
<b>Previously seeing LF case</b>						
Saw	47 (35.61)	85 (64.39)	1			
Didn't see	2 (13.33)	13 (86.67)	0.27 (0.06, 1.28)	0.1	-	-
<b>Thinking being susceptible to LF</b>						
Susceptible	10 (20.83)	38 (79.17)	1		1	
Not susceptible	39 (39.39)	60 (60.61)	2.47 (1.1, 5.52)	0.02*	2.83 (1.15, 6.98)	0.02*

**Abbreviations:** OR = odds ratio; \* = statistically significant; CI = confidence interval

#### **4.6 Health system factors and non-compliance to MDA targeting LF**

A total number of 30 health workers involved in MDA supervision were interviewed to look for issues related to the health system. All of them claimed that drug distributors are trained before each MDA targeting LF and that activities are supervised on the field. In addition, they all reported that they didn't face any issue related to drug availability. Almost 90 % of the interviewed health workers reported that MDA was done in one week. Ninety three percent of them (93%) claimed that they were motivated enough to undertake MDA activities effectively. All the health workers interviewed reported thinking that all the eligible individuals didn't take part to the MDA. To the health workers, the non-compliance in the Ankobra community could be explained by the fear of AE (56.67%), absence at the MDA moment (23.33 %), pregnancy (10 %), not suffering from LF (6.67 %) and taking other medications (3.33 %).

#### **4.7 Drug distribution factors and non-compliance to MDA targeting LF**

All the five drug distributors in the Ankobra community were interviewed to identify the issues related to the drug distribution system. All of them claimed to have been informed by the district about an impending MDA targeting LF at least five days before its implementation. They all reported to have informed in their turn their community members at least five days also before MDA. Two out of the five (40 %) reported that MDA duration was five days while the other three reported three, four and six days, respectively. Three claimed to have received remuneration for six days while the two other reported five and seven days, respectively. Three reported the insufficiency of the drugs they received for the MDA while the two others didn't echo this claim.

For the drug distributors, the main reasons for non-compliance in the Ankobra community were by decreasing order of frequency fear of AE, absence at the MDA moment and pregnancy.



## CHAPTER FIVE

### DISCUSSION

#### 5.1 Summary of objectives

The aim of this study was to determine the level of non-compliance to the MDA targeting LF and also to determine its contributing factors in the Ankobra community of Ellembelle health district in 2016.

#### 5.2 Key findings of the study

The study showed a non-compliance rate to the MDA equal to 33.33 %. Young people, women, educated and singles in the Ankobra community had increased odds of being non-compliant. Thinking being not susceptible to LF was significantly associated with non-compliance to the MDA targeting LF in the Ankobra community in 2016.

#### 5.3 Comparison of key findings with literature

The present study reported a non-compliance rate of 33.33 %. This rate is highly superior to that expected for an effective MDA. For a drug distribution campaign to be successful, it requires a compliance rate of more than or equal to 80 % (or a non-compliance rate of less than 20 %). Worldwide, it has been reported a high non-compliance rate to MDA targeting LF throughout the years. In India, non-compliance rates of 32.3 % (Nandha et al., 2013), 70.5 % (Hussain et al., 2014), 29.93 % (Roy et al., 2013) have been reported. In Cameroon and Kenya, it has been found respectively a non-compliance rate of 30 % (Senyonjo et al., 2016) and over 40 % (Njomo et al., 2012), respectively. In Ghana, it has been reported a non-compliance rate of 56.2 % in the Ahanta West district (Offei & Anto,

2014). In Sri Lanka, Weerasooriya et al. reported a non-compliance rate of 28.6 % (Weerasooriya et al., 2007). High rates of non-compliance have drastic negative consequences on the success of LF elimination process. It leads to a high proportion of the population left untreated, therefore susceptible to still harbor some microfilariae in their blood making them a potential reservoir for the persistence of the disease especially in an environment where mosquito vectors are always present.

There is a need for LF elimination Programs to adopt the same operational definition when assessing non-compliance. The high proportion of non-compliance reported in some studies such as the one conducted by in India by Weerasooriya et al. is due to the fact that they considered people who didn't receive MDA drugs as non-compliant (Weerasooriya et al., 2007). The operational definition used in this study and in most of the other studies done about non-compliance (Shuford et al., 2016) considered people who received the drugs, but for any reasons decided to not swallow them.

One major finding of this study is that people who think being not susceptible to LF have increased chance to be non-compliant. Similar findings have been reported in India (Pattanshetty et al., 2010; Kumar et al., 2015). Therefore, there is a crucial need to undertake health education activities about LF and the importance of community members' compliance to MDA for the disease elimination. People need to know that since they are living in an endemic area with the presence of mosquito vectors in the environment, they are susceptible to LF. The best way to prevent himself from getting the disease or hindering its spread is to comply with the MDA campaigns.

Only 16.5 % of the study participants really knew that LF is transmitted by mosquito bites. This proportion is comparable ( $\text{Chi}^2 = 0.45$ ,  $p = 0.5$ ) to that reported by Cabral et al. (20 %,  $N = 102$ ) in Brazil (Cabral, Bonfim, Oliveira & Oliveira, 2017). However, in India it has been reported a proportion of 88 % of study participants which knew that LF is transmitted by mosquito (Hussain et al., 2014). This may be explained by the fact that intensive behavior change communication took place in the India study sites before the study initiation (Hussain et al., 2014).

Most of the non-compliant were young (less than 30 years old), female, educated and single. In Brazil, non-compliance has been reported to be associated with females and single individuals (Cabral et al., 2017). In Cameroon, females and young adults have been found to be more often non-compliant compared to the general population (Senyonjo et al., 2016). Surprisingly, in Mali, being a female has been found to be a protective factor against non-compliance (Dicko et al., unpublished data). The difference between the findings of the current study and the one conducted in Mali may be explained by the fact that in Mali the study has been conducted in an area where a lot of health education activities about LF and MDA importance have previously been done. In addition, in the Malian study area, women are known to agree more with health activities than males as a result of their position in the family. Despite the fact that most of the study participants were educated, the non-compliance rate in the Ankobra community was still high. Similar finding has been reported in India (Hussain et al., 2014).

The reasons reported for the non-compliance during this study were fear of adverse events, not willing to take the drugs, pregnancy, not suffering from LF and taking other medications. In India, Babu et al. found fear of AE (82.1 %, N = 2,898) to be the main reason of non-compliance cited by study participants (Babu & Kar, 2004). The proportion of study participants who reported fear of AE as main reason of their non-compliance in this study is comparable to that reported by Babu et al. ( $\text{Chi}^2 = 1.41$ ,  $p = 0.23$ ). Fear of AE, not willing to take the drugs and pregnancy have been found by several authors as being the main reasons reported for non-compliance to the MDA (Senyonjo et al., 2016; Hussain et al., 2014; Elaziz, El-setouhy, Bradley, Ramzy & Weil, 2013; Roy et al., 2013; Njomo et al., 2012; Kumar et al., 2015). This current finding highlights the need of a robust AE reporting and management system not only in the Ankobra community, but also in all endemic areas to ensure a high MDA compliance of communities. In addition, health education activities should be done before and during MDA campaigns to discuss with community members and make sure they understand that almost all the AE related to the drug distribution are minor or mild in intensity and that they can be easily managed by the health workers if declared on time. It will be helpful to let them know that the observed AE are mainly due to the microfilaricidal activity of the drugs they are taking (drugs killing microfilariae in the blood) and that the frequency of AE will decline with consecutive rounds of MDA.

An important aspect of the distribution system highlighted by the drug distributors was that the drugs were not sufficient to treat all the eligible individuals. This may be explained by the inaccuracy of the data used to estimate the total number of eligible population in the

community. This issue should be fixed so that to hinder drug shortages during MDA campaigns. One way to overcome it is to sensitize community members about the fact that if they don't report accurate information about the community size, it can lead to an underestimation of the population and therefore to drug shortage during the MDA. All the health workers interviewed claimed thinking that all the eligible population doesn't take part to the MDA. Therefore, there is a crucial need to adapt the MDA period to the availability of the targeted individuals to reach a maximum number of people. In addition, drug distributors should be encouraged to revisit the households to reach an adequate coverage and compliance levels.

Morbidity management is an essential component of the GPELF strategy in addition to MDA. Beside the MDA, health education focused on the techniques used at individual level to manage lymphedema cases should be promoted at both the health worker and patient level. In addition, all the hydrocele cases throughout the entire Ellembelle health district must be recorded for surgery to alleviate the hydrocele resulting handicap.

Finally, an integrated approach of the efforts of funders, policymakers, health workers, drug distributors, community members and all the stakeholders will be suitable to achieve the LF elimination goal in the Ankobra community and Ellembelle health district by 2020.

#### 5.4 Limitations of the study

- The present study used only a quantitative design. A mixed design (both quantitative and qualitative) would better identify the reasons and factors associated with non-compliance.
- There is the potential of risk of recall bias since the answer of some of the questions requested participants to think to past events.



## CHAPTER SIX

### CONCLUSION AND RECOMMENDATIONS

#### 6.1 Conclusion

The present study found a MDA coverage rate of 73.5 % and a non-compliance rate of 33.33 % in 2016 in the Ankobra community of Ellebelle health district.

The major reason reported for non-compliance was fear of adverse events. Women, young people, singles, and community members who thought being not susceptible to LF have an increased chance of being non-compliant. Well-elaborated health education strategies targeting these people should be initiated to meet the GPELF elimination goal by 2020.

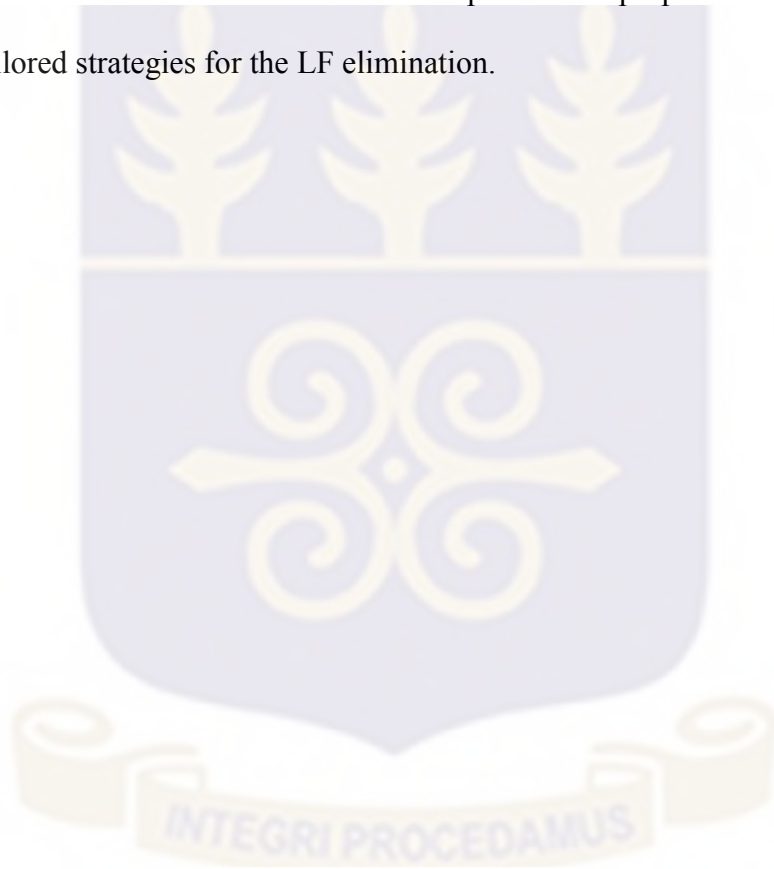
Considerable progress has been made in LF elimination at the national level in Ghana. However, some specific areas like the Ankobra community have still high microfilaremia and high non-compliance rates to MDA targeting LF. This could compromised all the efforts done so far in reaching the GPELF elimination goal by 2020. Tailored MDA strategies should be adopted for the Ankobra community and all the areas nation-wide where a high non-compliance rate to MDA targeting LF has been reported.

#### 6.2 Recommendations

Based on the results of the present study, we recommend to:

- **Ellebelle Health District:** To ensure health education about LF and the importance of MDA in its elimination is done in the communities before and during the campaigns;

- **Drug distributors:** To reach as much as possible a high drug coverage, compliance and to report in a timely fashion all the AE notified to them during the MDA;
- **Community members:** To report all experienced AE to the drug distributors;
- **Researchers:** To undertake further research studies in the Ghanaian communities with LF prevalence  $\geq 1$  % microfilaremia using both quantitative and qualitative approaches and involving many more communities to find the non-compliant and the factors associated with non-compliance to propose and develop efficient tailored strategies for the LF elimination.



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**APPENDICES**  
**APPENDIX 1: Consent form**

**Introduction and Information about the research**

Lymphatic Filariasis (LF) is parasitic disease endemic in Ankobra. Since 2000, the MDA to eliminate it started but until now the prevalence of the disease is above the elimination threshold recommended by the World Health Organization (WHO). Normally, after 5-6 rounds of MDA, LF should be eliminated. Many factors can be involved in the persistence of the disease after the required rounds of MDA. One of the most important among them is the non-compliance to the treatment. We invite you to take part in a research study entitled “Factors associated with non-compliance to mass drug administration for lymphatic filariasis in Ankobra” to help us to eliminate the disease in your community. We want to be sure that you understand clearly the purpose of this research study before you decide to participate. Please ask us to explain any words or information that you may not understand.

**Possible Risks**

There is no risk associated with the participation to this study. It doesn't necessitate any invasive or discomforting procedures to the participants.

**Possible Benefits**

The study will provide information to understand factors associated with the non-compliance in Ankobra. This information will be used by National Lymphatic Filariasis Control Program to develop targeted interventions for LF elimination.

**Participation to the research study**

You are free to participate or not to this research study.

**Confidentiality**

All the information about you will kept confidential. We will neither use your name in any reports nor discuss your participation (without your authorization) with anyone outside the research team.

**Payment**

No payments will be made for the participation to this research study.

**Leaving the Research**

You may end your participation to this study at any time you want.

**If you have any questions about the study**, please call 0555252592.

**VOLUNTEER AGREEMENT**

I understand all that has been explained to me about the study – objectives, benefits, risks and my rights, and I agree to participate in this study.

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Signature of respondent	Date
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Signature of investigator	Date
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**APPENDIX 2: Questionnaires**

**Questionnaire for community members**

Question Number	Questions	Variable name
Q1	Interviewer ID: <input type="text"/> <input type="text"/> <input type="text"/>	
Q2	Date:           D    D    M    M    Y    Y <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
Q3	Name of respondent: _____	
Q4	Locality name: _____	
Q5	Sex of respondent: [M] Male <input type="checkbox"/> [F] Female <input type="checkbox"/>	
Q6	Age of respondent (in completed years): <input type="text"/> <input type="text"/>	
Q7	Marital status of respondent: [1] Single <input type="checkbox"/> [2] Married <input type="checkbox"/> [3] Divorced <input type="checkbox"/> [4] Widowed <input type="checkbox"/>	
Q8	Education level of respondent: [1] No formal education <input type="checkbox"/> [2] Primary education <input type="checkbox"/> [3] Secondary education <input type="checkbox"/> [4] Higher education <input type="checkbox"/>	
Q9	Occupation: [1] Farmer <input type="checkbox"/> [2] Fisherman <input type="checkbox"/> [3] Craftsman <input type="checkbox"/> [4] Seller <input type="checkbox"/>	
Q10	Do you know about lymphatic filariasis (Elephantiasis or hydrocele)? [1] Yes <input type="checkbox"/> [0] No <input type="checkbox"/>	

Q11	Do you suffer from it (interviewer will look at presence of elephantiasis or hydrocele)? [1] Yes [0] No	<input type="checkbox"/>	
Q12	Have you ever seen a case of elephantiasis and/or hydrocele? [1] Yes [0] No	<input type="checkbox"/>	
Q13	Do you know what transmits lymphatic filariasis? [1] Yes [0] No	<input type="checkbox"/>	
Q14	If yes, please say it: [1] Poor sanitation [2] Mosquito [3] Food habits [4] Other (to specify): _____ _____	<input type="checkbox"/>	
Q15	Do you think you are susceptible to filarial infection? [1] Yes [0] No	<input type="checkbox"/>	
Q16	Did you receive the drugs during the last MDA in your community? [1] Yes [0] No	<input type="checkbox"/>	
Q17	Did you swallow the drugs? [1] Yes [0] No	<input type="checkbox"/>	
Q18	If no, what was the reason? [1] Not aware [2] Absence [3] Fear of adverse events [4] Pregnancy [5] Non-attendance of the health staff [6] Assumption that free medicines will not work [7] Large number of pills to be swallowed [8] Taking other medications [9] Not suffering from lymphatic filariasis [10] Other (to specify): _____ _____	<input type="checkbox"/>	

**Questionnaire for health workers**

Question Number	Questions	Variable name
Q1	Do the drug distributors undergo training before each mass drug administration (MDA) for lymphatic filariasis (LF)? [1] Yes [0] No	<input type="checkbox"/>
Q2	What is the duration of LF drug distribution (in days)?	
Q3	Do you have issues with availability of drugs during the MDA? [1] Yes [0] No	<input type="checkbox"/>
Q4	Are you motivated to undertake LF MDA activities? [1] Yes [0] No	<input type="checkbox"/>
Q5	Do you supervise the distribution activities on the field on each MDA? [1] Yes [0] No	<input type="checkbox"/>
Q6	If no to Q5, why? [1] Burden of activities [2] Lack of motivation [3] Lack of personal [4] Other reason (to specify)	<input type="checkbox"/>
Q7	Do you think all the eligible population takes part to MDA? [1] Yes [0] No	<input type="checkbox"/>
Q8	If no to Q7, what do you think are the reasons for the non-compliance to MDA in Ankobra community? [1] Unaware of MDA [2] Absence at MDA moment [3] Fear of adverse events [4] Pregnancy [5] Non-attendance of the health staff [6] Assumption that free medicines will not work [7] Large number of pills to be swallowed [8] Taking other medications [9] Not suffering from LF [10] Other reason (to specify)	<input type="checkbox"/>

**Questionnaire for drug distributors**

Question Number	Questions	Variable name
Q1	How early are you informed about an impending mass drug administration (MDA) in your community? [1] 1-2 days [2] 3-4 days [3] more than or equal to 5 days	<input type="text"/>
Q2	How early do you inform community leaders about the MDA starting? [1] 1-2 days [2] 3-4 days [3] More than or equal to 5 days	<input type="text"/>
Q3	How long is the drug distribution in your community?	
Q4	How many days remuneration do you receive for drug distribution?	
Q5	Are the drugs you receive enough to treat all the eligible population? [1] Yes [0] No	<input type="text"/>
Q8	For you, what are the reasons for the non-compliance in Ankobra? [1] Unaware of MDA [2] Absence at MDA moment [3] Fear of adverse events [4] Pregnancy [5] Non-attendance of the health staff [6] Assumption that free medicines will not work [7] Large number of pills to be swallowed [8] Taking other medications [9] Not suffering from LF [10] Other reason (to specify)	<input type="text"/>

**APPENDIX 3: Approval Ghana health service ethics review committee**

**GHANA HEALTH SERVICE ETHICS REVIEW COMMITTEE**

*In case of reply the number and date of this Letter should be quoted.*



My Ref. GHS/RDD/ERC/Admin/App/17/396  
Your Ref. No.

Research & Development Division  
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ILO DICKO  
School of Public Health  
University of Ghana  
Legon

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol.

GHS-ERC Number	<b>GHS-ERC: 24/12/2016</b>
Project Title	Factors Associated with Non-Compliance to Mass Drug Administration for Lymphatic Filariasis in Ankobra
Approval Date	21 <sup>st</sup> March, 2017
Expiry Date	20 <sup>th</sup> March, 2018
GHS-ERC Decision	<b>Approved</b>

**This approval requires the following from the Principal Investigator**

- Submission of yearly progress report of the study to the Ethics Review Committee (ERC)
- Renewal of ethical approval if the study lasts for more than 12 months,
- Reporting of all serious adverse events related to this study to the ERC within three days verbally and seven days in writing.
- Submission of a final report **after completion** of the study
- Informing ERC if study cannot be implemented or is discontinued and reasons why
- Informing the ERC and your sponsor (where applicable) before any publication of the research findings.

Please note that any modification of the study without ERC approval of the amendment is invalid.

The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Kindly quote the protocol identification number in all future correspondence in relation to this approved protocol

SIGNED.....  
DR. CYNTHIA BANNERMAN  
(GHS-ERC CHAIRPERSON)

**Cc:** The Director, Research & Development Division, Ghana Health Service, Accra