UNIVERSITY OF SUNDERLAND

CONTRIBUTORY ROLE OF SOCIOECONOMIC FACTORS IN THE DEVELOPMENT AND SPREAD OF ANTIMALARIAL DRUG RESISTANCE

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AUTHOR'S DECLARATION

I **PHILIP EMEKA ANYANWU** declare that this thesis is my own and that it has not been submitted, in whole or in part, in any previous application for a degree. Except where stated otherwise by reference or acknowledgment, the work presented is generated from my own original research.

DEDICATION

This work is dedicated to the memory of Professor Dora Nkem Akunyili for her role in fighting fake drugs in Nigeria.

ACKNOWLEDGEMENT

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TABLE OF CONTENTS

ABSTRACT

Background

Malaria remains a global health issue with the burden unevenly distributed to the disadvantage of the developing countries of the world. Nigeria, a middle-income country in sub-Saharan Africa, is one of the countries with high malaria burden in the world. As a socioeconomic issue, the high level of poverty in Nigeria is an important factor that reinforces the persistent malaria burden in the population. Poverty contributes to the malaria burden as it can affect integral aspects of malaria control like treatment seeking behaviours, access to preventive measures and treatment. Presently, there have been renewed efforts in the global malaria control resulting in reductions in the global malaria burden over the last decade. However, the development of resistance to artemisinin-based combination therapies threatens the sustainability of the present success in malaria control. The mechanism behind the development and spread of antimalarial drug resistance is a complex one with multiple factors in play. Nevertheless, antimalarial drug use behaviours remain critical drivers of drug resistance as they can affect some of the other factors. This study adopted a social epidemiological stance in exploring existing antimalarial drug use behaviours that have the potential to drive drug resistance development and spread. The study went further to investigate the role of socioeconomic factors in the adoption of the identified behaviours when treating malaria.

Methods

An exploratory mixed methods research design was adopted in this study. This design involved an initial systematic review of the literature to create a holistic picture of what is known about the issue under study. The systematic review informed the design of a qualitative study involving the use of interviews to explore the existing antimalarial drug use practices in the Nigerian population; and the different socioeconomic factors influencing the behaviours. The qualitative interviews informed the design of a measurement instrument and hypotheses that were tested in a survey with larger number of participants from Nigeria

Findings

The important malaria treatment seeking and drug use behaviours identified in this study were the practice of mixing drug for malaria treatment, presumptive treatment of malaria, sharing of malaria treatment course, and saving antimalarial drugs for future use. When symptoms are experienced, socio-economic factors, like the educational level, type of settlement, and

household income level, tend to determine the treatment behaviours and therefore inform and determine the experience of malaria illness. There were statistically significant relationships between socioeconomic measures and drug use behaviours like the use of mixed drugs, stopping treatment to save drugs, sharing of antimalarial drugs, adherence to recommended dose and time of administration, presumptive treatment and use of recommended drugs for malaria treatment. These behaviours differ regarding the specific socioeconomic measures that are significantly associated with them.

Discussion

Physical and social environments can place constraints on an individual's choices as well as that of a population. As shown in this study, education, income level and type of settlement, as structural factors, affect the decision on how to seek malaria treatment, what antimalarial drug to get, and how to use antimalarial drugs. Practices like mixing, stopping treatment to save drugs, and sharing of antimalarial drugs with others have the potential to encourage the development and spread of antimalarial drug resistance by exposing the parasite to sub-therapeutic doses of antimalarial drugs. Also, mixing of drugs paves the way for the sale of fake as well as expired antimalarial drugs thereby affecting malaria morbidity and illness experience.

Conclusions and Recommendations

In malaria campaigns, there is need to broaden the scope of antimalarial drug resistance control strategies to include strategies targeted at improving the socioeconomic status of people in malaria endemic areas. The informal health facilities were significantly associated with most of the reported resistance-promoting drug use behaviours like mixing; as such efforts to improve the way antimalarial drugs are used should target these facilities. Population-wide improvements in income level, educational level, environmental and structural conditions of the rural areas in malaria endemic settings like Nigeria, will encourage behavioural changes on how antimalarial drugs are used.

List of Abbreviations

AA	Artesunate-Amodiaquine
ACT	Artemisinin-based combination therapy
ACTS	Artemisinin-based combination therapies
AIDS	Acquired Immune Deficiency Syndrome
AL	Artemether-Lumefantrine
AMFm	Affordable Medicines Facility-malaria
ASMQ	Artesunate-Mefloquine
CDC	Centre for Disease Control and Prevention
CMD	Chief Medical Officer
DHAPQ	Dihydroartemisinin-Piperaquine
GFFHTM	Global Fund to Fight HIV, TB, and Malaria
HIV	Human Immunodeficiency Virus
OTC	Over the Counter drug
PCR	Polymerase Chain Reaction
RDT	Rapid Diagnostic Test
SEA	South East Asia
SP	Sulfadoxine-Pyrimethamine
TB	Tuberculosis
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION

1.1 Introduction

This chapter offers an introduction to the study. It starts with a description of the problem under study; highlighting the rationale for this research. The chapter also provides an overview of the structure of the thesis as well as the research question, aims/objectives, and hypotheses.

1.2 Problem Statement

Malaria remains a global health issue with the burden more in the developing countries of the world (Miura, 2013; World Health Organization, 2013b). The renewed effort in global malaria control has resulted in a reduction in the malaria burden in the last decade (World Health Organization, 2014a). This reduction is partly due to the increase in access, availability, and affordability of artemisinin-based combination therapies (ACTs) in malaria endemic regions. However, the development and spread of resistance to ACTs are a major threat to the sustainability of the present success (World Health Organization, 2011).

ACT remains the most potent treatment available for malaria (World Health Organization, 2014a). With resistance to ACT confirmed in South East Asia, there is a high probability that this will follow the pattern of previous cases of resistance to antimalarial drugs, like chloroquine and sulfadoxine-pyrimethamine, that all originated in the Southeast Asia and spread widely to sub-Saharan Africa. As a result, the WHO in its January 12, 2011, news release stressed the urgent need for efforts to control the development and spread of resistance to ACTs. As the increased use of ACTs contributed significantly to the reduction in malaria burden, the development and spread of resistance to ACTs threaten not only the sustainability of this progress; but can also reverse the reduction trend, as cases of resistant malaria infections have higher mortality and morbidity outcomes.

Indeed the mechanism behind the development and spread of antimalarial drug resistance is a complex one with multiple factors -such as drug use practice/behaviours, drug half-life, transmission intensity, clone multiplicity, parasite density, host immunity, within-host dynamics and the genetic basis of drug resistance- in play (Huijben, 2010). Importantly, drug use behaviours have repeatedly been identified as a key factor in the development and spread

of resistance (Huijben, 2010; Talisuna, Okello, Erhart, Coosemans, & D'Alessandro, 2007). Amongst all resistance factors, antimalarial drug use behaviours –such as presumptive diagnosis/treatment, drug overuse, use of sub-therapeutic dose, non-adherence to the treatment regime, amongst others- are very important as they can affect some of the other factors (Huijben, 2010). Also, in comparison with the other factors associated with the development and spread of resistance, drug use practice can be controlled through changes in human behaviours and activities.

Although a global health issue, the burden of malaria is borne more by the African region (World Health Organization, 2016d). This region accounts for the majority (80%) of the malaria cases globally as well as malaria associated deaths (90%), with children under-5 years of age at high risk of malaria infection. Nigeria, a middle-income country in sub-Saharan Africa, is among the countries with the highest malaria burden in the world with 35% of the estimated 426,791 global malaria deaths in 2015 occurring in Nigeria (World Health Organization, 2016d). This percentage of mortality is an increase from 32% as of 2011 (Federal Ministry of Health Nigeria, 2011b).

With a population of about 178.6 million in 2014 (World Meter, 2017), Nigeria accounted for 13% of the global under five years deaths in 2012 (World Health Organization, 2014b) with one in every 15 Nigerian children dying before reaching age one; and one in eight not surviving till their fifth birthday (National Population Commission, 2013a). It is not surprising that malaria is among the leading causes of death in Nigeria, especially in infants and under-five children (National Population Commission, 2013a).

Some factors that drive the persistence of malaria in this population are the availability of conducive environment for vector breeding; the health policy and system in Nigeria in relation to malaria treatment; and the high level of poverty in Nigeria. As a socioeconomic issue, the high level of poverty in Nigeria affects the use of malaria treatment as well as preventive measures. The high cost of ACTs (especially in relation to other antimalarial drugs) constitutes a major barrier to adherence when using them. This factor also encourages the persistent use of artemisinin monotherapies in Nigeria (Ezenduka, Ogbonna, Ekwunife, Okonta, & Esimone, 2014) despite recommendations for their withdrawal by the WHO as their use contributes to the development of resistance against artemisinin derivatives by *Plasmodium* parasites (WHO, 2014).

Environmental factors are important contributors to the persistence of malaria burden in Nigeria. Several *Anopheles* mosquito species that transmit malaria –such as *A. gambiae, A. funestus,* and *A. arabiensis*- are present in Nigeria; with *A. gambiae* being the most common malaria vector in this area (Federal Ministry of Health Nigeria, 2011b). These vectors transmit the malaria parasites all year round. However, the rainy seasons, as compared to the dry seasons, are usually the peak transmission season for malaria in Nigeria (Federal Ministry of Health Nigeria, 2011b). The reasons for this include: increase in water surfaces and ponds which provide a breeding ground for the mosquito vector, hence the increase in mosquito population and bites during the rainy season; increased farming activity during the rainy season, among others (National Population Commission, 2013a). All these factors work hand-in-hand to bring about increased malaria morbidity and mortality during the rainy season (Federal Ministry of Health Nigeria, 2011b).

Like most malaria endemic countries, past episodes of resistance to anti-malarial drugs like Chloroquine and Sulfadoxine-Pyrimethamine (SP) spread quickly in Nigeria. As a result, in 2005, Nigeria adopted ACTs with artemether-lumefantrine (AL) as the first-line treatment for uncomplicated malaria, and Artesunate-amodiaquine (AA) later added as an alternative first-line drug to AL (Ezenduka, Ogbonna, et al., 2014). Other ACTs used in Nigeria for the treatment of uncomplicated malaria cases include dihydroartemisinin-piperaquine (DHAPQ) and Artesunate-mefloquine (ASMQ) (Ezenduka, Ogbonna, et al., 2014). With the increased use of artemisinin in Nigeria (both as monotherapies and in combination with other antimalarial drugs) and the fact that they are sold over-the-counter; their misuse (in relation to drug use behaviours like commonly practiced presumptive treatment (Isiguzo et al., 2014; Onwujekwe et al., 2005; Uzochukwu et al., 2011)), puts this population at risk of the development and spread of resistance to artemisinin by *Plasmodium falciparum*.

1.3 Rationale for the research

Most of the studies on antimalarial drug resistance have been conducted from parasitological (Anderson et al., 2010; Bustamante, Batista, & Zalis, 2009; Noedl et al., 2008; Phyo et al., 2012) and pharmacological (Hastings, 2003; Huijben, 2010; Nayyar, Breman, Newton, & Herrington, 2012) perspectives. Although these studies have contributed to the fight against resistance by providing evidence on the mechanisms involved, the persistent development of resistance to new antimalarial drugs despite these efforts, calls for a new approach to studying this important global health issue. To the best of the researcher's knowledge, there has been no

study on the role of socioeconomic factors in the adoption of drug use behaviours that can promote the development and spread of antimalarial drug resistance. The existing studies on malaria treatment behaviours have focused on describing these behaviours. However, this study went beyond offering description by also studying the underlying causes and outcomes from antimalarial drug use behaviours. From a public health perspective, treating the cause of a health condition does not necessarily bring about improvement in health, especially when the underlying cause of the cause persists. As such, focusing on behaviours and outcomes alone does not bring about the required sustainable change in treatment practices as would be achieved by understanding and addressing the underlying factor reinforcing the behaviours.

Therefore, this study, by adopting a social epidemiological stance, explored how socioeconomic measures, as underlying structural factors, influence malaria treatment seeking behaviours and drug use practices in a way that can promote the development and spread of antimalarial drug resistance. The intrinsic relationship between poverty and malaria (Gallup & Sachs, 2001; World Health Organization, 2012) -which is evident in the fact that poverty as a socioeconomic issue, is a major feature of all malaria endemic populations- is an indicator of a likely important interaction between socioeconomic factors and antimalarial drug resistance.

The decision to conduct this study using the Nigerian population is underpinned by the high malaria burden in Nigeria; previous cases of widespread of antimalarial drug resistance in Nigeria; and the high rate of poverty in Nigeria (with about 46% of the population living below the World Bank poverty line of $1.25 per day (World Bank, 2014)). In addition, although there is currently no detailed study or surveillance programme on antimalarial drug resistance in Nigeria; most of the factors that have been implicated in the development of resistance to artemisinin and other antimalarials in areas like Southeast Asia (high drug pressure, fake antimalarial drugs, high rate of poverty, mass medication, use of monotherapies) have also been well reported in Nigeria (Chuma, Okungu, & Molyneux, 2010; Ezenduka, Ogbonna, et al., 2014; Federal Ministry of Health Nigeria, 2011b; Onwujekwe, Uzochukwu, et al., 2009). These similarities with malaria endemic settings in Southeast Asia suggests the likely existence of artemisinin resistance in Nigeria.

An exploratory mixed method design, involving a systematic review, qualitative interviews, and a survey, was used to answer the research question. The entire process of this study was underpinned by the social production of disease theory, rooted in social epidemiology.

1.4 Research Question

What are the resistance-promoting drug use behaviours adopted in malaria treatment in Nigeria?

How do socioeconomic factors contribute to the adoption of identified malaria treatment seeking and drug use behaviours that can promote the development and spread of antimalarial drug resistance?

1.5 Research Aim and Objectives

The overall aim of this study is to offer an insight into the contributory role of socioeconomic factors in the development and spread of antimalarial drug resistance in Nigeria.

The Objectives of this research are:

- To assess the antimalarial drug use behaviours in the Nigerian population
- To identify antimalarial drug use behaviours that can promote development of drug resistance
- To explore the distribution of the identified antimalarial drug use behaviours among people of different socioeconomic positions.
- To offer insight into the role socioeconomic factors in decision making when seeking malaria treatment and using antimalarial drugs.
- To make recommendations for improving antimalarial drug use behaviours.

1.6 Research Hypotheses

Based on the results of the systematic review and the qualitative interviews, eleven (11) hypotheses were generated and tested using statistical tests. These hypotheses were grouped into major (hypotheses 1 to 7) and auxiliary (hypotheses 8 to 11) based on their importance in answering the research questions and achieving the aim and objectives of this study.

Hypothesis One

H0: Socioeconomic position is not related to adherence to malaria treatment course

H1: Socioeconomic position is related to adherence to malaria treatment course

Hypothesis Two

H0: Socioeconomic position is not related to the use of the recommended antimalarial drugs

H1: Socioeconomic position is related to the use of the recommended antimalarial drugs

Hypothesis Three

H0: The practice of mixing drugs for malaria treatment does not vary according to socioeconomic position

H1: The practice of mixing drugs for malaria treatment varies according to socioeconomic position

Hypothesis Four

H0: The use of malaria diagnostic testing prior to treatment does not vary according to socioeconomic position

H1: The use of malaria diagnostic testing prior to treatment varies according to socioeconomic position

Hypothesis Five

H0: The experience of treatment failure is not statistically associated socioeconomic position

H1: The experience of treatment failure is statistically associated with socioeconomic position

Hypothesis Six

H0: The type of facility malaria treatment is sought is not associated with the outcome of treatment failure

H1: The type of facility malaria treatment is sought is associated with the outcome of treatment failure

Hypothesis Seven

H0: Antimalarial drug use practices are not associated with the experience of treatment failure.

H1: Antimalarial drug use practices are associated with the experience of treatment failure.

Hypothesis Eight

H0: Socioeconomic position does not affect knowledge about malaria infection.

H1: Socioeconomic position affects knowledge about malaria infection.

Hypothesis Nine

H0: Socioeconomic status does not affect perceptions about malaria infection.

H1: Socioeconomic status affects perceptions about malaria infection.

Hypothesis Ten

H0: The use of preventive measures is not associated with level of socioeconomic measures

H1: The use of preventive measures is associated with level of socioeconomic measures

Hypothesis Eleven

H0: There is no difference in malaria treatment seeking behaviours for children across the levels of socioeconomic measures

H1: There is difference in malaria treatment seeking behaviours for children across the levels of socioeconomic measures.

1.7 Structure of the thesis

This thesis is arranged in chapters which are structured around the key stages of this work. Chapter One, as you have just read, introduced the study, giving a general overview of the problem under study and the research questions, aim and objectives, and hypotheses. Chapter Two contains a detailed review of existing studies about the subject area. It contextualises the research problem and provides evidence of what is already known. This chapter is followed by chapter three which explains the theoretical framework adopted in this study and how it fits into the wider discipline of epidemiology. The research methods that were chosen in this

inquiry, and their broad philosophical underpinning, were reported in Chapter Four. Chapters Five, Six and Seven reported the results of the systematic review, qualitative interviews and the survey strands of this study respectively. These results are discussed together in Chapter Eight, enabling a comparative and complementary discussion of the implications of the results and how they relate to the existing body of knowledge on the subject area. Chapter Nine, the final chapter of this thesis, provides a conclusion of the entire study and recommendations based on the findings.

1.8 Contributions to knowledge

- This research is the first study that, in studying malaria treatment seeking and drug use behaviours, has gone beyond the description of the phenomenon by creating an insight into the causes and consequences of these behaviours. As such, this study provides evidence on the significance of socioeconomic measures in predicting specific drug use behaviours, and possible treatment outcomes like drug resistance.
- Identification of the practice of mixing of drugs for malaria treatment, which has not been reported in malaria literature and has the potential to encourage the development of antimalarial drug resistance; and other important public health implications.
- Another of the original contributions of this study to malaria research is the development and design of a validated measurement instrument (questionnaire) that can be used in identifying groups vulnerable to adopting behaviours that can promote the development and spread of antimalarial drug resistance in Nigeria.

1.9 Publications

Over the course of this study, some parts of the results of this thesis have been published in peer-reviewed Journals and conference proceedings. Publications were made on the individual strand of this study. Below are the citations for the publications.

[1] Anyanwu, P., Fulton, J., Paget, T., & Evans, E. (2016). Socioeconomic Determinants of Antimalarial Drug Use Behaviours: A Systematic Review. *Journal of Community and Public Health Nursing*, *2*(2). pp.123. DOI: 10.4172/2471-9846.1000123

[2] Anyanwu, P., Fulton, J., Paget, T., & Evans, E. (2017). Exploring the role of socioeconomic factors in the development and spread of antimalarial drug resistance: a qualitative study. *Malaria Journal.*

[3] Anyanwu, P. (2016). Contributory role of socioeconomic factors in the development and spread of antimalarial drug resistance: a qualitative study of antimalarial drug use behaviours. Presented at EuroSciCon Parasitic Infection Conference, 2016 at London O2 Arena, London. Abstract available at http://lifescienceevents.com/wp-content/uploads/ParasiticABSTRACTS2016.pdf accessed on 12/02/2017

[4] Anyanwu, P. (2017). Exploring the role of socioeconomic factors in the development and spread of antimalarial drug resistance: a qualitative study. Presented at Keystone Symposia Malaria from innovation to eradication 2017 at Speke Resort, Kampala, Uganda.

1.10 Chapter Summary

The development and spread of antimalarial drug resistance remain a major threat to the current achievements in global malaria control. Currently, resistance to artemisinin-based antimalarial drugs by the *Plasmodium* parasite has been confirmed in Southeast Asia. Given the pattern of spread of resistance to previous antimalarial drugs, the African population stands at risk of artemisinin drug resistance. This study aimed to contribute to the urgent need to control the development and spread of antimalarial drug resistance by exploring the existing antimalarial drug use behaviours in Nigeria and their distribution among those at different levels of socioeconomic measures. Eleven hypothesis generated from the initial strands of this study were tested in the survey strand. One major contribution of this study to the subject area is in its identification of an important antimalarial drug use behaviour with potentials of driving the development of resistance which has not been reported in malaria literature.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter provides a detailed review of existing studies on malaria. It includes the literature sources consulted in creating an understanding of the research problem and what is already known about it. The chapter also contextualises the research problem and the need for the study.

The chapter sets out providing a general overview of malaria, highlighting its epidemiology, prevention, treatment and control. The role of resistance in malaria control was also reviewed; this was followed up later on in the chapter by a detailed review of the mechanisms and history of antimalarial drug resistance. Also, the cause-and-effect relationship existing between malaria and poverty was explained. The rest of the review focused on providing an insight into malaria treatment-seeking behaviours in the highly-endemic Nigerian population, highlighting the existing practices that can encourage the development of drug resistance in this population.

2.2 Overview of Malaria

Malaria has been a major global health issue for centuries. Its burden goes as beyond the discovery of the causal parasite in the 19th century by Alphonse Laveran in Algeria (Harrison, 1978). It is a tropical disease caused by *Plasmodium* parasites transmitted through the bites of *Anopheles* mosquitoes (World Health Organization, 2014a).

Of the *Plasmodium* parasite species, only five have been identified to cause malaria in humans. These include *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale* and *Plasmodium knowlesi* (World Health Organization, 2013b). Amongst these five species, the *P. falciparum* and *P. vivax* cause most of the malaria cases globally (World Health Organization, 2013b). Nevertheless, *P. falciparum* is the most common species causing malaria morbidity and mortality in sub-Sahara Africa and South-eastern Asia -both regions bear the highest global burden of malaria- (World Health Organization, 2013b). Also, *P. falciparum* causes most of the malaria mortality in non-immune individuals (World Health Organization, 2012).

Unlike *P. falciparum*, *P.vivax* infection is more in South-eastern Asia than in Africa (World Health Organization, 2013b). The low rate in of *P.vivax* in Africa has been attributed to the high frequency of the Duffy negativity trait among Africans. The absence of the Duffy antigen

(which is the receptor protein for *P. vivax*) in the red blood cells confers resistance to *P. vivax* infection (World Health Organization, 2013b). Therefore, transmission of the *P. vivax* parasite by mosquitoes to Duffy negative individuals does not lead to infection (World Health Organization, 2013b).

Furthermore, the female *Anopheles* mosquito is the vector responsible for the spread of the malaria parasite. As in the parasite, different species (about 30) of the *Anopheles* mosquitoes are involved in malaria transmission (Huijben, 2010; Y. Kim & Schneider, 2013; World Health Organization, 2013b). The distribution of the *Anopheles* species that transmit malaria varies in different regions and areas of the world. For example, in Nigeria, the most dominant species of *Anopheles* that are involved in malaria transmission include *A. funestus*, *A. gambiae complex*, *A. arabiensis* and *A. melas* (Jimoh, Sofola, Petu, & Okorosobo, 2007). The population of these vector in an area will affect malaria transmission intensity.

Importantly, the transmission mechanism of malaria is an integral aspect of the infection. The *Plasmodium* parasite has a complex life cycle, parts of which are spent in a human host (asexual reproductive stage) and a mosquito host (sexual reproductive stage) (Huijben, 2010; Y. Kim & Schneider, 2013). Therefore, for a successful life cycle and transmission of the infection, the parasite requires both human and mosquito host. Hence, most of the prevention and treatment measures are centred around interrupting the life cycle of the *Plasmodium* species.

2.3 Epidemiology of Malaria

According to the WHO World Malaria Report (2016d), 91 countries have ongoing malaria transmission as at the end of the year 2015. Nevertheless, the burden is more in the sub-Saharan African region of the world.

Over the last decade, the global burden of malaria has experienced significant reduction. Between the year 2010 and 2015, the WHO reported a 21% and 29% reductions in global malaria incidence and mortality respectively (World Health Organization, 2016d). The 2015 estimate for global malaria-related deaths was approximately 429,000 (World Health Organization, 2016d). This recent data show progress in the fight against malaria. However, the burden of malaria is still very significant especially when one considers other effects and outcomes of this entirely preventable and treatable infection. It is still one of the leading causes of under-five mortality globally (World Health Organization, 2016c). No wonder six of the seven countries with the highest rate of under-five mortality in 2015 are malaria endemic

countries (Angola, Chad, Central African Republic, Sierra Leone, Mali, and Nigeria) (World Health Organization, 2016c, 2016d).

Although a global health burden, malaria is not uniformly distributed in all regions of the world (Miura, 2013). The WHO malaria report (2016d), showed that most of the global malaria cases (90%) and deaths (92%) in 2015 still occurred in sub-Saharan Africa; with about 70% of the deaths occurring in children under-five years of age. Given that health records and data from health facilities in most areas of Africa are incomplete, and the fact that most malaria treatments in this region are sought outside the formal health facilities that produces the available records (Ansumana et al., 2013; Chuma et al., 2009; Cohen, Yavuz, Morris, Arkedis, & Sabot, 2012; Jombo, Araoye, & Damen, 2011), the malaria burden in this region is most likely underreported. The high prevalence of malaria in endemic areas in Africa is further sustained by the year-round transmission in most of these areas.

Malaria is an all-season infection; nevertheless, the prevalence varies throughout the year (Chuma et al., 2010). The peak period is usually during the rainy season (Chuma et al., 2010). As the parasites need the vector for a successful transmission and life cycle, heavy rainfall in the tropical areas increases the population of mosquito vectors by providing breeding sites (water surfaces) for them (Miura, 2013). These conditions lead to higher rate of transmission and subsequent increase in the rate of malaria infection during this time of the year.

2.3.1 Who is at Risk?

Living in a malaria endemic area puts one at risk of malaria infection (World Health Organization, 2016d). As earlier stated, presently, 91 countries still have ongoing malaria transmission, with about half of the world population at risk of the disease (World Health Organization, 2016d). The risk of malaria infection usually increases with increase in the vector population, increased exposure to mosquito bites, and reduction in the level of immunity. The *Anopheles* mosquitoes that transmit malaria are widely distributed in tropical countries unlike in temperate regions.

As stated, the level of immunity is an important factor in determining an individual's level of risk to malaria infection. On top of the list of groups at high risk of malaria infection due to the level of immunity are children under five years of age and people from non-endemic areas. To understand the reason why these groups are at high risk, there is a need to briefly explain the concept of acquired (partial) immunity to malaria.

Notably, acquired immunity to malaria is a debated concept as there is no consensus on the mechanisms of the protection (Doolan, Dobaño, & Baird, 2009). However, it involves enhancement in the immune mechanism of a host, that is acquired as a result of previous malaria infection (Doolan et al., 2009). This means that for people who are living in endemic countries, subsequent malaria infections after their debut will be less severe, and in some cases, might not result in disease (CDC-Centers for Disease Control and Prevention, 2012). It is also worth noting that this protection is usually not complete, hence the word 'partial'.

Neonates of mothers living in malaria endemic area are temporarily protected by the passive (acquired) immunity from the mother (Federal Ministry of Health Nigeria, 2011b). This partial protection is lost after the first three months of life (Federal Ministry of Health Nigeria, 2011b). The loss of this partial protection in children under-five years of age exposes them to high risk of malaria infection (Nayyar et al., 2012). Therefore, malaria infection in this age group is usually complicated and severe.

Similarly, people living in non-endemic countries who have no recent exposure to malaria, and so have no partial immunity against malaria, are at a high risk of severe and complicated malaria infection (Federal Ministry of Health Nigeria, 2011b; World Health Organization, 2014a). International travelers from non-endemic areas fall into this category.

Other malaria high-risk groups include pregnant women, people with compromised immune system like HIV/AIDS patients, amongst others (World Health Organization, 2014a). Pregnant women in malaria endemic areas are at increased risk of malaria disease. This is as a result of the biological changes (hormonal changes in their body which reduces their immunity) as well as reduced mobility (which can affect their access to malaria treatment) as a result of their pregnancy (Grietens et al., 2010; Hartman, Rogerson, & Fischer, 2010; Nosten et al., 1999).

In addition to these, poverty is another risk factor that increases people's risk of malaria (Gallup & Sachs, 2001). The association between poverty and malaria is demonstrated in the fact that most of the countries with high burden of malaria are characterized by high level of poverty, infant mortality and poor access to health care.

2.3.2 Malaria and Epidemiological Transition

Going back some centuries, the global distribution of malaria has changed over time (Hay, Guerra, Tatem, Noor, & Snow, 2004; Kiple, 1993). Some countries that were previously malaria endemic have successfully eliminated the disease (Aregawi, Cibulskis, Otten, &

Williams, 2009). The WHO Global Malaria Eradication Programme in 1955-1968 saw the elimination of malaria in many areas of the world (Aregawi et al., 2009). By 1970s, malaria was eradicated in 24 countries, mostly from the North American and European regions (Kiple, 1993) -these include Spain, Bulgaria, Hungary, Italy, Netherlands, Portugal, Jamaica, USA, Australia, amongst others (Aregawi et al., 2009). The period from 1950's and 1970's also comes under the Post-World War II period of economic expansion that saw the boom of the economy of the Western countries (Bullock & Yaffe, 1979; Marglin, 1990). In evaluating the history of these countries and the processes they have undergone in eradicating malaria, the issue of epidemiological transition stands out as an important factor in explaining malaria eradication in these regions.

One of the features that most of the countries that have achieved malaria eradication share is the fact that they have all undergone epidemiological transition. Epidemiological transition is a term used to refer to the general shift in a country's disease burden from acute infectious and deficiency diseases to chronic non-communicable diseases (Harper & Armelagos, 2010; Wahdan, 1996). The key indicators of an epidemiological transition are changes in the leading causes of death and morbidity in a country (Wahdan, 1996). These changes are usually driven by changes in the socioeconomic, demographic, technological and environmental conditions of a population. With the Post-World War II economic growth in Europe, there was a reduction in infectious diseases especially those referred to as "diseases of the poor", like malaria. Most of the current malaria endemic countries, especially from sub-Saharan, are characterized by the high rate of poverty (Gallup & Sachs, 2001; World Health Organization, 2012) and are yet to undergo or are currently undergoing epidemiological transition. Features of poverty like the low standard of living, poor housing, dilapidated environment amongst others, further expose people in tropical areas to the mosquitoes that transmit malaria.

2.4 Malaria Prevention

Malaria preventive measures are usually centered on vector control by reducing the population of the vector and personal protection from the vector (mosquito bites) (Miura, 2013; World Health Organization, 2014a). The currently used malaria preventive measures can be broadly categorized into two: those that involve the use of preventive tools and those that do not (hence are centered mainly on human behaviours).

The malaria preventive measures that involve the use of preventive tools include the use of insecticide treated nets (ITN), indoor residual spraying with insecticide (IRS) (World Health

Organization, 2016d), use of nets on windows and doors amongst others. The major barrier to the use of these preventive tools is the financial cost of acquiring them (Choonara, Odimegwu, & Elwange, 2015). This issue is more pronounced in the highly endemic areas where almost the entire population is constantly at risk of malaria infection; therefore, affording these preventive tools all year round becomes a challenge for the poor.

In addition to vector control, malaria can also be prevented using prophylaxis (Miura, 2013). This option is more common in travelers from non-endemic areas, and pregnant women in endemic areas (like the use of sulfadoxine–pyrimethamine as intermittent preventive therapy for malaria by pregnant women) (World Health Organization, 2015d). As with the use of the above mentioned preventive tools, the cost of the prophylaxis can be a barrier to their constant use in malaria prevention.

Furthermore, the malaria preventive measures that do not involve the use of tools include: avoiding stagnant water around the home, avoiding staying or sleeping outside at night, wearing long sleeved shirts and trousers at night times, closing doors and windows at night time amongst others. As stated earlier, these measures are centered mainly around human behaviours and require little or no financial cost.

2.5 Malaria Diagnosis

Early diagnosis and treatment of malaria remain a key aspect of malaria control. Presently, the WHO have recommended that all suspected malaria cases be confirmed using a parasite-based diagnostic testing prior to treatment (World Health Organization, 2016d). Test before treatment is important in controlling overuse of antimalarial drugs by ensuring only those who need the antimalarial drugs are treated (World Health Organization, 2015d). It has also been described as more cost-effective than presumptive treatment (Ansah, Epokor, Whitty, Yeung, & Hansen, 2013; Ansah et al., 2013; Parikh et al., 2010). Consequently, the need for a confirmatory test for malaria prior to treatment informed the Test, Treat and Track (TTT) strategy rolled out by the WHO in 2012 (World Health Organization, 2012). The available parasite-based diagnostic tests for malaria are microscopy, rapid diagnostic test and Polymerase chain reaction (PCR). In the Nigerian population, microscopy is the most commonly used parasite-based method of malaria diagnosis.

Microscopy: The use of microscopy in malaria diagnosis is considered the ‘gold standard’. The test is based on examination of a Giemsa-stained blood smear using a microscope (CDC-Centers for Disease Control and Prevention, 2015). One basic of the basic requirements for

malaria microscopy is a qualified microscopist. A microscopist and other basic requirements for conducting a malaria microscopy test (like a microscope) constitute an important barrier to its widespread use, especially in remote areas with high level of malaria transmission (Mokuolu et al., 2016). Also, the use of microscopy for malaria diagnosis faces the challenge of quality control especially with the subjectivity attributed to the reliance on the expertise of the microscopist/laboratorian. This issue is further exacerbated by the fact that there is no global standard regarding the qualification of microscopists (Ayalew, Tilahun, & Taye, 2014; CDC-Centers for Disease Control and Prevention, 2015; Nateghpour et al., 2015).

Rapid Diagnostic Test (RDT): RDTs for malaria diagnosis are based on detection of *Plasmodium* parasite antigens (CDC-Centers for Disease Control and Prevention, 2015). Using a small amount of blood, RDTs conduct immunochromatographic assay with specific antigens, like Histidine-Rich Protein 2 and lactate dehydrogenase, targeted (Tiono et al., 2014; Wongsrichanalai, Barcus, Muth, Sutamihardja, & Wernsdorfer, 2007). RDTs are slightly less specific and sensitive than the microscopy (World Health Organization, 2015d); however, they require less training and skills to use. Also, the basic requirements for microscopy are not required, making RDTs an effective diagnostic tool in resource-poor settings. In addition, RDTs usually require less time to produce malaria test result (usually takes between five to twenty minutes) and are cheaper than the microscopy and PCR methods (CDC-Centers for Disease Control and Prevention, 2015). Based on its features, the use of RDTs offers a better opportunity for scaling up diagnostic testing to remote areas as it requires less supportive infrastructure and skilled labour than microscopy (Batwala, Magnussen, Hansen, & Nuwaha, 2011; Mokuolu et al., 2016). Some of the common RDTs available for malaria diagnosis include Quality assured Histidine-Rich Protein II (HRP2) based RDTs; Plasmodium Lactate Dehydrogenase (PLDH); and Aldolase based RDTs (Federal Ministry of Health Nigeria, 2011b).

Polymerase chain reaction: PCR is currently the most sensitive parasite-based test for malaria confirmation (CDC-Centers for Disease Control and Prevention, 2015; Hermsen et al., 2001). This test is based on detection of the *Plasmodium* parasite nucleic acid (CDC-Centers for Disease Control and Prevention, 2015). In relation to the other tests, PCR is very important for malaria detection in cases of sub-clinical infections, that is cases of malaria infection where the parasite rate is low (Coleman et al., 2006; Snounou et al., 1993). Nevertheless, PCR malaria test although used in some clinical settings, its use is mainly seen in malaria research (Bharti, Letendre, Patra, Vinetz, & Smith, 2009). This low usage of PCR in clinical settings despite its

importance in detecting low rate of parasitemia is as a result of the high cost of conducting it (Bharti et al., 2009; CDC-Centers for Disease Control and Prevention, 2015), as well as the longer time it takes for results to be ready (CDC-Centers for Disease Control and Prevention, 2015).

Another commonly used method of malaria diagnosis is presumptive diagnosis based on clinical symptoms present (Miura, 2013). According to the latest WHO malaria treatment guideline, presumptive treatment of malaria should only be used in suspected malaria cases where a parasite-based diagnostic testing is not possible (World Health Organization, 2015d). Presumptive diagnosis of malaria happens when the diagnosis and treatment of the condition is based mainly on clinical symptoms, which is usually fever (Masanja et al., 2012). As a form of clinical diagnosis, presumptive treatment is of low specificity compared to parasite-based methods because of the similarity between malaria symptoms and that of other diseases like typhoid (Wongsrichanalai et al., 2007). Presumptive diagnosis is not a confirmatory test of malaria and is not parasite based, as such its use is not encouraged in malaria treatment. Nevertheless, presumptive treatment remains the most used method of malaria diagnosis in most endemic areas, and a driver of self-treatment of malaria (Isiguzo et al., 2014; Wongsrichanalai et al., 2007).

2.6 Malaria Treatment

Malaria remains a treatable infection. The primary objective of treatment of uncomplicated malaria case is to eliminate the malaria parasite from the body (World Health Organization, 2015d). In other words, the treatment should be able to improve the patient's health by inhibiting disease progression, reducing the transmission intensity (as a public health goal) and control antimalarial drug resistance development and spread (Bloland, 2001)

Malaria treatment dates back to several centuries ago. One of the first treatment measures for malaria was the use of cinchona bark in the 16th century in America by the Spaniards (Huijben, 2010). It was not until 1820 that the active antimalarial compound in the cinchona bark 'quinine' was isolated (Huijben, 2010). All these developments in treatment were achieved before the microscopic identification of the malaria parasite by Alphonse Lavaran in 1880 (Huijben, 2010; Laveran, 1880). Following these discoveries, other scientists like Robert Koch were able to establish the sensitivity of the blood-stage malaria parasite to quinine (Huijben, 2010). However, quinine treatment was expensive at that time and out of the reach of the poor, and so recorded little success in malaria eradication. Although its use is currently less common,

quinine is still used for the treatment of uncomplicated and severe malaria in some settings (Achan et al., 2011)

Following the discovery of quinine, a new antimalarial compound was discovered in 1934, chloroquine. Unlike quinine, chloroquine was more successful in malaria eradication program as it was much cheaper than quinine. Chloroquine, alongside DDT (dichlorodiphenyltrichloroethane) spraying, contributed to the huge success of the Global Malaria Eradication Program in 1955 that saw malaria reduction and elimination in most western countries (Huijben, 2010). Chloroquine was used globally for malaria treatment. The widespread use of chloroquine led to the development of resistance in *Plasmodium* (Ridley, 2002).

Other antimalarial drugs include:

- Sulfadoxine and pyrimethamine
- Atovaquone-proguanil (Malarone)
- Other quinoline medicines: amodiaquine, mefloquine, halofantrine amongst others (Ridley, 2002).

Another class of drugs used for malaria treatment are the artemisinin compounds. Artemisinin has been used to treat malaria over the past decades in places like China (Miura, 2013). Artemisinins are extracted from *Artemisia annua* plants of Asian origin (Miura, 2013). In relation to other antimalarial drugs, artemisinin drugs are very effective in parasite clearance; can relief the malaria clinical symptoms faster (Cui & Su, 2009; Ridley, 2002; White, 1996); and can affect the transmissible gametocyte stage of the malaria parasite (Okell, Drakeley, Ghani, Bousema, & Sutherland, 2008). However, they are relatively more expensive than other antimalarial drugs (Yeung, Pongtavornpinyo, Hastings, Mills, & White, 2004). Another issue with the use of artemisinin compounds is that they have short half-lives, and so treatment with artemisinin monotherapies takes about 5 to 7 days (Saunders et al., 2012). This issue with the half-life and prolonged treatment encourages the development of resistance to artemisinin drugs by the *Plasmodium* parasites (Ridley, 2002; WHO-Roll Back Malaria & Organization, 2001). To ensure and protect the effectiveness and continued use of artemisinin in malaria treatment, there was need to use these drugs in combination with other antimalarial drugs with a longer half-life and different targets (Ridley, 2002; WHO-Roll Back Malaria & Organization, 2001). This is one of the rationales for the use of artemisinin-based combination therapies. As

Artemisinin derivatives produce a rapid parasite clearance in the first days of treatment; subsequent complete clearance of parasites is dependent on the partner drug (Huijben, 2010; Premji, 2009).

Certainly, ACTs are presently the most effective antimalarial drugs available for treatment of uncomplicated malaria cases (World Health Organization, 2014a). It was recommended as the first-line treatment for uncomplicated malaria cases by the WHO in 2006. This recommendation has been adopted by over forty (40) African countries (Bosman & Mendis, 2007). Some of the commonly used ACTs include:

- artemether-lumefantrine (Coartem®),
- Artesunate+amodiaquine,
- Artesunate+mefloquine
- Artesunate+SP, and
- dihydroartemisinin-piperaquine

The combination that is used as the first line treatment in each country can differ depending on the level of resistance to the partner drug (lumefantrine, amodiaquine, mefloquine or SP) in the area (Huijben, 2010).

Early and proper treatment of malaria is effective in reducing the level of morbidity and mortality from the infection, as well as reducing further transmission to others. Proper treatment requires correct diagnosis and use of recommended drug (World Health Organization, 2016d). This is however not always obtainable in highly endemic countries where treatment is usually preceded by presumptive diagnosis (Miura, 2013). The cost of malaria treatment in the midst of high level of poverty poses a barrier to proper malaria treatment. This effect is more with ACT which is significantly expensive (with a median cost of a complete course of the adult dose at about USD $3.87 in high poverty endemic areas like Nigeria) (Ezenduka, Ogbonna, et al., 2014).

Another factor to consider in ensuring proper malaria treatment is the source of the treatment. Several studies in malaria endemic areas have shown that the informal sector is the most popular source for malaria treatment (Chuma et al., 2010; World Health Organization, 2012b). The use of the informal sector for malaria treatment promotes presumptive and self-treatment (Erhun & Osagie, 2004; McCombie, 2002; Onwujekwe et al., 2005).

2.7 Malaria Resistance

One of the greatest challenges to effective control of malaria globally is the development and spread of resistance to antimalarial drugs by the *Plasmodium* parasites (Federal Ministry of Health Nigeria, 2011b; World Health Organization, 2016d). It has repeatedly been identified as one of the major drives to the persistent burden of malaria in developing countries (World Health Organization, 2016d). According to the WHO, antimalarial drug resistance is defined "as the ability of a parasite strain to survive and/or multiply despite administration and absorption of a drug given in doses equal to or higher than those usually recommended, but within the tolerance of the subject" (Bloland, 2001, p. 12). In other words, the parasites undergo changes that render the medication used to cure the infections they cause ineffective.

The development of resistance to antimalarial drugs is not a new phenomenon. As far back as 1844 and 1910, there were reports of quinine resistance; although these reports were not supported by a clear evidence (Talisuna, Bloland, & d'Alessandro, 2004). After the introduction of chloroquine, the first report of resistance against it (1957 in Asia) emerged rapidly. The spread of chloroquine resistance led to its replacement with SP as the first line drug in many countries in Asia, South America, and Africa. However, resistance to SP also emerged soon after its introduction (Talisuna et al., 2004). These resistance developments were all first reported and confirmed in Southeast Asia, then subsequently spread widely to sub-Saharan Africa region.

Presently, the use of ACTs has contributed to the recent reduction in global malaria burden since 2000 (World Health Organization, 2014a). The development of resistance to artemisinin is, therefore, a major challenge to sustaining the current achievement in malaria control. Artemisinin resistance by *Plasmodium* parasites has been detected in four countries in Southeast Asia: Cambodia, Myanmar, Thailand and Vietnam (Enserink, 2008; Lim et al., 2009; World Health Organization, 2014a). Considering the fact that resistance against other antimalarial drugs in the past –like chloroquine- first emerged in Southeast Asia and subsequently spread rapidly to other areas, the effectiveness of ACT as the first-line treatment for malaria is in jeopardy. This poses a major threat to the global efforts to control and indeed, eradicate malaria (Newman, 2011; Tanner & Savigny, 2008).

Indeed, antimalarial drug resistance has a broad-spectrum effect that cuts across several areas of an individual or a population's overall health and well-being. Health-wise, drug-resistant

cases of malaria infection usually result in higher rates of morbidity and mortality, especially when the available antimalarial drugs are not effective in inhibiting the disease progression.

2.8 Malaria Control Programmes

The achievement of malaria eradication in Western (developed) countries contributed to the reduction in the attention given to the eradication program in other parts of the world after the 1970s. Interest in malaria eradication, research, and drug development started dwindling after the elimination of malaria in western countries (Greenwood & Mutabingwa, 2002). For instance, between the period of 1975 and 1996, there were about 1,223 new drugs developed. Despite the persistent burden of malaria during this period (which was more in developing countries), only 3 of these drugs were antimalarial (Greenwood & Mutabingwa, 2002). The neglect of malaria in the past is partly responsible for the high burden of malaria in the current era (World Health Organization, 2005a).

Interestingly, the last decades have seen renewed interests in the fight against malaria with several organizations and non-endemic countries increasingly getting involved in malaria control program(Carter, Escalada, & Singh, 2017; Koram, 2016; Mueller, Bassat, Lacerda, & del Portillo, 2017). This renewed interest aligns with the increased globalization, with the burden of malaria transcending geographical boundaries and impacting on the economy and health of people in endemic as well as non-endemic areas. Hence, malaria eradication and control programs are gathering momentum globally. Some of the organizations currently involved in global response to malaria control include

- Roll Back Malaria partnership by the World Health Organization (WHO)
- Bill and Melinda Gates Foundation
- Global Fund to Fight HIV, Tuberculosis (TB), and Malaria (GFFHTM)
- The Affordable Medicines Facility-malaria (AMFm) managed by the GFFHTM (The AMFm has contributed to the increased access to ACTs- (Ezenduka, Ogbonna, et al., 2014))
- US President's Malaria Initiative
- World Bank's Booster Programme

Despite the existence of these malaria control programs, there have been persistent challenges to the control and elimination of malaria. Part of the challenges includes early treatment of

malaria, treatment seeking behaviours, the development and spread of resistance, poverty, drug distribution and use system, amongst others.

2.9 Human and Economic Cost of Malaria

Malaria has an insidious effect that cuts across population health, economic and social development (Ricci, 2012). Apart from the health effects of morbidity and mortality, malaria has a huge impact on the economy of endemic countries. The economic burden of malaria has been studied from both the micro- and macro- economic perspectives. While studies on the microeconomy of malaria concentrate on the direct cost of prevention and treatment at individual, household or health services level; macroeconomy studies measure the effect of malaria at country or population level, assessing its long-term effect on the economy.

At the microeconomic level, the cost of malaria includes treatment and prevention costs, loss of productivity, reduced educational attendance and achievements, reduced saving/investment, reduced standard of living by spending a significant amount of income on treatment, amongst others (Nonvignon et al., 2016; Sachs & Malaney, 2002).

At the macroeconomic level, malaria affects the economic development of endemic countries. The total sum of economic loss from productivity attributed to malaria has a resounding effect on the economy of developing countries (Miura, 2013). The high burden of malaria has also been identified to discourage foreign investment and tourism in endemic areas (Malaney, Spielman, & Sachs, 2004; Miura, 2013; The World Bank, 2015). There are indications that the fear of contracting malaria will discourage foreign investors from non-endemic areas from investing in malaria endemic areas. One of the most cited cases in this regard is that of the Billiton, an Anglo-Australian multinational mining, metals, and petroleum company that invested $1.4 billion in Mozambique. In the next two years, the company had 7000 cases of malaria among its workers; including 13 British workers who died as a result of malaria infection (Sachs & Malaney, 2002).

Correspondingly, on the impact of malaria on businesses, the World Economic Forum in 2006 reported that of the 8000 business leaders from across the world who participated in the Executive Opinion Survey in 2004, 22% reported that malaria affects their business (Bloom, Bloom, & Weston, 2006). Also, 10% of the participants perceived the negative effect of malaria on their business as serious (Bloom et al., 2006). The proportions were higher for business leaders with business interests in sub-Saharan Africa with 72% reporting that malaria affects their business, and 39% describing the negative effect of malaria on their business as serious

(Bloom et al., 2006). These findings were similar to those from the study by Nonvignon et al. (2016) on the economic burden of malaria on businesses in Ghana, which reported that malaria affected business productivity (through employee absenteeism), increased the cost of operation (through increased cost of medical expenses paid for employee's malaria treatment) amongst others. These impacts of malaria on businesses will subsequently affect the wider society through reduced tax revenue from businesses to the State, and reduced income tax from individuals.

With these economic impacts of malaria, it is not surprising that poverty and malaria go together as these negative effects of malaria go a long way in keeping and dragging people further down the poverty line. It is worth noting that given the higher mortality and morbidity attributed to drug-resistant cases of malaria infection, one will expect the micro- and macro-economic impacts to be more than that of malaria cases not associated with resistance. Indeed, malaria and poverty can both be a cause and effect of each other (Gallup & Sachs, 2001).

2.10 Poverty and Malaria

Historically, malaria, like most communicable diseases was distributed globally in the present developed and developing countries of the world. However, as earlier stated, with the epidemiological transition and economic development in western countries that saw the replacement of communicable diseases with the non-communicable disease of the affluent (McKeown, 2009), malaria became a burden of the developing world alone. Unlike developed countries, most of the poor, low-income countries do not have sufficient resources to provide adequate prevention and treatment measure to eradicate malaria; which make them more vulnerable to malaria infection and deaths (Miura, 2013). High level of infant and under-five years old mortality in Africa contribute to the high fertility rates as couples tend to reproduce more to make up for the children lost to malaria. This is typical as developing countries are still characterized by high fertility and birth rates (United Nations, 2015) as well as large family size. As the rate of fertility and birth increases, the proportion of the population at high risk of malaria infection (under-five years children and pregnant women) also increases because pregnancy elevates the risk of malaria infection.

Evidence from all over the world suggests a strong relationship between poverty and health (Ainsworth & Over, 1999; David E. Bloom, Sachs, Collier, & Udry, 1998; Eastwood & Lipton, 1999). Poor people suffer a multiplicity of deprivations that results in poor health outcomes (Claeson et al., 2001). The link between the concepts of health and poverty is intertwined with

causality running in two directions. Poor people in malaria endemic areas are thus caught in a vicious circle: poverty breeds ill health, ill-health maintains poverty.

2.10.1 Effects of Poverty on Malaria Burden

One of the factors that contribute to persistent malaria burden globally is the global poverty rate. Poverty level affects the malaria burden in the following ways:

- The poor are less likely to seek prompt and effective malaria treatment when infected (Chuma, Thiede, & Molyneux, 2006; Schellenberg et al., 2003)
- Less access (affordability, acceptability, and availability) to malaria preventive measures, and prompt and effective malaria treatment (Chuma et al., 2010)
- Less likely to use health facilities and more likely to self-medicate or use traditional herbalists when they have malaria.
- Less likely to adhere to drug dosage (Chuma et al., 2010).
- Poor quality information on malaria cause, prevention, and treatment usually as a result of the low educational level (Dike et al., 2006).
- Poor living conditions which promote malaria transmission.
- Jobs like hunting, and peasant farming, which pushes poor people to the fields and forests every day thereby exposing them to mosquito bites (Teklehaimanot & Paola Mejia, 2008).

2.10.2 Effects of Malaria Burden on Poverty

As stated earlier, malaria and poverty are correlative regarding their effect on each other. Population health is an important tool in attaining human development and in sustaining economic growth. Population health has been identified as central to poverty reduction (Gallup & Sachs, 2001) because, the healthier a population, the more productive the people becomes. Malaria burden can drag people down and/or keep people below the poverty line. The economic and social burden of malaria affects the poor more. For example, the cost of antimalarial treatments like ACT is the same for everyone irrespective of their socioeconomic status. However, the economic burden of spending about US$3.7 on ACT is felt more by someone who is living below the poverty line of US$1.25 per day, than someone of high-income (Miura, 2013). As such, malaria works in maintaining and keeping poor people poor. There are indications that global eradication of malaria will have a great impact on global poverty reduction (Miura, 2013), which is a major precursor of most infectious diseases (Jimoh et al., 2007).

2.11 Malaria in Nigeria

The West African region remains a major contributor to global malaria prevalence. In 2016, the World Malaria Report estimated that 355 million people from the West African region are at risk of malaria. According to the report, Nigeria is the leading country in terms of malaria burden in West Africa. As shown in Figure 2.11, more than half (55%) of the estimated 111.8 malaria cases in West Africa occurred in Nigeria (World Health Organization, 2016d).

Nigeria is a lower middle-income country in sub-Sahara Africa with gross domestic product (GDP) of US$481.1 billion; and 48% of its population live below the World Bank poverty line (World Bank, 2016). It is one of the most endemic countries for malaria with about 97% of its 178.6 million population at risk of malaria. It is estimated that about half of the Nigerian adult population will experience at least one malaria episode annually (Federal Ministry of Health Nigeria, 2011b). For children under-five, estimated number of malaria episodes is between two and four annually (Federal Ministry of Health Nigeria, 2011b). About 29% of the 211.8 million global malaria cases, as well as 55% of the cases in West Africa in 2015, occurred in Nigeria (World Health Organization, 2016d) (see figure 2.1). Also, of the estimated 426,791 global malaria deaths in 2015, 35% occurred in Nigeria (World Health Organization, 2016d). This high malaria burden in Nigeria is partly due to the demography, environmental factors, healthcare system, and the level of poverty in the population, amongst others.

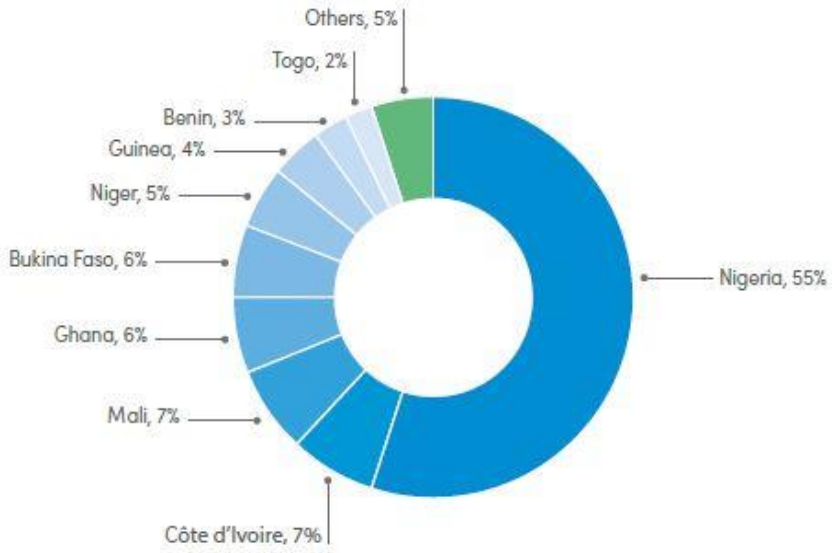

Figure 2.1: Adapted from WHO World Malaria Report 2016: Share of malaria cases in West Africa in 2015

The Nigerian demography shows a high proportion of high-risk malaria groups, especially children under-five years old and pregnant women. The Nigerian Demographic and Health Survey (2013b) results indicate that the Total Fertility Rate of Nigeria is 5.5 births per woman. This means that on average, a Nigerian woman will give birth 5.5 times by the end of her childbearing years. This high rate of fertility, which results in high percentage of neonates in the population, contributes to the high population of pregnant women and children under-five at every point in time in Nigeria. Malaria is among the leading causes of infant and under-five mortality in Nigeria; which is still so high with one in every 15 Nigerian children dying before reaching age one, and one in eight not surviving till their fifth birthday (National Population Commission, 2013b).

As a tropical climate, one of the major drives to the persistence of malaria in this area is the availability of conducive environment for vector breeding. As such malaria vectors such as *Anopheles gambiae*, *Anopheles funestus* and *Anopheles arabiensis* are present in Nigeria, but *A. gambiae* is the most prevalent in Nigeria (Federal Ministry of Health Nigeria, 2011b). The dilapidated environmental condition that characterizes most rural, and indeed some urban areas, in Nigeria, is also contributory to the high transmission of the *Plasmodium* parasite. The most common specie of *Plasmodium* parasite in Nigeria is *Plasmodium falciparum* which constitutes about 98% of the total malaria cases in the country (Federal Ministry of Health Nigeria, 2011b).

Although the mosquitoes transmit the malaria parasites all year round in Nigeria, the rainy season, as compared to the dry season, is usually the peak transmission season for malaria in Nigeria (Federal Ministry of Health Nigeria, 2011b). In addition, the rainy season is also the farming season in Nigeria. With more than two-third of the Nigerian labour force involved in farming (World Bank, 2015), people spend more time out on the farms and fields during the rainy season, which subsequently increases exposure to mosquitoes. These factors work together to bring about increased malaria morbidity and mortality during the rainy season. This seasonal difference in malaria is more striking in the northern part of the country than in the south (Federal Ministry of Health Nigeria, 2011b).

2.11.1 Nigerian Health System and Malaria treatment

The Nigerian health system, as with the health system of most countries, constitutes both the public and the private sector. According to the Nigerian Federal Ministry of Health (2011a),

about 40% of the 34,173 health facilities registered in Nigeria as at the end of the year 2011 were private. Nevertheless, the private health sector caters for a greater proportion of the population than the public health sector (60% for private vs. 40% for public) (National Population Commission, 2013a).

In Nigeria, malaria treatment can be sought from different levels of health facilities (primary, secondary and tertiary healthcare facilities) from both private and public sectors (Federal Ministry of Health Nigeria, 2011b). However, most malaria treatments are sought from the private sector. Within the private health sector in Nigeria, the informal health facilities/providers -that is the patent medicine vendors or drug retailers (locally known as the chemists and pharmacies)- are the most used source for malaria treatment with about 45.6% of the population seeking malaria treatment from these sources (National Population Commission, 2013b). The patent medicine sellers (chemists) in Nigeria are usually traders with little or no pharmaceutical training or qualification, who sell drugs in a small shop or carry them around the streets and market areas (Onwujekwe, Obikeze, Uzochukwu, Okoronkwo, & Onwujekwe, 2010). They are mostly common in the rural and suburban settings in Nigeria. The pharmacies, on the other hand, are usually owned and/or run by a trained pharmacist (Onwujekwe, Obikeze, et al., 2010). Some pharmacies in Nigeria are however run by pharmacy attendants or nurses and are usually found in the urban areas. Although the Ministry of Health in Nigeria has the statutory responsibility for supervising the activities of the private and public health sectors in Nigeria, the health sectors, especially the private, are poorly regulated with a low standard of care offered to users (National Population Commission, 2013b). The poor regulation of the health sector promotes bad practices among providers and users that further complicates the malaria burden in Nigeria (Isiguzo et al., 2014).

Evidently, the weak healthcare system in Nigeria is a key contributor to the high malaria morbidity and mortality in this country (Federal Ministry of Health Nigeria, 2011a; Welcome, 2011). Poor access to formal health care facilities is a common feature of most areas in Nigeria. Nevertheless, for those who have access to formal healthcare facilities in Nigeria, malaria is the leading cause of visits to the outpatient clinics -with about 60% of those visiting outpatient clinics seeking malaria treatment- (Federal Ministry of Health Nigeria, 2015).

These features of the healthcare system in Nigeria interact in sustaining the high burden of malaria in Nigeria. Another important factor in the persistent malaria burden in Nigeria is the issue of antimalarial drug resistance which has a serious impact on public health.

2.11.2 Public health burden of malaria in Nigeria

Like most malaria endemic countries, resistance to anti-malarial drugs, such as chloroquine and SP, spread to Nigeria quickly. As a result, in 2005 Nigeria adopted ACT artemether-lumefantrine (AL) as the first-line treatment for uncomplicated malaria with Artesunate-amodiaquine (AA) later added as an alternative first-line drug to AL. (Ezenduka, Ogbonna, et al., 2014). Other ACTs used in Nigeria for the treatment of uncomplicated malaria cases include dihydroartemisinin-piperaquine (DHAPQ) and Artesunate-mefloquine (ASMQ) (Ezenduka, Ogbonna, et al., 2014).

The complexity of the malaria burden in Nigeria goes beyond the mortality and morbidity attributed to the disease. The individuals, households, and government of Nigeria suffer huge economic loss as much as 132 billion Naira (about US$740 million) annually as a result of malaria treatment cost, loss of productivity, absenteeism from schools amongst others (Federal Ministry of Health Nigeria, 2011b). This economic effect of malaria burden has the ability to impede human development and so can contribute to persistent underdevelopment and poverty in Nigeria.

The cost of treatment of malaria can be more devastating for some households than others. The poor suffer more from the financial cost of malaria treatment as they spend a larger proportion of their income in seeking malaria treatment than the rich. According to Xu et al. (2003), a household with more than 40% of their non-food expenditure gulped up by treatment cost are most likely to be living in poverty. The impact of malaria treatment cost becomes more significant when one considers the recurring nature of malaria in individuals in endemic countries in a year (Onwujekwe et al., 2005). Also, in cases of resistant infection, where repeated treatment with different drugs will be needed to reduce parasitemia, the financial, health and social costs of malaria is expected to be much higher.

2.12 Access to Malaria Treatment and Drugs

Access to the antimalarial drug is an integral aspect of malaria control programs (World Health Organization, 2016d). The concept of ‘access’ in public health goes beyond mere availability. For a treatment to be accessible to the population, it should be readily available, through a reliable source (example from hospitals, clinics), affordable, and of good quality.

In Nigeria, antimalarial drugs are over the counter drugs (OTC) (Federal Ministry of Health Nigeria, 2015); as such, when available in a facility, they can be easily purchased without a prescription (Ikwuobe, Faragher, Alawode, & Lalloo, 2013). One of the rationales for the OTC

status of antimalarial drugs in Nigeria is to make them accessible to the members of the population with less restriction, given the high prevalence and burden of malaria in Nigeria, and the high proportion of patients to providers (Ogundipe, Obinna, & Olawale, 2015).

As stated earlier, although antimalarial drugs can be accessed from all types of health facilities and at all levels, the private sector retail drug outlets (informal health facilities) remain the most common source of malaria treatment in Nigeria (Uzochukwu & Onwujekwe, 2004), as in most malaria endemic countries (Cohen et al., 2012; Hill, Kendall, Arthur, Kirkwood, & Adjei, 2003; Khatib et al., 2013; Littrell et al., 2011; Nonvignon et al., 2010; Rutebemberwa, Pariyo, Peterson, Tomson, & Kallander, 2009). With the existing poor level of regulation of the activities of the private health sector in Nigeria (SHOPS Project, 2012), the private healthcare facilities have been reported to offer a lower quality of health care services and products (SHOPS Project, 2012). In addition to this, the poor level of regulation in this sector means their activities, in terms of compliance with national malaria treatment policy, quality of care offered to patients, drug dispensing and quality of antimalarial drugs used, are not necessarily controlled (Chuma et al., 2009; Cohen et al., 2012; Division of Malaria Control, 2012).

The cost of antimalarial drugs is a major factor that determines access to appropriate malaria treatment for those at lower socioeconomic levels. Despite current efforts through initiatives like AMFm (World Health Organization, 2012), cost/price remains one of the major issues with the ACTs class of drugs. The high cost of ACT is partly because the active compounds are extracted from plant (*A. annua*) and not from chemical synthesis (Chuma et al., 2010; Kindermans, Pilloy, Olliaro, & Gomes, 2007). Therefore factors that can affect the availability of the *A. annua* plant, such as market events (like demand and supply), agricultural events (like poor harvest), as well as climatic conditions, can affect the output and price of ACT.

Indeed, the high cost of ACT is one of the reasons for its frequent shortage and unavailability. ACT shortage or stockout in public health facilities is common in malaria endemic areas (Chuma et al., 2010). The qualitative study by Chuma et al., (2010) in Kenya reported a frequent shortage of ACTs. The anti-malarial drug reported to be readily available was fansidar (SP -which is more of a prophylaxis therapy and not recommended for malaria treatment in endemic areas). According to the findings from the study by Chuma et al. (2010), 95 (30.0%) of people who visited public health facilities did not get drugs from the hospital's pharmacy and were given a prescription to buy drugs elsewhere (Chuma et al., 2010). Of these, only 31 (32.8%) individuals bought the prescribed drugs (Chuma et al., 2010). This study further shows

that about 64 (20.2%) of the people who visited public health facilities and were attended to by a health practitioner did not get required drugs for treatment (Chuma et al., 2010). Also, antimalarial drugs being out of stock was commonly reported from the exit interview of participants with 140 (38.8%) not receiving the antimalarial drug as a result of this (Chuma et al., 2010). The persistent cases of antimalarial drug shortage in formal public health facilities contribute to the people's perception of these facilities as unreliable and so discourage them from using them. This perception about formal public health facilities further exposes patients, especially the poor, to the option of drugs from vendors –which can be counterfeit and usually come at a cheaper price.

Although there is free malaria treatment in some endemic countries, the reality in such countries, like Nigeria and Kenya (Onwujekwe et al., 2005; Chuma et al., 2009), is that despite the existence of this free treatment, the policy is not well implemented, and the coverage is low. As such, treatment charges remain a significant barrier to access to malaria treatment (Onwujekwe et al., 2005).

Furthermore, the physical location of health facilities in relation to service users and availability of transport is an important aspect of access to treatment as they can influence the decision on where, when and what sort of treatment people will seek (Chuma et al., 2010).

2.13 Development and Spread of Antimalarial Drug Resistance

2.13.1 Overview

According to the WHO publication by Bloland (2001), drug resistance has led to the spread and resurgence of malaria in areas where the disease has been eradicated in the past. The present era of rapid and intense globalization has favoured the spread of resistant malaria parasites from one part of the world to another in short periods of time (Bloland, 2001). Infections by drug-resistant strains of *Plasmodium* are usually more severe with a higher rate of morbidity and mortality than infections by drug-sensitive malaria parasites (Bloland, 2001). *P. falciparum*, which causes most of the malaria cases globally, has developed resistance to all antimalarial drugs presently in use globally (Bloland, 2001).

Drug resistance happens when drugs that were previously effective against malaria parasite loses some or all of its potency as a result of selection of the *Plasmodium* parasite genetics, making them less susceptible to the effects of the drugs (World Health Organization, 2015a). In cases of uncomplicated malaria, this means the inability of the antimalarial drug, when

administered in the correct concentration, to inhibit the multiplication of the *Plasmodium* parasite (White, 2004).

Indeed the mechanism behind the development and spread of resistance is multifactorial with host and parasite factors (such as drug use practices, drug half-life, transmission intensity, clone multiplicity, parasite density, host immunity, within-host dynamics and the genetic basis of drug resistance) in play (Huijben, 2010). The effects of these factors have been reported in the literature, but their exact impacts are not well established (Huijben, 2010). For instance, there has been persistent controversy on whether drug resistance is more likely to evolve in areas of low or high transmission intensity (Bloland, 2001).

Studies supporting the claim that drug resistance tendency is higher in high transmission intensity areas (De Roode, Culleton, Bell, & Read, 2004; I. M. Hastings & d'Alessandro, 2000; Mackinnon, 2005; Wargo, Huijben, De Roode, Shepherd, & Read, 2007) argue that high transmission areas are characterized by higher clone multiplicity and as such favours drug-resistant parasites co-infecting a host with drug-sensitive parasite when the infection is treated. Nevertheless, some studies have also supported the claim that drug resistance evolves more in low transmission intensity areas. Some of the reasons supporting this claim is that low transmission areas are usually characterized by more non-immune individuals than high transmission areas; and individuals in the low transmission areas are more likely to have symptomatic malaria infections, hence an increased use of antimalarial drugs.

Another factor important in parasites' evolvement of mechanisms for drug resistance is drug half-life. In malaria treatment, drugs with long half-lives are preferred to drugs with short half-life (Bloland, 2001). The reason for this is because using drugs with short half-life, like artemisinin (especially as a monotherapy) (Ridley, 2002; WHO-Roll Back Malaria & Organization, 2001), will require repeated dosage, which invariably increases the likelihood of non-adherence in administration. This subsequently increseases the risk of exposure of the parasite to sub-therapeutic dosage while using drugs with short half-life; thereby paving way for the development of resistance. As such, adherence is usually higher, with drugs that have a longer half-life, like SP, as they are usually single-dose regime on shorter regimen (Bloland, 2001). Having said that, there are also arguments that long half-life, which means prolonged presence of the drug in the system, can encourage resistance as the concentration of the drug the parasite is exposed to reduces over time (Bloland, 2001).

An equally important mechanism of antimalarial drug resistance is the genetic diversity of malaria infection (Huijben, Sim, Nelson, & Read, 2011). Several studies have demonstrated that multi-genotype malaria infection occurs (Baruah, Lourembam, Sawian, Baruah, & Goswami, 2009; Jafari, Le Bras, Bouchaud, & Durand, 2004; Nwakanma et al., 2008; Soulama et al., 2009). As such, mixed infection with resistant and sensitive strains of the *Plasmodium* parasite occurs in human malaria infection (Huijben et al., 2011). The study by Huijben et al. (2011) showed that drug treatment in cases of mixed infection with resistant and sensitive parasites favours drug resistant parasites through competitive release as well as a survival advantage.

As earlier stated, high drug pressure, which can be a product of the unnecessary use of drugs, encourages the emergence and spread of resistance (Huijben, 2010). Presumptive treatment has been recognized as a driver of high drug pressure. Presumptive treatment using antimalarial drugs can encourage the spread of resistance especially in cases of mixed infections. It is important to note that mixed infections of various genotypes are very common in human malaria infections (A-Elbasit et al., 2007; Arnot, 1998a; Baruah et al., 2009; Jafari et al., 2004; Snounou et al., 1993; Soulama et al., 2009; Thaithong, 1983; Vafa, Troye-Blomberg, Anchang, Garcia, & Migot-Nabias, 2008), therefore, mixed infections with resistant and sensitive parasites are also common especial in high transmission areas (Arnot, 1998b; Juliano et al., 2010). The study by Bushman et al. (2016) in which blood samples from 1,341 children with malaria drawn from Angola, Ghana and Tanzania were analyzed to determine densities of chloroquine-sensitive and chloroquine-resistant strains found that 15% (n=198) of the sample were cases of mixed infection of both sensitive and resistant strains.

In a mixed infection without drug treatment, the drug-sensitive parasites usually exert a competitive suppression on the drug-resistant parasite thereby restricting their multiplication (Bushman et al., 2016; Huijben, 2010). This was referred to as 'fitness disadvantage' by White (2004). Bushman et al. (2016) reported that the fitness cost of the resistant traits in chloroquine-resistant *Plasmodium falciparum* manifests as in the reduction in parasite density. And this reduced density is reported in both cases of single infection with chloroquine-resistant strains alone as well as cases of mixed infection of both chloroquine resistant and susceptible strains. According to White (2004), in the absence of antimalarial drugs in a mixed infection, the drug-resistant parasites are less fit and have reduced multiplicity compared to the drug-sensitive parasites. Treatment with antimalarial drug removes the sensitive parasites and hence their competitive suppression, thereby increasing the relative frequency of resistant parasites

(Hastings, 2003). This competitive release allows the resistant parasites to fill up the ecological space left by susceptible parasites (Huijben, 2010). Therefore, the competitive release partly explains the danger that drug misuse poses to the spread of resistance especially in cases where people in the endemic country who usually have the malaria parasites, but not necessarily causing disease at that point, usually practice presumptive diagnosis or self-treatment for any fever or common symptom.

In addition to the above factors, drug use behaviours have repeatedly been identified as a key factor in the development and spread of resistance (Huijben, 2010; Talisuna et al., 2007). Antimalarial drug use behaviours –such as presumptive diagnosis/treatment, drug overuse, use of sub-therapeutic dose, non-adherence to the treatment regime, amongst others- are very important as they can affect some of the other factors. Also, in comparison with the other factors associated with the development and spread of resistance, drug use practice can be controlled through changes in human behaviours and activities.

Drug use behaviours like presumptive treatment can lead to the overuse of antimalarial drug; which in turn increases the incident of altering the within-host ecology of drug-resistant parasites; and the removal of the drug-sensitive competitors has a significant impact on transmission potential of drug-resistant parasites (Huijben, 2010).

Furthermore, the story of the development and spread of drug resistance cannot be complete without mentioning the Thai-Cambodia border. The Thai-Cambodia border has been the hub of the emergence and spread of antimalarial resistance (Huijben, 2010). In the past, the emergence of resistance to chloroquine, SP and mefloquine have all originated from this area. Although quite intriguing, it is however not a surprise that the first report of reduced ACT sensitivity, which is an indicator of the development of resistance, originated from this area too (Wongsrichanalai & Meshnick, 2008). There have been several attempts to explain the persistent development of antimalarial drug resistance from this area. Most of the explanations are based on the

- Socioeconomic features reflected in the level of poverty, poor ability to diagnose malaria using laboratory or RDT (Wongsrichanalai & Meshnick, 2008).
- Drug use system with a combination of high drug usage and low immunity (Pongtavornpinyo et al., 2008). The intensity of malaria transmission in SEA, in relation to sub-Saharan Africa, is low; resulting in low level of partial immunity against

malaria in the Southeast Asia region, and so infections in this area are usually drug-treated (Huijben, 2010).

- Population demography
- Existence of fake drugs because of the high level of antimalarial drug usage (Hall et al., 2006)
- Distinctive ability of the parasites in this region to develop *de novo* resistance mutations (Rathod, McErlean, & Lee, 1997).

The above are speculated explanations. However, there is currently no conclusive evidence on the reason for the persistent development of antimalarial drug resistant in this area. One key point about these explanations in relation to the present study population is that, apart from some features like a low level of transmission and lower multi-genotype infection, these suspected resistance-driving factors also describe the current state of malaria in Nigeria.

Furthermore, in discussing the issue of malaria drug resistance, it is worth distinguishing treatment failure from true drug resistance. Although treatment failure and drug resistance are caused by similar factors, they are different. Treatment failure occurs when the administration of antimalarial drug fails to clear malaria parasitemia or resolve clinical symptoms. While drug resistance can manifest as treatment failure, not all cases of treatment failures are caused by drug resistance (Bloland, 2001). Several factors like incorrect dosing, poor compliance with treatment regimen, fake drug, sub-therapeutic drug concentration, drug interactions, poor absorption or rapid elimination of the drug, and wrong diagnosis can cause treatment failure (Bloland, 2001). All these factors can also contribute to the development of drug resistance (Bloland, 2001). One significant difference between the two is that, for treatment failure, repeating the treatment using the correct drug quality, dosage and regimen can clear the parasite, however, for drug resistance repeated treatment may make little or no any difference in parasite clearance.

Persistence of treatment failure in a population can be a sign of increasing spread of resistance (World Health Organization, 2013b). The WHO currently recommend that endemic countries should change their antimalarial treatment policy when the treatment failure rate for its first line antimalarial drug in a 28 or 42 days follow up exceeds 10% (World Health Organization, 2013b). The number of the follow-up days can vary with different antimalarial drugs.

2.13.2 Chloroquine and Sulfadoxine-Pyrimethamine Resistance

Resistance to Chloroquine by *Plasmodium falciparum* malaria parasites first emerged in Thailand in 1957 (Packard, 2014). From the Thailand-Cambodia border regions, chloroquine resistance spread to other parts of the world including Africa (Bruce-Chwatt, 1970; Mbomo & Ochrymowicz, 1969). In addition, there were also speculations of chloroquine resistance emerging from South America about the same period in the 1950s (Fançony, Brito, & Gil, 2016). Strangely, none of the reported chloroquine resistance sweeps began in Africa. However, this region bore the highest burden of chloroquine resistance (Huijben, 2010). The rapid spread of chloroquine resistance in Africa led to a rise in malaria-related mortality in this region (Packard, 2014).

There are indications that the demography, environmental and socioeconomic characteristic of the Thailand-Cambodia border were important factors in the development and rapid spread of chloroquine resistance like the mining activities, high immigration, amongst others (Packard, 2014). These conditions led to high incidence of malaria disease in this area. As a control measure, the public health authorities adopted a mass drug administration strategy that included administering chloroquine indirectly through medicated salt (Payne, 1988). With this strategy, coverage was increased, however, it offered no control of the dosage and adherence to the treatment. The repeated application of sub-curative concentrations of chloroquine to a highly infected population set the stage for the emergence of chloroquine-resistant strains of *P. falciparum* (Packard, 2014). Following the emergence, chloroquine-resistant strains of *P. falciparum* were spread to new workers who were non-immune to malaria; and the resulting high drug pressure (caused by high drug use in the treatment of resistant malaria in non-immune workers) further encouraged resistance (Packard, 2014). As at 1973, almost all (90%) cases of *P. falciparum* malaria were chloroquine-resistant (Packard, 2014).

In reaction to the increased spread of chloroquine resistance, it was soon replaced as the first-line drug in most endemic countries with Sulfadoxine-Pyrimethamine (SP- Fansidar). However, resistance to SP emerged swiftly (less than one year after its introduction as first line treatment in countries like Thailand) (Huijben, 2010). Although most studies reported that development of SP resistance first appeared in Southeast Asia (Cortese, Caraballo, Contreras, & Plowe, 2002; Ian M. Hastings, 2004; Nair et al., 2003; Roper et al., 2003), some studies have demonstrated that the original development of SP resistance was in Africa (Mita, Tanabe, & Kita, 2009; Severini et al., 2006).

2.13.3 Artemisinin Resistance

Artemisinin resistance is described as reduction or delay in the rate of parasite clearance following malaria treatment with the appropriate dose of an artemisinin-based drug (WHO, 2015). In cases of treatment of sensitive *P. falciparum* with artemisinin, parasite clearance is achieved within two days in approximately 95% of patients (White, 2004); however, artemisinin-resistant *P. falciparum* infections remain slide positive for 3 or more days post-treatment (Phyo et al., 2012). The idea of combination therapy using artemisinin and other antimalarial drugs is targeted at preventing the development of resistance to artemisinin (Packard, 2014). Nevertheless, the confirmed resistance to artemisinin compounds by *P. falciparum* is likely spreading (Arjen M. Dondorp et al., 2009; Noedl et al., 2008; World Health Organization, 2013b). There have been observed reduction in parasite clearance and unusual treatment failure rates for both Artemether-Lumefantrine and Artesunate-Mefloquine especially in Cambodia and Thailand where resistance to the partner drugs already exists (World Health Organization, 2015b).

According to the WHO World Malaria Report (2013b), there is a difference between suspected and confirmed artemisinin resistance. Suspected resistance to artemisinin is defined as "an increase in parasite clearance time, as evidenced by 10% or more cases with parasites detectable on day 3 of treatment with an ACT" (World Health Organization, 2013b, p. 45). While confirmed resistance is defined as "treatment failure after treatment with an oral artemisinin-based monotherapy (administered under special study conditions) with adequate antimalarial blood concentration, as evidenced by the persistence of parasites for seven days, or the presence of parasites on day 3, and recrudescence within 28 or 42 days (depending on the drug)" (World Health Organization, 2013b, p. 45).

Undoubtedly, the emergence of artemisinin resistance is a serious threat to the global malaria control. This threat is further amplified by the fear that artemisinin resistance might follow the same pattern of other antimalarial drugs (like chloroquine and SP) whose resistance emerged in Thailand-Cambodia border and rapidly spread to other parts of the world. The public health impact of artemisinin resistance spread to Africa will be severe in endemic countries as there are currently no new front-line drugs to replace ACT as the first-line drug.

Unfortunately, there have been indications of increased spread of artemisinin resistance (Enserink, 2008; Lim et al., 2009; Wongsrichanalai & Meshnick, 2008), made possible by the increased globalization. Nevertheless, the WHO still insists that there has been no definitive

evidence of artemisinin resistance outside the Greater Mekong sub-region (World Health Organization, 2016d). This claim, however, does not rule out the possibility of the existence of resistance to ACT in endemic areas like Nigeria. Like in chloroquine and other antimalarial resistance that spread to Africa from Asia, it is likely that the established ACT resistance in Southeast Asia may have spread to Africa by now. Also, the continuous use of artemisinin monotherapies like Artesunate in malaria endemic areas, like Nigeria, is an indication of the possibility of the development of resistance in this area. Contrary to the WHO report (World Health Organization, 2013b) that included Nigeria as one of the countries where artemisinin monotherapy is no longer in use or on sale, recent studies from Nigeria found that Artesunate is very much available and in circulation in the Nigerian market with no restrictions (Bamiselu et al., 2016; Ezenduka, Ogbonna, et al., 2014; Kaur et al., 2015; Liu, Isiguzo, & Sieverding, 2015).

2.14 Drivers of Antimalarial Drug Resistance

Amongst the factors that contribute to the development and spread of drug resistance, drug use practice stands out especially in endemic countries like Nigeria with a history of poor compliance and regulation of antimalarial drug use (Oyeyemi, Ogunnowo, & Odukoya, 2014; Palafox, Tougher, Patouillard, Goodman, & Hanson, 2009). The rest of this review will focus on the drug use related factors that can contribute to the development and spread of antimalarial drug resistance. These factors will be discussed under the following headings:

- Compliance with drug use policies
- Presumptive diagnosis, self-treatment, and drug overuse
- Poor drug quality
- Malaria treatment-seeking behaviours and their determinants

2.14.1 Compliance with Drug Use Policies

The antimalarial drug use pattern of a population can be a major drive to the development of resistance (Omole & Onademuren, 2010). One of the fears raised by the WHO prior to recommending ACT as the first-line treatment for uncomplicated malaria cases is that it will promote overuse of Artemisinin, which will subsequently increase the risk of emergence of resistance. This is because drug overuse in the past provided an intense selection pressure on the malaria parasites enabling them to develop mechanisms of resistance (White, 2004).

Moreover, some of the issues with compliance to treatment guidelines which encourage antimalarial drug resistance include the use of monotherapies, incorrect dosing, non-compliance with the dosing regimen, among others. At the 60th World Health Assembly in 2007, WHO recommended that oral artemisinin monotherapies should no longer be used in the treatment of uncomplicated malaria because this practice is a major contributory factor to the development of resistance to artemisinin derivatives (World Health Organization, 2007). Nevertheless, as stated earlier, artemisinin monotherapy is still widely used in Nigeria (Bamiselu et al., 2016; Ezenduka, Ogbonna, et al., 2014; Kaur et al., 2015; Liu et al., 2015).

Part of the reasons for the continuous use of artemisinin monotherapies, especially Artesunate in Nigeria is because of the high rate of poverty in the country and high prevalence of self-medication as the main source of drug utilization (Ezenduka, Ogbonna, et al., 2014). Artesunate offers a better buying choice for the poor in Nigeria because of its affordability (in relation to ACT) and effectiveness (in relation to other non-artemisinin compounds like SP and chloroquine). The poor level of education of those at the lower level of the socioeconomic gradient (Ferguson, Bovaird, & Mueller, 2007) is an indication of possible difficulty by this group in understanding the long-term effect of the use of artemisinin monotherapies practice, which can affect the entire population in the form of resistance.

Correct use and dosing of antimalarial drugs have always been identified as key to not only therapeutic success but also in deterring the intensification of drug resistance (Oboli & Harrison-Church, 1978). Incorrect dosing occurs when wrong quantities of antimalarial drugs are administered. Incorrect dosing may occur by overdosing or under-dosing. Similar to incorrect dosing is the inappropriate duration of drug regime. Some people stop treatment before the recommended duration (Chuma et al., 2010). Administering under-dose of antimalarial drug and short duration of treatment course both expose the parasites to sub-curative or sub-optimal drug level, which can promote the development of resistance (Omole & Onademuren, 2010). The important question to ask at this point is ‘what are the factors that can lead to a patient administering under-dose of antimalarial drug?’ to this question, treatment costs; lack of information about appropriate treatment; and difficulties in assessing good quality treatment by patients (Hanson et al., 2004) comes to mind. Compliance to treatment policy is a responsibility of the patients as much as that of the prescribers.

2.14.1.1 Patients' Compliance

The Nigerian National Antimalarial Treatment Policy (2005b) advises that the patients have a responsibility to ensure compliance with treatment policies so as to protect the effectiveness of antimalarial drugs. Many studies on antimalarial treatment compliance in Africa identified poverty as a major determinant of compliance by the patients (Chuma et al., 2010).

Several reasons underpin the noncompliance to antimalarial drug treatment by the poor. According to a qualitative study in Kenya by Chuma et al. (2010), some reasons given by participants for non-adherence to the dosage include stopping treatment once there are signs of recovery so as to save drugs for future use, and inconvenience of drug administration times especially when this coincides with the time spent on their farms.

Additionally, the drug distribution system in Nigeria intensifies the poor drug use in this area. In Nigeria, all antimalarial drugs are over the counter (OTC) drugs (Federal Ministry of Health Nigeria, 2011b) and patients have the option of buying as much courses or doses as they want or can afford. This poor regulation of the healthcare system (National Population Commission, 2013b), in collaboration with the high cost of ACT (Opiyo, Yamey, & Garner, 2016) allows for under-dosage and shorter duration of drug regime.

Another treatment factor related to socioeconomic status is the lack of information by patients on the correct dose. A study by Oguonu (2005) on knowledge of correct dose by caregivers for children found that only 29% of the caregivers who participated in the study knew the correct chloroquine dose in children. Fifty-eight percent of them mentioned sub-therapeutic doses while 13% mentioned toxic doses. Also, caregivers in urban cities had statistically significant better knowledge of the treatment regimen of chloroquine than rural caregivers. Nevertheless, this study was carried out when chloroquine was the first-line treatment for malaria in Nigeria.

2.14.1.2 Prescribers' Compliance

Prescribers of antimalarial drugs include health practitioners, pharmacists, medicine vendors, drug retailers among others. These prescribers have a duty of care by ensuring they comply with the malaria treatment policies in the area they are operating. In most malaria-endemic populations, the informal health care facilities, like the drug retail sector, is the main source of malaria treatment (Ezenduka, Ogbonna, et al., 2014); because they offer less expensive services in relation to formal health facilities. In Nigeria, the drug retail sector has a role to play in the control of the development and spread of drug resistance by ensuring compliance with treatment policies documented in the National Malaria Policy by the Federal Ministry of

Health, Nigeria (Ezenduka, Ogbonna, et al., 2014). However, the reality is that this sector represents a great risk of policy failure with regards to inappropriate drug use. For instance, the informal health facilities in Nigeria are not licensed to offer diagnostic testing (Millar et al., 2014), hence most of the malaria treatments from this sector are not based on the results of a parasite-based diagnostic testing (except for those who have had parasite-based diagnostic testing prior to their visiting the informal health facility to source for antimalarial drugs). Also, most of the artemisinin monotherapies in circulation and use in Nigeria come from the informal healthcare facilities like the drug retail shops (Ezenduka, Ogbonna, et al., 2014). The high demand for Artesunate because of its cheaper cost compared to ACT reinforces its supply by the drug retail sector.

Furthermore, the private drug retail sector is a major market for the sale of drugs of substandard quality. It is important to note that the providers in the retail sector are driven by economic gain, and so their prescription patterns are influenced by profit maximization, competition, patients' demand, and the severity of regulatory sanctions (Hanson et al., 2004; Onwujekwe, Uzochukwu, et al., 2009). Correspondingly, the issue of noncompliance of prescribers is not peculiar to drug retail sector alone; health workers from formal health facilities also contribute to the noncompliance from prescribers. Health care facilities in Africa were reported to still prescribe non-artemisinin monotherapies, like amodiaquine, for uncomplicated malaria cases long after the adopting of ACT as the first-line treatment (Faye et al., 2010; Schramm et al., 2013). The inability of patients to pay for ACT is also a contributory factor to the prescription of monotherapies by health workers in Africa (Chuma et al., 2010).

In addition, studies on adherence to the results of malaria diagnostic test in prescribing treatment showed that in some instances where the test result is negative, practitioners in formal health facilities still prescribe antimalarial drugs (Ansah et al., 2010; Skarbinski et al., 2009; Uzochukwu et al., 2011). This non-adherence to test result can contribute to drug resistance by increasing the drug pressure in the population (Tanner et al., 2015). Also, practitioners' non-adherence to test results will affect patients' perception of the importance of malaria diagnostic test prior to treatment, which can subsequently reinforce the practice of presumptive and self-treatment among the patients.

2.14.2 Presumptive Diagnosis, Self-Treatment, and Antimalarial Drug Overuse

As in the treatment of most disease conditions, diagnosis is very necessary to ensure a proper and effective treatment especially as many disease conditions can present common symptoms

like fever, dizziness among others. Testing of every suspected malaria case ensures appropriate and effective treatment and improves malaria surveillance (World Health Organization, 2013b). Currently, the WHO recommends TTT-strategy (test, treat and track) in malaria case management (World Health Organization, 2012). This recommendation implies that for all suspected malaria cases, a parasite-based diagnostic test should first be conducted to confirm malaria status. This diagnostic test, should then be followed by proper malaria treatment if the patient is malaria positive; and subsequent follow-up monitoring to ascertain implementation and progress (Ezenduka, Ogbonna, et al., 2014; World Health Organization, 2012).

As earlier stated, the difference between the two available parasitic diagnostic test for malaria in clinical settings -microscopy and RDT- is that microscopy offers a more definitive diagnosis of malaria compared to RDT (CDC-Centers for Disease Control and Prevention, 2015). However, RDT is less expensive and can produce rapid test results (CDC-Centers for Disease Control and Prevention, 2015).

Over the last decade, there have been an increase in sales of RDT from 200,000 in 2005 to above 108 million in 2012 as more endemic areas adopt different types of RDT for *P. falciparum*-specific test, and for combination test that can detect more than one species (World Health Organization, 2013b). Most of the increased use of RDT occurred in Africa, with approximately 78% of the RDT delivered in 2012 used in the African region (World Health Organization, 2013b). However, considering the population at risk of malaria in Africa and the rate of unavailability of proper parasite-based diagnosis of malaria, this is like soothing one bee sting in the midst of hundreds. There is a need for scale-up of diagnostic testing through RDT in both public and private sectors in malaria-endemic areas where presumptive treatment is still highly practiced.

Indeed, presumptive treatment is a major challenge to malaria control. This practice has been identified as a major drive to self-medication and drug overuse which promote the development and spread of resistance to drugs by malaria parasites (World Health Organization, 2013b). Unlike presumptive diagnosis, parasite-based confirmation of malaria helps to ensure proper diagnosis of patient's condition to minimize the overuse of antimalarial drugs, provide best practice in malaria treatment and rationalize antimalarial drug use to avoid the onset of parasite resistance to antimalarial drugs (Federal Ministry of Health Nigeria, 2011b).

2.14.2.1 Practice of Presumptive Diagnosis in Nigeria

It is surprising that in this present era of increased threat to malaria control by drug resistance, with the existence of cheaper diagnostic testing, like RDT, presumptive diagnosis and treatment of malaria is still very common in malaria endemic populations like Nigeria (Bamiselu et al., 2016; Onwujekwe et al., 2005). This practice is common both in the public and private health facilities as well as among drug retailers and pharmacies. The high rate of presumptive diagnosis and treatment of malaria in Nigeria calls for major actions. Part of the reasons for this trend is the National Policy on Malaria in Nigeria that still permits malaria treatment for suspected cases of fever. The study by Mangham et al. (2011) on the treatment of uncomplicated malaria at public health facilities and medicine retailers in southeastern Nigeria found that very few health facilities in the area offered malaria microscopy testing. The study also reported that amongst all health facilities –both public health facilities and retail outlets- surveyed, none offered RDTs. This finding goes further to show the poor practice in malaria treatment in Nigeria which paves way for the development and spread of antimalarial drug resistance. The findings from other studies on antimalarial use in Nigeria further highlights the intensity of this problem. Some of these studies, like Onwujekwe et al. (2005) and Uzochukwu et al. (2010), have shown that treatment through the medicine outlets is mostly based on presumptive diagnosis, and this has been shown to result in over 50% of those treated for malaria being non-malaria cases.

The low demand for diagnostic testing and limited accessibility for laboratory and RDT is a major barrier to proper malaria diagnosis. Again, poverty as a socioeconomic issue is a major underlying factor that promotes these barriers to proper diagnosis. For the poor, the use of parasite-based diagnostic testing prior to malaria treatment means more money will be spent in treating malaria. Also, the limited access to malaria test (both laboratory microscopy and RDT) is more pronounced in the rural areas and villages where the burden of malaria is more (Onwujekwe et al., 2005)

2.14.3 Poor Drug Quality

The quality of an antimalarial drug also contributes to the development and spread of resistance by the *Plasmodium* parasites (Ambroise-Thomas, 2012; Nayyar et al., 2012). Substandard drugs can be products of unintentional negligence in drug production or storage which results in poor quality in terms of the drug composition (Kaur et al., 2016; World Health Organization, 2016a). However, some cases of substandard drugs are intentional; these are classed as counterfeit drugs (World Health Organization, 2006). The WHO Fact Sheet on Counterfeit

Medicines described counterfeit as “deliberately and fraudulently mislabeled with respect to identity and/or source” (World Health Organization, 2006, p. 1). Counterfeited or fake drugs are products of malpractice in drug production, sometimes leading to sub-therapeutic level or complete absence of the active pharmaceutical ingredients in a drug.

Overall, substandard drugs are very important factor in malaria treatment and control. The use of substandard drugs in malaria treatment poses a huge public health issue to the entire population. They are an obvious contributor to antimalarial drug resistance as sub-therapeutic concentrations of antimalarial drug contributes to the selection of resistant parasites (Nayyar et al., 2012; White, 2004; World Health Organization, 2015a). Modeling analyses have demonstrated that administration of under-dose of artemisinin plays an important part in the spread of artemisinin resistance (White et al., 2009). In addition to this, use of substandard drugs affects treatment experience by increasing morbidity, mortality (Jaiteh et al., 2016; World Health Organization, 2006) and economic cost of malaria infection.

Although there have been increasing reports of poor quality antimalarial drugs in the past decade (Dondorp et al., 2004; Newton et al., 2006), there is speculation that the issue may be much greater than it seems as most counterfeit drug cases are unreported, reported to the wrong agencies, or kept confidential by pharmaceutical companies involved/affected for business reasons (Basco, 2004; P. Newton et al., 2001).

The practice of drug counterfeiting is spread all over the world and constitute approximately 10% of the global medicines trades (World Health Organization, 2006). However, the prevalence and risk are more in low and middle-income countries (Kaur et al., 2016) with weak drug regulation, control and enforcement (World Health Organization, 2006; P. Newton et al., 2001). The existence of fake antimalarial drugs has also been repeatedly reported in the Nigerian population (Kaur et al., 2015; Onwujekwe, Kaur, et al., 2009).

Several factors have been identified to encourage the thrive of antimalarial counterfeit medicine trade in Nigeria. As mentioned above, the nature of a country’s drug regulation and control policies have an effect on the prevalence of counterfeit drugs. In Nigeria, the insufficiency of facilities and strategies to check the quality of antimalarial drugs is a major challenge to the fight against fake drugs. Some years ago, the renewed fight against fake drugs in Nigeria by the National Agency for Food and Drug Administration and Control under the watch of Late Prof. Dora Akunyili witnessed unprecedented success in the history of the fight against fake drugs. However, the rate of fake drugs especially antimalarial, in Nigeria is still

high. The study by Onwujekwe et al. (2009) on the quality of antimalarial drugs provided by public and private healthcare providers found that 60 (37%) of the anti-malarial tested did not meet the United States Pharmacopoeia (USP) specifications for the number of active ingredients present, as they either lacked the active drug ingredient or contained sub-therapeutic quantities of it. Also, 78% of the suspected fake drugs were from private facilities, mostly low-level retailers, such as patent drug vendors (Onwujekwe, Uzochukwu, et al., 2009).

In addition to drug use regulation and control, poor consumer and prescriber knowledge about antimalarial drugs and how to identify counterfeit ones, allow the counterfeit ones to thrive among the good quality drugs (Bate, Coticelli, Tren, & Attaran, 2008). Poor level of education in areas of high poverty disempowers people and constitutes a barrier to accessing quality information and gaining knowledge on drug use and health in general.

A similar factor that encourages the circulation of counterfeit antimalarial drugs is the cost of the good quality drugs (Bate et al., 2008; Newton et al., 2006). Using ACT as an example, in relation to good-quality ones, counterfeit drugs are usually cheaper and more affordable to the poor. As such, with the poverty rate in Nigeria, it becomes imperative and convenient for many people to go for the cheaper, poor-quality antimalarial drugs. An evidence of how this works is in the case of the Pailin province of Cambodia where cheap counterfeit drugs containing subtherapeutic quantities of antimalarial is widely available (Dondorp et al., 2010). The existence of high level of self-treatment through private sectors in Nigeria, also makes it easier for the poor to go for counterfeited drugs.

Finally, the financial incentive to pharmaceutical and retail outlets involved in counterfeit drug business is another factor that encourages its thrive. Trade in counterfeit drugs is lucrative, thus making it more attractive to criminal networks. A report released by the Centre for Medicines in the Public Interest, in the United States, projects counterfeit drug sales to reach US$ 75 billion in 2010, a 92 % increase from 2005 (World Health Organization, 2006).

2.15 Malaria Treatment Seeking Behaviours and their Determinants

Public health studies are usually interested in the treatment seeking behaviours of a population (Musoke, Boynton, Butler, & Musoke, 2014; Uzochukwu & Onwujekwe, 2004). This interest is because the overall profile of the treatment seeking behaviours of a specific population -with regards to a specific disease or health condition, like malaria- is very important in determining the epidemiology of the disease in the population (Dixit et al., 2016). As such, studies on treatment seeking behaviours concentrate on factors like the time between the onset of disease

symptoms and treatment seeking, source of treatment, type of drugs used, adherence to treatment guideline, amongst other (Balasundaram, Sarkar, Hamide, & Lakshminarayanan, 2014; Karyana et al., 2016; J.-W. Xu, Xu, Liu, & Zeng, 2012). The interest in these factors goes beyond their importance in determining treatment outcomes (such as an individual's experience of illness); it includes the overall effect on public health through disease transmission, morbidity, and mortality. Hence the factors that determine health seeking behaviours are very important to public health researchers.

Evidently, determinants of treatment seeking behaviours have long been identified in the literature (Kroeger, 1983). On a broader level, these factors include physical, political, cultural, and importantly, socioeconomic (Kroeger, 1983). Other determinants of treatment seeking behaviour include environmental conditions, sociodemographic factors amongst others (Ogunlesi & Olanrewaju, 2010).

Physical factors such as the location of health facilities and road network can affect treatment seeking behaviours by determining access and source of treatment, as well as the availability of healthcare professionals (Chuma et al., 2010). The location of a facility can influence its usage and the characteristics or demography of its users. These physical factors are usually effects of political forces in the population.

The political activities in a population can affect treatment seeking behaviours and overall public health through the decisions on the location of health facilities, construction of roads leading to health facilities, and policies and guidelines on the treatment of health conditions. The organization of healthcare in a society is also an important determinant of treatment seeking behaviour (Shaikh & Hatcher, 2005).

Similarly, culture also exerts an important influence on treatment seeking behaviours by shaping norms, practices, and perceptions about illnesses, recognition of illness, and decision on where to seek treatment (Brieger & Arlington, 2003; Colvin et al., 2013). For instance, some cultural norms and practices in the Nigerian population context (such as storage of water in open pots and containers around the house, and the structure and location of the houses in rural areas (Ojua, Ishor, & Ndom, 2014)) can affect malaria transmission and treatment seeking behaviour.

Indeed, socioeconomic factors remain key determinants of treatment seeking behaviours as they have the ability to influence the other factors, as well as to reduce the impact of the other

factors in determining health-seeking behaviours. Evidently, socioeconomic factors have always been key players in malaria treatment seeking (Uzochukwu & Onwujekwe, 2004). The main indicators of socioeconomic factors important in malaria research are educational level, income level, type of settlement and employment status (Uzochukwu & Onwujekwe, 2004). Income level as a socioeconomic factor reflects financial abilities which can determine treatment seeking behaviours like the choice of health facility for treatment (Kiwanuka et al., 2008), and the use of diagnostic test prior to treatment (Uzochukwu & Onwujekwe, 2004). Income and educational level have repeatedly been reported to affect adherence to malaria treatment guideline especially among the poor (Beer et al., 2009; J. L. Cohen et al., 2012; Onyango et al., 2012; Simba et al., 2012). Certainly, educational level as a socioeconomic factor can also impact on the ability to source for adequate information needed to make an informed malaria treatment decision (Hanson et al., 2004).

The interaction of these socioeconomic factors is important in determining malaria treatment seeking behaviours of a population; and subsequent treatment outcomes like recovery, treatment failure, drug resistance or death. Understanding the contributory role of these factors in malaria treatment seeking is very crucial in ensuring malaria control through accurate diagnosis, effective treatment, and protecting the efficacy of antimalarial drugs. As a key determinant of treatment seeking behaviour, the contributory role of socioeconomic factors to behaviours that can promote the development and spread of antimalarial drug resistance is the main focus of this study.

2.16 Chapter Summary

Although a global health issue, the burden of malaria is unevenly distributed to the disadvantage of the developing countries of the world, mainly in Africa. The intrinsic relationship between malaria and poverty remains a major factor in sustaining this preventable and treatable disease. The *Plasmodium* parasites have developed resistance to all antimalarial drugs in use. The development of resistance is a complex issue with factors like drug half-life, transmission intensity, clone multiplicity, parasite density, host immunity, within-host dynamics, the genetic basis of drug resistance, and drug use practices affecting it. Drug use practices like non-adherence to treatment regimen, presumptive treatment, poor drug quality, and malaria treatment seeking behaviours are important contributors to resistance. As such, there is the possibility that socioeconomic measures may have the ability to impact on drug use behaviours in a way that can promote the development and spread of antimalarial drug resistance.

CHAPTER THREE

CONCEPTUAL AND THEORETICAL FRAMEWORK

3.1 Introduction

This chapter explains the conceptual and theoretical framework of this study. It starts up with an explanation of the role of frameworks in research and goes further to explain the conceptual framework of the study. The rest of the chapter explain the theoretical underpinning of this study, starting with a brief discussion of the need for theory in this research. This is followed by an overview of epidemiological theories, which creates a background for the social production of disease theory used in this study.

3.2 Research Frameworks

Frameworks are important in research as they help researchers to structure their work by offering a pathway to adopt in organising and explaining research ideas (Pye Tait, n.d.). Overall, frameworks play an important role in the description of the research problem by using a concept to explain the problem and the likely direction of the findings of the study (Imenda, 2014). The commonly used frameworks in research are conceptual and theoretical frameworks. Although different (Imenda, 2014), both frameworks are complementary and important in the structuring of ideas and providing a foundation for the interpretation of results and drawing of conclusion based on the outcome of a study (Sinclair, 2007). While theoretical frameworks offer explanations on the relationships between broader constructs and the phenomenon of interest, conceptual frameworks are narrower and more specific.

3.3 Conceptual framework

A conceptual framework is an organised way of considering the phenomenon or research problem under study, and what processes and activities will be required in the conduct of the study (Imenda, 2014; World Health Organization, 2010). The phenomenon of interest in this study is antimalarial drug use behaviours that have deleterious effects on drug resistance. In conceptualising this problem, a detailed review of the literature was conducted to identify some factors that can influence this phenomenon. As such, the review of the literature was important in the conceptualization of this phenomenon, and in the construct of the research question.

The conceptual framework of this study includes the idea that antimalarial drug use behaviours can be affected by different factors like socioeconomic, psychosocial, cultural amongst others.

Nevertheless, as a process which involved revisions, the conceptual framework was revised based on evidence from malaria literature, with the focus of the study directed at the socioeconomic position. Consequently, the conceptual framework of this study depicts that socioeconomic position, which is affected by social and environmental structures that stratifies the society, might affect how malarial treatment is sought and how antimalaral drugs are used. Just like the Russian dolls where each doll is fitted inside the next larger one, antimalarial drug use behaviours were conceptualized to be constrained by social stratifications, which are in turn shaped within the social and environmental structures of the society.

In addition to its role in the conceptualization of the problem and the structuring of the research question, the conceptual framework was also important in the alignment of the research methodology. As such the research question, which is a product of the conceptual framework of this study, was the basic factor that determined the research processes like data collection, analysis and interpretation. Importantly, the conceptual framework played a major role in the construct of the research hypotheses by identifying variables that are important to the phenomenon under study, and which of the variables are independent or otherwise.

Correspondingly, the conceptual framework of this study is related to that of the Commission on Social Determinants of Health (CSDH) (WHO, 2010) shown in Figure 3. The CSDH conceptual framework was a product of the commission set up by the World Health Organization to explain the complexity of health by summarizing the evidence on the role of societal structures in population health outcome (WHO, 2010). The CSDH conceptual framework also identifies the role social, economic and political mechanisms in determining socioeconomic positions (WHO, 2010). And that the stratification of the society according to income, education, occupation, gender, race/ethnicity and other factors affects disease exposures, vulnerabilities, illness experiences amongst others; thereby leading to inequalities in health outcomes (WHO, 2010).

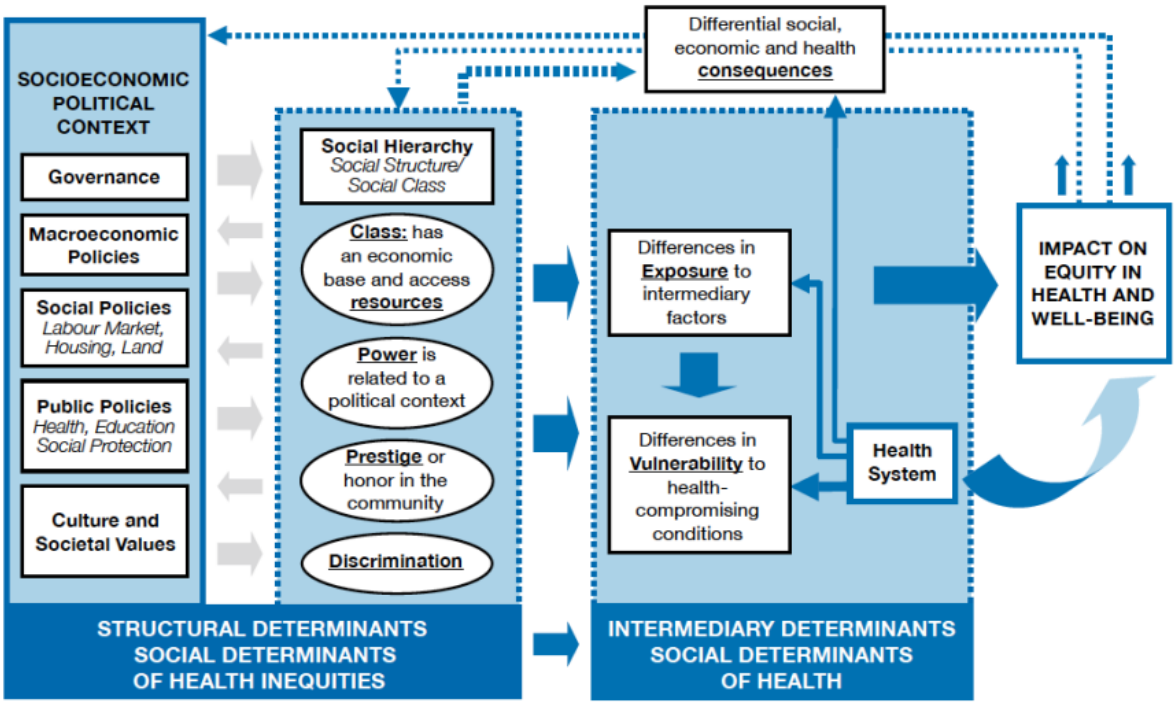

Figure 3: CSDH Conceptual Framework (WHO, 2010)

As stated earlier, conceptual and theoretical frameworks need to be complimentary, with both contributing to the structure of the whole research process. Theories make unique contributions in research, leading to their central role in research interpretation.

3.4 Theoretical Framework

3.4.1 Why do we need theory in this study?

The word 'theory' has become commonly linked to academic research. The New Oxford Dictionary of English defined it as "a supposition or a system of ideas intended to explain something, especially one based on general principles independent of the thing to be explained" (Peasall, 2001, p. 1922). This definition captures what a theory is, what it is used for, and how it can be applied.

In research, a theory is a framework for articulating and conceptualizing logical explanations for observations (Krieger & Zierler, 1996; Reeves, Albert, Kuper, & Hodges, 2008). By adopting a particular theoretical framework in a study, researchers can link a single study to an existing body of knowledge or evidence.

Generally, theories offer an insight on what we observe, how we observe them and help us make sense of the observations. In other words, they enable researchers to explain observed

relationships between variables and also to make some predictions on how the society works (Reeves et al., 2008). Nevertheless, it is worth mentioning that theories are not only used in explaining the interaction between variables in the research findings. They are crucial right from the designing stage of a study (idea formulation, formulation of the research question and hypothesis) to the execution (data collection and analysis of the variable) and the explanation of the findings (Krieger & Zierler, 1996). In addition to these, theories can also be useful in making recommendations for the control of a phenomenon under study (Krieger & Zierler, 1996).

Furthermore, as seen in the Oxford dictionary definition of a theory, theories are usually underpinned by a general principle that might not be necessarily dedicated to the concept or phenomena they explain. This means that a particular theory, like life course theory, can be applied to different issues in health and otherwise. Similarly, a particular problem or issue can be studied through different theoretical lenses (Reeves et al., 2008) as different theories offer different perspectives or insights to a particular issue or problem.

3.4.2 Social Epidemiologic theories

As in other disciplines, public health, and epidemiological studies adopt theoretical frameworks in investigating patterns of population health. Krieger and Zierler (1996), referred to epidemiologic theories as 'interconnected ideas' that help explain the distributions and patterns in the health of a population. As epidemiology is a multidisciplinary science, the theories that underpin epidemiological studies are usually based on connected ideas that originate from different disciples. For instance, in social epidemiology, which is a sub-disciple of epidemiology concerned with the connection between social systems and population health (Cwikel, 2006), the theories specific to studies adopting this stance are usually based on the interplay between social systems and human biology (Krieger & Zierler, 1996). In explaining the interaction between social and biological processes -both at individual (micro) and population (macro) levels-, social epidemiologic theories structure research findings into logical and coherent interactions that describe population health patterns. The theories go further to offer clear philosophical and ideological assumptions about the disparity in health outcome among groups in a population (Krieger, 2001a; Krieger & Zierler, 1996).

The origin of the term 'social epidemiology' can be attributed to the work of Alfred Yankauer published in 1950 by the *American Sociological Review* (Krieger, 2011a). Over the last century, social epidemiology has gained momentum with an increase in the number of studies that

explore the interaction between social and economic structures and population health outcomes (Berkman, Kawachi, & Glymour, 2014). The fundamental difference between social epidemiology and other sub-disciplines of epidemiology is in its broader scope to disease aetiology that goes beyond the biomedical model to include a social and economic model to population health (Berkman et al., 2014). In studying disease patterns in a population, it extensively includes sociological variables and theories in the analysis and interpretation of population health (Kaufman, Kaufman, & Poole, 2003).

The biomedical model of health, which has enjoyed dominance in health studies in past centuries, is based on assumptions that biological factors are the primary determinants of health outcomes while other 'distal' contributory factors to health are secondary, with less significance. It also assumes that the population is a mere sum of the individuals that constitutes it (Fee & Krieger, 1993; Lock & Gordon, 2012; Tesh, 1988a). As such, this model has been criticized for its individualistic stance that promotes victim-blaming with little consideration of social systems and structures that play important role in an individual's health decisions (Krieger, 2001a). These limitations of the biomedical model led to the renewed interest in investigating the effect of social factors in disease causation (Kaufman & Kaufman, 2001).

As this study is underpinned by the concept of social causation of disease which is aligned with the social epidemiology discipline, it looked beyond biological factors in assessing the contributors to the development and spread of antimalarial drug resistance. By adopting a social epidemiologic stance, one of the questions this study poses is 'are biological mechanisms of antimalarial drug resistance (like drug half-life, transmission intensity, clone multiplicity, parasite density, host immunity, within-host dynamics and the genetic basis of drug resistance) more legitimate contributors to antimalarial drug resistance than the 'distal' socioeconomic factors (such as low household income, low level of education, and dilapidated environment that characterize rural settlements in Nigeria) may determine health seeking and drus use behaviour? Attempts to answer this question involve critical analysis and consideration of what contributory factors to antimalarial drug resistance merit the term 'significant'. It also calls for the questioning of our restricted focus on a biomedical model that considers disease causality only at the individual level. Indeed the social context can affect physical health and outcomes (Krieger, 2001a); and the social inequality existing in societies translates to the disparity in health and disease outcome (Singer, Ryff, Council, & others, 2001).

The inequality in health that exists in most societies is a manifestation of the underlying class conflict, as well as socio-political problems. According to Karl Marx, the distribution of the means of production is the major determinant of social class (Marx, Engels, & Moore, 1959). Societies are structured in a way that allows the accumulation of the surplus of production by some small groups -capitalists- at the detriment of a larger proportion of the society who stand to be exploited by the small proportion enjoying the production surplus (Berkman et al., 2014). Concepts like neoliberalism have seen to the increase of capitalism in the present era.

Neoliberalism is a theory that stems from the theory of liberalism. Neoliberalism champions the course of free trade, privatization and deregulation of markets (Eliason, 2015; McGregor, 2001). It is based on the three principles of individualism, privatization and decentralization (McGregor, 2001). In public health, neoliberalism dismantles healthcare systems through privatization thereby making access to health care services unequal to the members of a population. In addition, through its privatization and individualist stance, neoliberalism has been accused of breaking down societal structures and systems that exist to protect the less well-off in the society (Eliason, 2015). As a theory rooted in individualism, it aligns with the notion of victim-blaming while denying the significance of social factors in determining health.

In examining the process of social inequalities in health and how socioeconomic position affects health inequality, Diderichsen stated that the social context of a population, in the form of social structure, system, and policies, can to stratify the population into different levels or positions (Diderichsen, 1998; Diderichsen et al., 2001). Furthermore, with the different levels of social position comes differences in access to material resources; and subsequently, differences in the level of exposures to disease and its outcomes for people at different positions of this social stratification (Diderichsen, 1998; Diderichsen et al., 2001; Solar & Irwin, 2007). This pattern is evident in the fact that the social structural line that stratifies a society into different levels of socioeconomic measures, also happen to be among the important determinants of population health patterns (Berkman et al., 2014). As such, social epidemiologists are concerned about the health consequences of these social class stratification in a population.

Generally, social epidemiologists employ different theories, usually from sociological and biological disciplines in explaining disease distribution pattern and the causal or contributory

factors to health outcomes. Some social epidemiologic theories are underpinned by evidence from both disciples. Theories like lifestyle theory, psychosocial theory, the theory of the social production of disease or political economy of health, and ecosocial frameworks have been developed to help understand the interaction between social and biological factors in determining disease patterns in a population. Other epidemiologic theories that recognize the role of social structure on population health include social (Bronfenbrenner, 2009; McLeroy, Bibeau, Steckler, & Glanz, 1988) and system theory (Churchman, 1968).

The lifestyle theory is more biomedical-model-based than social or socioeconomic. In using this theory, disease patterns in a population is attributed to behavioural or cultural factors that are peculiar to certain groups of people (Tesh, 1988b). The lifestyle theory was the main theoretical framework used by most of the initial epidemiological studies on HIV (Krieger & Zierler, 1996) that explained the pattern of HIV transmission based on the sexual behaviours of groups like men who have sex with men and prostitutes. Apart from this theory leaning more towards the biomedical model, it has also been criticized for its victim-blaming approach. By attributing lifestyle as an explanation of disease pattern, like HIV transmission, a lifestyle theoretical framework sees individuals in this group as people who decided to make the wrong choices amidst other alternatives (Krieger & Zierler, 1996). It fails to recognize the impact of the social structure in constraining options and choices in health decision making. Indeed, the realities and possibilities that exist in making health-related decisions are influenced by individual status as well as other factors like social context.

Contrary to the lifestyle theory, the theories of psychosocial, social production of disease, and ecosocial frameworks (collectively termed 'theories of disease distribution' by Krieger (2001b)) all emphasize the concept of social position in population health. These theories are also similar in their interest to explain the social inequality in health. Nevertheless, they differ in relation to their specific emphasis on the degree to which social and biological conditions determine population health patterns, their use of social and biological explanations of population health, and subsequently their respective recommendations on how to control the disease pattern in a population (Krieger, 2001a, 2005).

In relation to their difference, Psychosocial theory which originated from the work of Cassel (1976), as the name goes, strongly emphasizes more on the role of psychosocial factors in determining the health of individuals in a population. It proposes that the perceptions and experiences of individuals in an unequal society will affect their health (Raphael, 2006;

Raphael & Bryant, 2006). This theory has been criticized for adopting a micro-level approach to population health by concentrating on the role of social and biological factors on health at the individual level alone as opposed to the population level. This micro-level stance is one of the differences between the psychosocial theory and the social production of disease theory which adopts a macro-level approach in studying health patterns in a population.

The ecosocial theory, which is relatively new and originated from the works of Nancy Krieger adopts a multilevel approach in integrating the role of social and biological factors in health (Krieger, 2001a, 2005). In addition, it also incorporates the historical and ecological perspective thereby introducing a new lens for conceptualizing the determinants of disease distribution in a population health (Krieger, 2001a, 2005).

3.4.3 Social production of disease theory

Over the last two decades, there has been a shift in the focus in the biomedical model of health. Other factors previously perceived as 'distal' in terms of defining disease causality have experienced increased interest and research (Shy, 1997; Syme, 1992). These 'distal' factors brought a new perspective to population health studies as such changed the focus of the epidemiologic investigations from micro individual level to a macro population level. Peculiar among these factors are social structure/position and socioeconomic position. With the increased research on the influence of social position on population health, a theoretical framework that explains the patterns and interactions that produce social inequality in health was imminent.

The social production of disease theory, also known as the political economy of health theory is a social epidemiologic theory that re-emerged in the 20th century following the increased interest on social determinants of health (Conrad, 2008; Doyal & Pennell, 1979). The theory was said to have, in the words of Kaufman and Kaufman (2001), 'waxed and waned' in epidemiologic studies for about two centuries. Some of the 19th and 20th-century epidemiologists whose works have been linked to the development of the theory of social production of the disease include Virchow Ackerknecht (Ackerknecht et al., 1953) and Cassel (Cassel, 1976). In addition to these, the re-emergence of the theory has also been attributed to the work of Vincente Navarro (1976), a Spanish physician with a particular interest in the sociological influences on health. Other recent epidemiologists that have propelled the use of the theory of social production of disease include Krieger Nancy, Sally Zierler, and Carl Shy.

The basic principle of the social production of disease theory is drawn from the broader political economy theory which emphasizes the influence of social, political and economic structure on the lives of the members of the population (Alford & Friedland, 1985). The broader political economy theory adopts a multidisciplinary perspective in investigating the interaction of social, political and economic factors in determining inequalities in access to the means of production and life opportunities in the society (Minkler, Wallace, & McDonald, 1994). The social production of disease theory uses the 'social causation pathway in explaining disease causation and outcomes in a population; as such, social position is a prominent concept of this theory.

Consequently, the theory of social production of disease proposes that health-related behaviours and disease outcomes and their unequal distribution in a population are products of the interplay between different socio-structural factors in the population (Solar & Irwin, 2007). Subsequently, in explaining population health pattern, the social production of disease theory looks at the social, political and economic context in which diseases develop, treatments are sought (Minkler et al., 1994), and disease outcomes establish.

As a macro-level theory, social production of disease theory focuses on the social, political and economic determinants of population health, while recognizing the health impact of negative psychosocial outcomes of social inequality. Social production of disease theorists argue that socioeconomic structure, as well as the political context, shape the pattern of inequalities in health in any particular population (Lynch et al., 1997); and can sometimes constitute barriers to individuals making healthy decisions (Doyal, 1979; Conrad, 1981).

Amongst all the social epidemiologic theories, the social production of disease theory stands out as the appropriate theory in investigating the socioeconomic determinants of antimalarial drug use behaviours that promote drug resistance as its theoretical assumptions aligns with the conceptual framework of this study. This is because, compared to the other theories, social production of disease is ideal in explaining the interaction of the socioeconomic position and context in determining behaviours that promote the development and spread of antimalarial drug resistance.

Furthemore, social production of disease theory, with its macro-level perspective, provides a conceptual framework for understanding public health problems and in devising effective approaches in controlling them (Minkler et al., 1994). As such, studies adopting this theory aim at conducting a detailed inquiry to understand the role of social, political and economic structures and context on public health; and how these interact with the human biology in determining health outcomes and disease pattern in a population.

Importantly, the social production of disease theory belongs to the school of thought that disagrees with the concept that health outcomes are randomly distributed in nature. One of the underlying assumptions of this theory and other theories that share this perspective is that population health outcomes are patterned in the society along some key social factors. For social production of health theorists, this pattern is in line with the socioeconomic structure and political context of the society.

Likewise, social production of disease theorists assumes that socioeconomic resources are not distributed in the society based on relative efficiency but the possession of power (Vicente Navarro, 1984; O'Connor, 1976). The state in its role of resource allocation and distribution has the power to influence the socioeconomic inequalities in a society (Estes, 1991), by shaping the nature and availability of public infrastructures like education, healthcare services, good quality housing (Solar & Irwin, 2007), rational living wage, amongst others. The exercise of this power structures the socioeconomic context in which people seek treatment.

Although almost the entire population in areas highly endemic for malaria (like Nigeria) are at risk of malaria infection, however, the relative socioeconomic position of people can shape their exposures and experiences of malaria infection. The disparity in socioeconomic position reflects in the use of malaria preventive measures (Adedokun & Adeyemi, 2013; Worrall, Basu, & Hanson, 2002), most of which are cost-intensive and require constant renewal as they offer short time protection from the mosquito vector that transmits the plasmodium parasite. An example of this is the insecticide residual spray (IRS). These cost-related factors make the consistent use of preventive measures like IRS, difficult for those at the lower levels of socioeconomic measures. With this, those of lower income level are likely to have more chances of exposure to malaria transmission, as well as the transmission of drug-resistant strains when present in the population.

Even when malaria infection does occur, the interaction of social, political and economic structures -like location of health facilities, types of health facilities available, existing policies on antimalarial drug distribution and dispensing, individual or household income, educational level, type of settle amongst others- may affect the treatment decisions and behaviours.

By comparing the frequency of malaria treatment behaviours that promote the development and spread of antimalarial drug resistance among socioeconomic groups that are differentially favoured or constrained by the social and economic structure, this study aims at establishing key contributory factors to the persistent issue of antimalarial drug resistance.

As stated earlier, in addition to offering a conceptual framework for explaining health inequalities along the socioeconomic gradients, social production of disease theory also goes further to devise strategies aimed at reducing the social inequality in health. Such strategies are usually based on improving the social structure as well as the economic and political context in which health-related decisions and behaviours emerge (Minkler et al., 1994). Pioneers of this theory, like Cassel, have recommended that with regards to controlling population health and disease trends, improving the social structure and support will go further than reducing exposure to the stressors (Cassel, 1976). In suggesting such strategies, social production of disease focuses on the cause of the cause in recommending strategies to reduce disease trends and social inequality in population health.

In addition to this, social production of disease theorists, in devising control strategies for public health issues, look beyond achieving equality. By adopting a vision of social justice aimed at reducing unjust social and economic policies and constructions (J. Y. Kim, Millen, Irwin, & Gershman, 2000), social production of disease theorists focus more on equity (Link & Phelan, 1996; Szreter, 2003). In other words, this means that, for instance, health promotion interventions underpinned by this theory are designed to ensure those with more needs have more access (equity) rather than ensuring everyone in the population has equal access to the intervention (equality).

As interesting and valuable as the social production of disease theory is in general and in relation to this study, it is not without limitations and criticisms. One of such is its adoption of a macro-level approach to social epidemiology (Camargo Jr, Ortega, & Coeli, 2013). Nevertheless, although a macro-level theory, the social production of disease does not deny the role of individual factors and the ability of individuals to carry out some unhealthy actions

intentionally (Estes, 1991). It recognizes that an individual or a group's social, economic and political context significantly influence the possibilities of their choosing an option that is beneficial or damaging to their health.

The use of the social production of disease theory guided the processes in this study from the designing and data collection stages, to the interpretation/discussion of the findings and recommendations.

3.5 Chapter Summary

The social production of disease theory, which is rooted in the broader disciple of Epidemiology, is based on the premise that health-related behaviours and outcomes are not randomly distributed; rather these are patterned along the social and economic structures of the society. The social production of disease theory offers a strong framework for studying the contributions of socioeconomic measures on how malaria treatment is sought and antimalarial drugs used in the Nigerian setting.

CHAPTER FOUR

METHODOLOGY

4.1 Introduction

In research, methodology guides the entire process as it is concerned with how the study will go about in answering the research question (Guba, Lincoln, & others, 1994; Jackson, 2013). The methodology chapter answers questions on why specific data are required, what data to be collected, where to collect required data from, when and how to collect data (Scotland, 2012). This chapter explains the methodology to be adopted in answering the research question and offers a rationale for the choice of methods selected. A mixed methods research was used in this study to answer the research question

4.2 Philosophical assumptions

In conducting research, researchers adopt different philosophical worldviews on what composes nature and being, what knowledge is and how knowledge can be learned (Crotty, 2005). The choice of philosophical assumption shapes the research process by determining the methodology to be used in answering the research question (Creswell, 2011). Consequently, the methodology and research design adopted in a study needs to align with the philosophical assumption of the study. In mixed methods research design, the philosophical worldview includes a basic set of beliefs or assumptions that guide the conduct of the study using different methods (Lincoln, Lynham, & Guba, 2011). Some of the most common worldviews used in mixed methods research include single worldviews like pragmatism, transformative-emancipatory paradigm (Creswell, 2010; Mertens, 2003). Also, there are multiple worldviews which involve the combination of two or more worldviews like post-positivism, positivism, constructivism, transformative amongst others (Creswell & Clark, 2007). To best answer the research question for this study, a pragmatic worldview is adopted.

Pragmatism, which originated in the United States during the latter quarter of the nineteenth century, is traced to the ideas of scholars like John Dewey (1859-1952), William James (1842-1910), Charles Sanders Peirce (1839-1914), and contemporary pragmatists like Cherryholmes (1992), Murphy (1990), Hilary Putnam, Nicholas Rescher, Jürgen Habermas, Susan Haack, Robert Brandom, and Cornel West. It is a philosophical assumption based on the concept of ‘practicability’, that is that an ideology or proposition is true if it works satisfactorily and that unpractical ideas or abstract questions should be abandoned (Feilzer, 2010; Small, 2011).

Pragmatists advocate that priority should be given to the act of discovery over the justifications for knowledge (Small, 2011).

For pragmatists, the research question should be the major determinant of the method adopted in the inquiry. Therefore, a pragmatism stance focuses on the research question and sees the methodologies as mere tools to be used in understanding the world (Creswell, 2011). It is based on "what works" using diverse approaches and valuing both objective and subjective knowledge.

Pragmatism, as a philosophical assumption in mixed methods research, provides an approach to combine principles from critical, interpretive, and positivist paradigm (Shaw, Connelly, & Zecevic, 2010) to achieve results that are meaningful and applicable in relation to the inquiry (Creswell, 2011; Creswell & Clark, 2007). The adoption of a pragmatist worldview provides a strong foundation for this study given the need for a pluralist stance (that is the use of both quantitative and qualitative approaches) in understanding the contributory role of socioeconomic factors in determining drug use behaviours. The inductive and deductive approaches may seem incompatible in a single study given the persistent debate on the differences and superiority between both approaches. However, pragmatists insist that a false dichotomy exists between quantitative and qualitative paradigms and their associated methodologies; and so advocate that the integration of both in a single study, allows for a more comprehensive approach to a research question (Sparkes, 2015).

Nevertheless, pragmatism as a philosophical assumption has been criticized for not recognizing the necessity of the connection between knowing and how we know thereby abandoning the notions of ontology and epistemology (Sparkes, 2015). As pragmatism is more interested in practicability and what works best, it disentangles itself from the entrapment of establishing what knowledge is and the way we know things as well as the paradigm debates between positivists and interpretivists.

4.3 Research Design

This study adopted an exploratory mixed method approach which provides a qualitative (textual) and quantitative (numeric) description of the issue under study using sample participants drawn from the Nigerian population. According to Johnson et al. (2007), the mixed method design involves the combination of elements of quantitative and qualitative research approaches in a study for the purpose of breadth and depth understanding and corroboration. Mixing in this study adopted a methodological orientation as described in Tashakkori and

Teddlie (1998) –this involved the combination of research methods and interferences. A mix of systematic review, qualitative interviews, and quantitative survey designs was used in this study.

For the purpose of addressing the research questions of this study, ordering of data collection in a sequential design is relevant. Sequential studies take advantage of several benefits of mixed methods studies, such as the ability to understand the mechanisms behind newly discovered associations (explanatory) or to test emergent hypotheses (exploratory) (Smith, 2008; Tarrow, 2004). Therefore, for the current study, the systematic review and the qualitative strand preceded the quantitative strand; however, priority was given to the quantitative strand so as to achieve the aims and objectives of this research better.

4.4 Data interpretation and discussion

Although the two types of data (qualitative data from interview and quantitative data from the systematic review and survey) were analyzed separately with the results from the systematic review and interviews informing the design of an instrument (questionnaire) for the survey, interpretation, and discussion of the findings from the three methods were interactive. The final interpretation of data involved comparison and a complimentary use of findings from all strands. For example, the findings from the qualitative phase might be used to explain further some of the findings or patterns observed in the quantitative phase and vice versa.

4.5 Rationale for the methods chosen

In relation to using either a quantitative or qualitative approach alone, mixed methods design was chosen as it was the best approach in answering the research question of this study. Although the use of quantitative design will be ideal in providing evidence on the extent of the role of socioeconomic factors in the development and spread of antimalarial drug resistance; however, the research problem is also qualitatively oriented. This is because of the need for an in-depth understanding of antimalarial drug use behaviours of the population, and how socioeconomic postion can affect an individual's antimalarial drug use behaviours. Also, with the subject of this study not well researched, there was a need to start from a systematic review to integrate the findings from the few existing studies that have reported on the relationship between socioeconomic factors and antimalarial drug use behaviours.

As an exploratory mixed methods study, one of the main aims of mixing in this study was the instrument development (Creswell, Fetters, & Ivankova, 2004). The purpose of mixing in this study was to ensure a rigorous study of the research problem by

- First identifying the important variables to measure (antimalarial drug use behaviours and their associated socioeconomic measures). As there is a gap in the literature on the subject area and no existing measurement tool to identify groups at high risk of developing drug resistance, the systematic review strand was important in creating a holistic picture of what is already known regarding resistance-promoting antimalarial drug use behaviours. Consequently, the qualitative strand was important in exploring and identifying the drug use behaviours of the population, and how socioeconomic factors contribute to these. The findings of the systematic review and qualitative strands of this study helped in identifying important variable to study using a larger number of participants.
- To further use the information (or variables) drawn from the initial strands (systematic review and qualitative interviews) of the research to develop an instrument (questionnaire) for the quantitative survey strand of the research.

A major advantage of the mixed methods design is that, in relation to the use of either qualitative and quantitative approach alone, combining the two methods offers a better understanding of the research problem (Creswell & Clark, 2007). Mixed methods studies enjoy the advantages of both qualitative and quantitative research methods while canceling out the disadvantages posed by using each method alone.

4.6 Study Population

The target population for this study was household heads (male or female) from both lower and upper socioeconomic gradients in Nigeria. The reason for the interest in this group is to ensure this study recruits participants who can provide information on the socioeconomic situation of the family as well as their malaria treatment seeking and drug use behaviours.

Nigeria is a sub-Saharan African country with a population of about 173 million people (World Bank, 2014). The country has a land mass of 923,768 square Kilometers and a tropical climate with two seasons, the wet and the dry seasons. The annual rainfall ranges between 550mm in some part of the north (mainly in the fringes of Sahara desert) to 4,000 mm (in the coastal region around Niger Delta area in the south) (Mouzin, 2012). The temperature in Nigeria oscillates between 25°C and 40°C. The climatic and geographic features of Nigeria make it a conducive environment for high malaria transmission.

All the states in Nigeria are holoendemic areas for malaria, and transmission is usually year round. However, the wet or rainy season is the peak malaria transmission period in Nigeria. In

addition, the duration of the peak transmission season differs in different locations with the areas in the north having a shorter duration of transmission (approximately three months) than the south (almost year round) (Mouzin, 2012). The *Plasmodium falciparum* is the most prevalent (97%) malaria parasite specie in Nigeria (Mouzin, 2012).

The decision to study this population is underpinned by three facts:

- Firstly, Nigeria is one of the leading countries in terms of malaria burden (with approximately 35% of global malaria death occurring in Nigeria). The population has also experienced high rates of antimalarial drug resistance which led to the review of the first line antimalarial treatment drugs in Nigeria and saw the switch to ACTs (Federal Ministry of Health Nigeria, 2011b).
- Secondly, Nigeria is characterized by a high level of poverty amidst its oil wealth with approximately 46.0% of the population living below the World Bank poverty line of $1.25 per day (World Bank, 2014).
- Thirdly, some features of the Nigerian health care system that contribute to the persistence of the disease burden in this population (by constituting a major barrier to early and effective treatment) include the lack of universal and equitable access to primary health care (as this is the level where conditions like malaria infection are managed) (Onwujekwe & Uzochukwu, 2005). Also, the current government policy of payment for health care in all public health facilities at the point of use which makes cost an important factor in treatment (Federal Ministry of Health, Nigeria (FMOH), 2001; Onwujekwe & Uzochukwu, 2005).
- Finally, the drug retail system in Nigeria, where antimalarial drugs are over the counter drugs (Federal Ministry of Health Nigeria, 2011b) with the masses having the option to purchase any quantity and dose they want, encourages development and spread of antimalarial drug resistance.

Data for the qualitative and quantitative strands of this study were collected from two locations in Nigeria: Abuja and Imo state (see Figure 4.1 showing a map of Nigeria with the study areas highlighted in green). Data were collected from both urban and rural areas in these locations so as to include the experiences and treatment seeking behaviours of people from both high and low socioeconomic positions. Both states had some similar population characteristics and differ in terms of predominant culture, language, and religion.

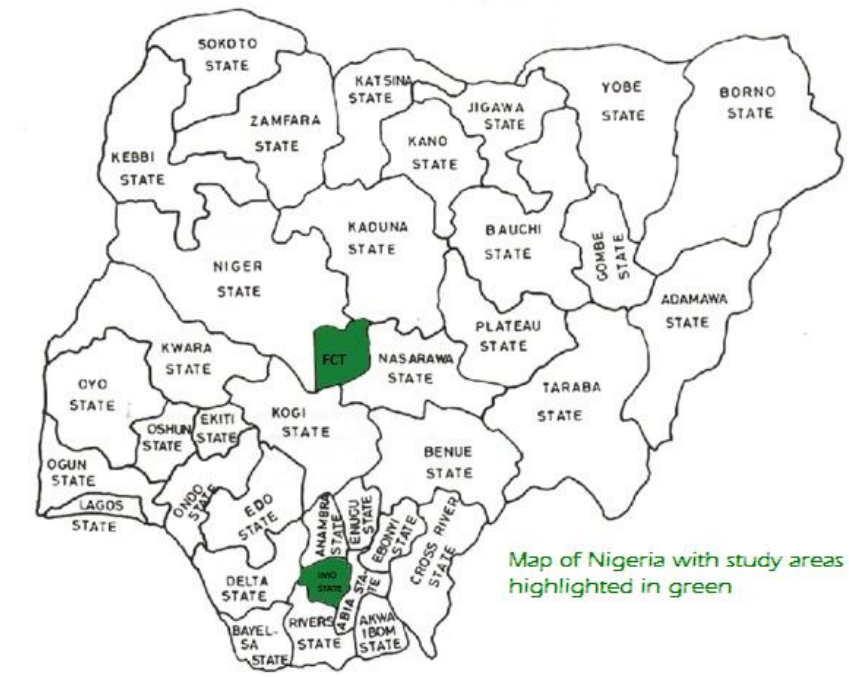

Figure 4.1: Map of Nigeria with study areas highlighted in green

4.7 Chapter Summary

This study adopts an exploratory mixed method approach which provides a qualitative (textual) and quantitative (numeric) description of the issue under study using sample participants from Nigeria. The systematic review was first conducted to ensure an in-depth understanding of what is already known on the subject area. This informed the conduct of the qualitative strand which was used to identify key variables to be tested using the questionnaire in the survey strand. The results of the survey were analysed for relationships using appropriate statistical techniques. The following three chapters provide a detailed account of the methodology adopted in each design as well as the results.

CHAPTER FIVE

SYSTEMATIC REVIEW

5.1 Introduction

This chapter presents the methodology and results of the systematic review, which was the first strand of this study. The results were structured around different socioeconomic measures and their respective antimalarial drug use behaviours, as reported in the included studies.

5.2 Overview

A systematic review is a type of research design that involves the integration of findings from existing studies (secondary data). It differs from the traditional or narrative review in that it adopts a scientific approach in conducting a systematic and comprehensive search of the literature, thereby reducing the selection bias and subjectivity that characterizes a traditional review (Bowling, 2014a). Systematic reviews play a key role in health studies and in informing policies and practice through the provision of evidence; as it collates the findings from all existing studies that meet the inclusion criteria, and creates a holistic picture of the issue under study.

Based on the type of data extracted from the included studies and the method of integration or analysis, a systematic review can be categories into a systematic review of qualitative studies (for example meta-synthesis, meta-ethnography), systematic review of quantitative studies (meta-analysis, votecount), and mixed methods systematic review. A systematic review of quantitative studies was conducted in this study as the relevant data to the research topic that were extracted from the included studies were quantitative.

5.3 Search strategy and selection criteria.

A systematic search of the literature on the socioeconomic factors associated with antimalarial drug use behaviors was conducted in May 2015. The following databases were searched: PubMed, EMBASE, Sociological Abstracts, and Biomedical. Keywords for the search included terms for socioeconomic factors (e.g. Poverty, income, treatment cost, educational level, rural area, occupation) together with terms related to antimalarial drug use behaviors (e.g. malaria drug adherence OR compliance, malaria drug use, antimalarial non-adherence OR non-compliance). In addition to the computerized search, a hand-search of relevant peer-

reviewed journals as well as reports/publications from malaria organizations and charities was carried out.

Inclusion criteria: To achieve the aim of this review, the following criteria were included for the selection of relevant articles:

- Measured antimalarial drug use behaviours in relation to socioeconomic factors.
- Published between the year 2005 up to 2015 so as to include studies conducted in similar economic era as present.
- Reported drug use behaviour for any of the antimalarial drugs in use
- Studies conducted in Africa or Asia
- Explicitly stated the research methods and defined the characteristics of the socioeconomic index as used in the study.
- Adopted a quantitative method of research or collected quantitative data.
- Included caregivers, parents or adults who bear the financial and social cost of malaria treatment for themselves or a member of their household.

The computerized search on PubMed, EMBASE, Sociological Abstracts, and Biomedical databases yielded a total number of 4,199 articles. Furthermore, the result was filtered to include only studies with the key words in their title and abstract. Afterwards, the titles and abstracts of the studies retained were screened for relevance with studies that did not report on socioeconomic and drug use behaviour variables being excluded. This process narrowed down the studies to 71 articles.

A hand search was also conducted by searching through journals on malaria research, checking the reference list of selected articles, the studies that have cited them and also related studies. This process was conducted to capture studies that might not have been picked up by the databases (for instance studies that have just been publish online by journals), to ensure an exhaustive search of literature is achieved. The hand search process yielded eight studies which were included in the selected studies making a total of 79 studies. Also, a search of grey literature including organizational sources like World Health Organization, conference proceedings, academic thesis among others was carried out. However, no relevant study was identified from this exercise. The 79 studies were further appraised for quality and relevance (see fig 4.2 for a flowchart of search process).

The appraisal stage involved reading through the full texts of the 79 articles. Appraisal of the studies was conducted using the Principles of Critical Appraisal for Quantitative Studies (PCAQS) recommended by the Cochrane Library. Based on the PCAQS guideline, the studies were assessed for validity and reliability, the study population, sampling method, sample size, data collection method and tool, statistical methods used in the analysis and level of statistical significance. At the end of the assessment and appraisal exercise, 17 studies that were of good quality based on the PCAQS assessment were included in this systematic review

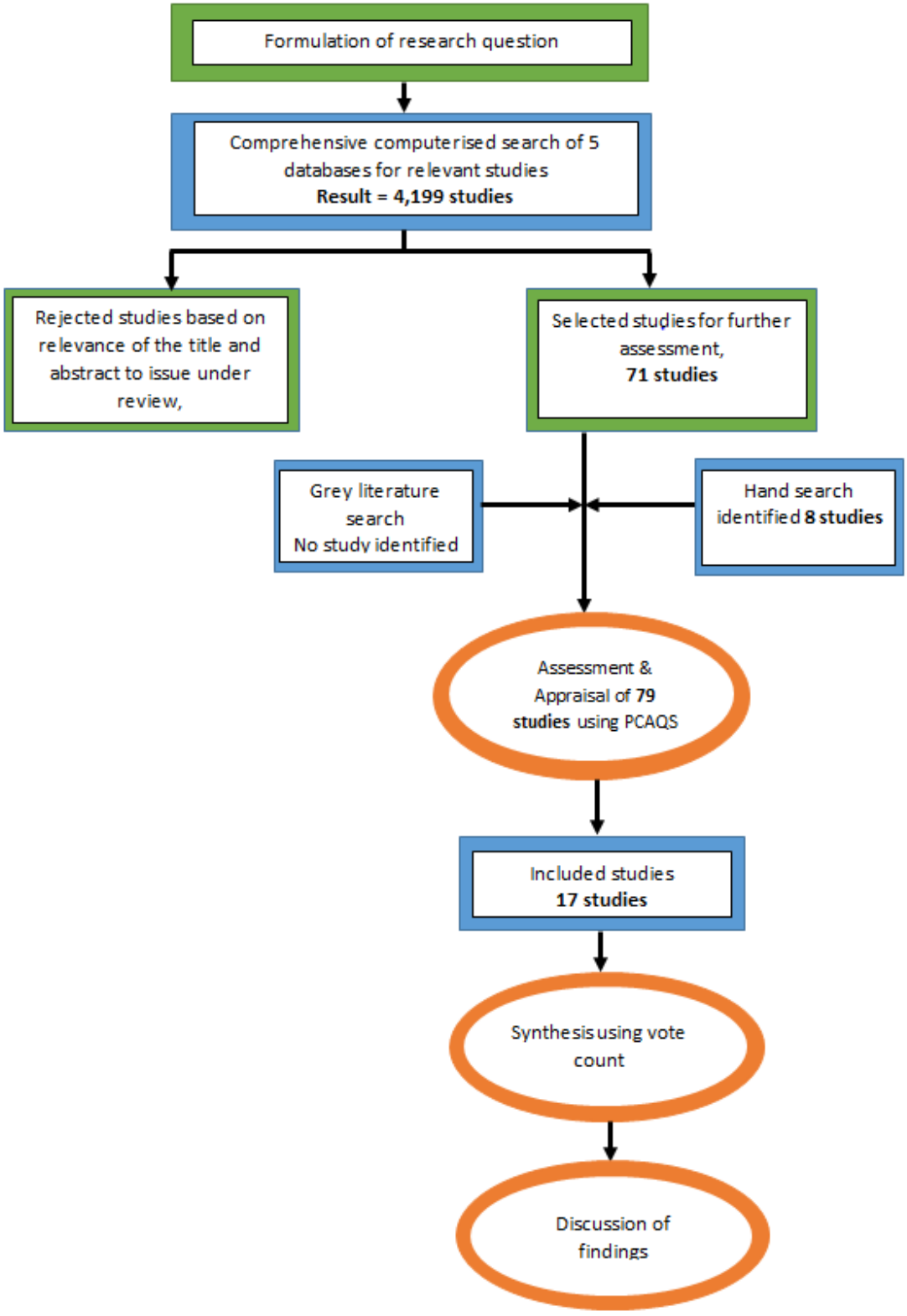

Figure 5.1: Flowchart of review process

5.4 Synthesis

This study adopted a narrative approach in synthesizing the results from the individual included studies. This approach was ideal for integrating the data considering the type of data extracted from the studies and the need to achieve the aim of this review.

Before the synthesis, relevant data from the studies included were extracted using a data extraction sheet. The data extraction was conducted by the researcher independently and then cross-checked by the director of study to ensure all data relevant to the review were extracted. An agreement was reached on the data finally extracted and used in the synthesis. Apart from the results, details of the studies, including the year of publication, source/publisher, study design, and setting, as well as number and type of participants, were also extracted.

As this study aims at identifying socioeconomic factors associated with antimalarial drug use behaviours, and considering the nature of the data collected, a vote count synthesis was chosen as the most appropriate method for synthesizing the quantitative data in this review.

Vote counting is a quantitative approach in a systematic review that consists of the identification and counting of the frequency with which a specific variable(s) is reported in all the included papers. It also uses the percentages or frequencies of these variables in the enitre data set in drawing conclusions about the issue under review (Heyvaert, Hannes, & Onghena, 2016; Light & Smith, 1971). The initial part of the vote counting process involves the sorting of the findings from the included studies into categories of those that are significantly positive, significantly negative and those that are non-significant (Heyvaert et al., 2016). The vote counting process for each of the variables reported in this review involved identifying the number of included papers that reported the variable and also considering the outcome and the strength of the statistical test for significance.

The results of the systematic review (see next chapter on systematic review results) informed the design of the qualitative strand of this study. The results were important in ensuring that the right questions are asked in exploring the existing behaviours that can promote drug resistance using individual face-to-face interviews.

Relevant data from the 17 studies that met the inclusion criteria for the systematic review were extracted and synthesized using the vote count table (see Table 5.1 on vote count). The data

extracted from these studies were all quantitative data. A survey design was the most adopted research design by the included studies (about 80%) -which was mostly cross-sectional with few longitudinal surveys. Only one of the 17 studies was conducted outside Africa (in Myanmar, Asia). Five studies were conducted in Tanzania; four studies each from Kenya and Nigeria, while Uganda, Ethiopia and Sierra Leone had one study each. The majority of the studies were conducted in rural areas, however, few were conducted in both rural and urban areas as well as urban areas only.

The synthesis of the findings from all the studies revealed different socioeconomic factors reported in relation to antimalarial drug use behaviours. These socioeconomic factors were categorized into Educational level (10 studies); Level of income/wealth (6 studies); Type of settlement (3 studies); Ability to read (2 studies); Occupation/Source of income (2 studies); and Household size (1 study). These factors were reported in line with antimalarial drug use behaviours such as non-adherence (12 studies); self-medication/presumptive diagnosis (5 studies) and non-compliance with malarial treatment guideline (4 studies).

5.5 Definitions used for antimalarial drug adherence

The definition of adherence was moderately standard across the included studies. The majority of the studies defined adherence as patients' administering the antimalarial drug according to the recommendations. In determining adherence, two common tools used by the studies were: counting remaining tablets/pill in the blister pack and/or verbal report of how many doses taken and at what time. Three studies added other measures like 'if the medication was administered with or without food' and 'the duration of the treatment'.

5.6 Measurement tool used for categorization of income/wealth level

For the studies that reported on income level and adherence, Principal component analysis (PCA) was used to classify income and wealth. However, there were differences in the inputs used for calculating the PCA. The inputs reported in all the studies on income/wealth level include educational level of household head or caregiver, data on household assets, housing construction and the main source of drinking water.

Statistical significance: For all the included studies, statistical significance was determined at a p-value of 0.05 and below.

Table 5.1: Vote count sheet			
Variables	**Expected outcomes**	**Unexpected outcomes**	**Studies**
Not acquiring the required dosage/regimen of drug and SES	60.9% of participants (from low SES villages) did not buy full dosage. 67.3% gave reasons for this as financial/affordability; 16.8% got better after starting; 14.4% said symptoms were mild and hence no need buying full dosage [23]		[23]
Adherence and education	A significant relationship with educational level and adherence P= 0.024 with 22% more adherence in participants with secondary education [21]	Caretaker's educational level and reported adherence showed no statistically significant relationship **(p=0.354)** [27]	[18 – 21; 24 – 29]
	A significant relationship between educational level and adherence P=0.005 with participants with ≥ 7ys of formal education more likely to adhere [18]	Participants educational level was not associated with reasons for non-adherence **(p=0.825)** [24]	
	P<0.01; OR 0.074; 95% CI 0.017-0.322. higher education level was associated with ACT adherence [20]	There was no statistically significant association between the educational level of patients or caregivers and probably adherence **(p=1.00)** [29]	
	Uptake of IPTp-SP increased with education, from as low as 38.9% among those who had no education to as high as **52.3%** among those with secondary and higher education. Women with secondary and higher education were almost twice as likely as those who had never been to school for formal education to receive complete IPTp-SP doses **(RRR=1.93, 95% CI 1.04 - 3.56). (P <0.001)** [26]	No association between educational level and adherence/non-adherence [19]	
	The adjusted odds of completed treatment for those who has finished primary school was 1.68 times that of patients who has not **(95% CI: 1.20, 2.36; p=0.003)** [28]	No significant association between mothers' attainment of tertiary (or higher) education and	

	There was a statistically significant association between fathers' attainment of tertiary (higher education) and use of ACTs, when compared to fathers who had not attained this level of education **(OR 0.054, CI 0.006-0.510; p=0.011)** [25]	the use of ACTs **(OR 0.905, CI0.195-4.198; p=0.898)** [25]	
Adherence and income	**p=0.003; OR 0.340; 95% CI, 0.167-0.694**. higher income level (Ksh >9000 (ie >GBP 66 monthly) was associated with better ACT adherence [20]		[14; 16; 20; 27; 31]
	p=0.034 with participants of higher income salary showing correct dosage of drugs [19]		
	Initiation of home treatment was higher in the poorer households. **25%** of the poorest will use home treatment first as against **14%** in wealthiest SE category [14]		
	Household monthly income significantly influenced dosage of the drugs used **(P = 0.034)** primarily because higher proportions of respondents with an income salary of **KShs. 4500-9000 (48.5%)** took the correct dosage of drugs as opposed to individuals with below **KShs 4500** and above **KShs 9000** [31]		
	Caretakers from the third SES quintile were most likely to adhere to treatment compared to the first quintile [27]		
Adherence and ability to read	P<0.01 OR 0.285; 95% CI 0.167-0.486. Ability to read was associated with ACT adherence [20]		[20; 21]
	Ability to read was statistically significant to the number of antimalarial tablets left **(p=0.049)** [21]		
Adherence and type of settlement	96% of rural dwellers dif not administer appropriate dosages [17]	65% of urbanites would use incomplete dose. Only 35% would administer correctly [17]	[16; 17; 27]

	The consumption of ACTS was more in the urban areas for both adults **(P=0.001)** and children **(P =0.005)** [16] Self-diagnosis was the most common diagnostic method in both rural and urban for adult and child diagnosis. There was higher proportion of self-diagnosis in rural than in urban areas for both adults and children. Rural self-diagnosis **(Adult=89.7%; children=85.9%),** Urban self-diagnosis **(Adult=83.3%; Children 79.2%)** [16] Urbanites are more likely to have blood test malaria diagnosis than rural dwellers [16]	Participants' residence and reported adherence showed no statistically significant relationship **(p=0.428)** [27]	
Adherence and source of drugs	P=0.005 those who source from pharmacy/chemists and government institutions were more likely to take correct dose than those from street vendors, private clinics, family/friends [16]		[16]
Self-diagnosis/medication and SES	25% of poorest SES will use home treatment first [14]	79% of the urbanites will use self-medication first [17] 20% of rural dwellers will self-medicate first [17]	[14; 16; 17; 23; 26; 30]
	61.6% took antimalarial drugs without prescription [23]	14% of wealthiest SES will use home treatment first [14]	
	Self-diagnosis was slightly higher in rural adults and children (A=89.7%; 85.9%) than in urban adults and children (A=83.3%; C=79.2%) [26]		
	Those in the poorer SES groups were, however, more likely to have previously sought treatment for their current illness prior to seeking treatment at the study facilities **(p = 0.002).** Of these, **62.7%** used patent medicine dealers [30]		

	Self-diagnosis was the most common diagnostic method in both rural and urban for adult and child diagnosis [16]		
Reasons for self-medication	For those who had no prescription, the reasons given were as follows: **39.0%** said procedure of acquisition (without prescription) was less costly; **23.0%** took the same drug for similar symptoms; **10%** said health institution was far from their location; **12.5%** said neighbour/friend/relative previously took the same drug (Watsirah et al., 2011)		[15; 23]
Presumptive diagnosis and SES	46% of rural dwellers will use drug vendors [17]		[17; 26]
	Urbanites were more likely to have a blood test than rural dwellers [26]		
Non-adherence and reasons given	14.7% of 34 interviewed [19]		[15; 19; 27; 23]
No food available for drug administration; and Sharing drugs with others	16.2% of 144 who were nonadherent [23]		
Saving drug for future illness	Reasons for not taking drugs according to advice were mainly; **41.4%** kept drugs for future episodes of the same illness, **33.0%** got better hence discontinued, and **16.2%** shared the dosage with another person [15]		
Nearness to treatment source	P=0.001 with the poorest SES more likely to travel further to seek treatment [30]		[30]
Household size and adherence	Household size significantly influenced the types of anti-malarial drugs used **(b = 0.092, P = 0.049)**. A higher proportion of the respondents whose household sizes were **3-5 (68.9%) or ≥6 (20.1%)** used SP as compared to households with **1-2** individuals **(11.0%) (P = 0.015)** [31]		[31]

Source of income/occupation and adherence	household source of income significantly influenced duration of antimalarial drug use **(P = 0.050)** with higher proportion of respondents who were salaried **(21.9%)** or self-employed **(38.6%)** reporting using antimalarial drugs within the specified duration relative to those with other sources of income (like farming, casual worker and petty trade) [31]		[16; 26; 31]
	Occupation of respondents was statistically significant to none uptake of IPTp-SP **(p= 0.040)** with participants who were farmers/livestock keepers **(29.4%)** and those with no job **(29.0%)** more likely not to take IPTp-SP than those employed/self-employed **(18.8%)** [26]		
	P=0.050 household source of income was associated with adherence, with salaried and self-employed more adherent than others like farmers, casual workers & petty traders [16]		

5.7 Educational level and antimalarial drug use behaviours

Educational level was the most reported socioeconomic factor in relation to antimalarial drug use behaviours across the studies. More than half of the studies (10 studies) reported on educational level in relation to adherence. Nine of these studies were conducted in the African region (Akoria & Arhuidese, 2014; Beer et al., 2009; Bruxvoort et al., 2015; J. L. Cohen et al., 2012; Exavery et al., 2014; Gerstl, Dunkley, Mukhtar, Baker, & Maikere, 2010; Ogolla, Ayaya, & Otieno, 2013; Onyango et al., 2012; Simba et al., 2012) while one study was conducted in Southeast Asia (Win, Zaw, Khin, & Tin, 2012). There was a high level of uniformity in the measurement tool used to assess educational level. Most of the studies used the classification of - no formal education; primary; secondary and tertiary education. One of the 10 studies (Beer et al., 2009) used a classification of 'no education; 1-7years of education; and >7 years' to report educational level.

The findings on educational level were not consistent in all the studies. Six studies (Akoria & Arhuidese, 2014; Beer et al., 2009; Bruxvoort et al., 2015; Cohen et al., 2012; Exavery et al., 2014; Onyango et al., 2012) reported a statistically significant relationship between higher educational level and adherence; four studies (Gerstl et al., 2010; Ogolla et al., 2013; Simba et al., 2012; Win et al., 2012) reported no statistically significant relationship between the variables.

In quantitative research, using a small number of participants (hence low statistical power) can lead to findings that may be nominally statistically significant but do not reflect the true effect (Button et al., 2013; Ioannidis, 2005; Simmons, Nelson, & Simonsohn, 2011). To ensure that the interpretation of the effects of the findings (using statistical significance) is not misleading, this review compared the sample size for studies reporting both statistically and no statistically significant relationship between educational level and adherence. The sample size in each of the studies that showed statistically significant relationship were between 217 to 1,267 while for those with no statistically significant relationship, the sample size for each of the studies was between 73 to 444.

5.8 Income level and antimalarial drug use behaviours

Income level was the second most reported socioeconomic determinant across the included studies. Four studies (Deressa, Ali, & Berhane, 2007; Onyango et al., 2012; Simba et al., 2012; Watsierah, Jura, Oyugi, Abong'o, & Ouma, 2010) reported on the association between income level and antimalarial drug use behaviours of non-adherence to the treatment dosage (Onyango

et al., 2012; Simba et al., 2012; Watsierah et al., 2010) and non-compliance to treatment guideline in the form of self-medication (Justin Cohen et al., 2010; Ibe et al., 2015; Watsierah et al., 2011). All of these studies were conducted in Africa. Of the three studies that reported on income level and adherence, two (Onyango et al., 2012; Watsierah et al., 2010) found a statistically significant relationship between low-income level and non-adherence. The other study (Simba et al., 2012) did not conduct a statistical analysis of this relationship but used percentages to indicate less-adherence in lower socioeconomic levels.

Of the three studies that reported on income/wealth level and noncompliance to treatment guideline, only one study [30] tested this relationship using statistical analysis and found a relationship between poorer socioeconomic status and presumptive treatment. The other two studies (Justin Cohen et al., 2010; Watsierah et al., 2011) only reported a higher percentage of presumptive treatment among poorer households.

5.9 Source of income/Occupation and antimalarial drug use behaviours

Among all the included studies, only three studies (Exavery et al., 2014; Onwujekwe, Hanson, et al., 2010; Watsierah et al., 2010) reported sources of income or type of occupation in association with adherence to malaria treatment. These two studies reported a statistical association between the source of income/occupation and adherence.

5.10 Ability to read and antimalarial drug use behaviours

Two studies (Cohen et al., 2012; Onyango et al., 2012) reported on adherence to antimalarial treatment and ability to read. Both studies found a statistically significant association between ability to read and adherence to antimalarial drugs.

5.11 Type of settlement and antimalarial drug use behaviours

In all, four studies (Exavery et al., 2014; Oguonu et al., 2005; Onwujekwe, Hanson, et al., 2010; Simba et al., 2012) looked at antimalarial drug use behaviour between participants from different types of settlements. Settlements in the four studies were categorized into two -urban and rural. The studies were conducted in Nigeria and Tanzania (two studies from each of the locations). Three studies reported on self-diagnosis/treatment (Exavery et al., 2014; Oguonu et al., 2005; Onwujekwe, Hanson, et al., 2010) while two reported on adherence (Oguonu et al., 2005; Simba et al., 2012).

Amongst the studies that reported on self-diagnosis/treatment, two studies (Exavery et al., 2014; Oguonu et al., 2005) found a statistically significant relationship between the type of

settlement and self-treatment/medication. The study by Exavery et al. (2014) reported that rural dwellers were more likely to self-medicate than urban dwellers. The other study which was conducted by Oguonu et al. (2005) reported a contrast finding with urban dwellers more likely to self-medicate than the rural dwellers.

In studying the relationship between the type of settlement and adherence, one study (Oguonu et al., 2005) reported a higher proportion of non-adherence (96%) among rural dwellers compare to urban dwellers (65%); it, however, did not conduct a statistical analysis to determine the significance of this relationship. In addition, the other study that reported on adherence and type of settlement (Simba et al., 2012) found a statistically insignificant relationship between the type of settlement and adherence.

5.12 Household size and antimalarial drug use behaviour

Only one study (Watsierah et al., 2010) reported household size and antimalarial drug use behaviour. The study, which was conducted by Watsierah et al. (2010) found that household size significantly influenced type of antimalarial drugs used; with a higher proportion of the respondents whose household sizes were 3-5 or ≥6 more likely to use the outdated first-line treatment of SP compared to households with 1-2 individuals (p=0.015).

5.13 Reasons for non-adherence and self-medication

Non-adherence to the antimalarial treatment regimen and noncompliance to the recommended treatment guideline through self-treating or presumptive diagnosis were the most reported drug use behaviours. Some of the included studies that reported these behaviours also reported some reasons given by participants for these behaviours.

For non-adherence, the reasons reported include: No food available for drug administration (Gerstl et al., 2010); sharing drugs with others (Cohen et al., 2010); and saving drugs for future (Watsierah et al., 2011)

For self-treatment and presumptive diagnosis, reasons given include: Less expensive than consultation (Justin Cohen et al., 2010; Watsierah et al., 2011); and health institution too far from home (Watsierah et al., 2011).

CHAPTER SIX

QUALITATIVE STUDY

6.1 Introduction

Chapter six presents the qualitative study, its methodology and interview results. As a thematic analysis method was adopted in this study, the results were structured around the themes (behaviours) identified from the analysis.

6.2 Overview

Qualitative studies are basically exploratory in nature and adopt an inductive approach in studying the world around us. The qualitative approach was used in this study to identify key variables (in relation to the research question) that the quantitative instrument investigated. As such, the qualitative study explored how the participants describe their experiences of malaria infection and treatment, and articulate reasons for their actions -such as how socioeconomic factors (such as educational level, income level, type of settlement) affect the way they use antimalarial drugs. Other information that were explored by the qualitative strand included participants' knowledge of malaria infection, socio-demographic features of participants amongst others.

6.3 Interviews

Data collection in qualitative studies is an integral part of the design with the researcher playing an important role in the collection and interpretation of the data, hence the subjective element of qualitative studies. Some of the commonly used methods of data collection in qualitative studies are observation (participatory or non-participatory), interviews, focus group discussions, documents like diaries, notes among others. These different methods of qualitative data collection have unique features which is evident in the type and richness of the data they collect.

The choice of a data collection method in this study is underpinned by the aim of the qualitative strand of this study, with considerations of which method can be feasible in collecting required data from appropriate respondents. Methods like focus group discussion which, in addition to their interactive nature, are time and resource saving (as data can be collected from many participants at the same time) were however not feasible in this study. For instance, based on the subject area and the interest of this inquiry, which will require participants to share their

treatment experiences and behaviours while discussing their socioeconomic situations (like household income, educational level), focus group discussion, which does not offer confidentiality, was not considered as appropriate. Overall the interview method of data collection was used in this study

The ability of one-on-one interviews to offer confidentiality to participants is one of its features that informed its use in this study. Also, with interviews (unlike focus group discussion), each participant gets one-on-one attention, which is important in gaining an in-depth understanding of their behaviours and also in ensuring other participants, as you would have in focus group discussion, do not dominate the discussions. As a primary data collection method, the use of interviewing is based on the need to understand people's perspectives about the issue under study. As such, participants are usually recruited based on their ability to provide relevant information.

Sampling

The issue of sampling and sample size is one of the key differences between a qualitative and a quantitative inquiry resources (Patton, 2002; Sayre, 2001). In the selection of study participants, quantitative studies, in order to achieve representativeness and generalizability, usually adopt a random probability sampling technique whereby all those meeting the inclusion criteria have an equal chance of being selected for the study (Teddlie & Yu, 2007). This need for representative sample is however not the same for qualitative studies where there are no specific rules on the approach to adopt in recruiting or sampling participants for the study. The overall guiding principle in sample selection in qualitative studies is to select participants who can provide valuable and rich information that will help in achieving the aim of the inquiry (Guest, MacQueen, & Namey, 2011). As a result, the purposive sampling technique is the most favoured in qualitative inquiries. Purposive sampling refers to the strategic selection and purposive recruitment of individuals who can provide accurate and rich information on the issue under study (Patton, 2002).

As an exploratory study, a purposive sampling technique was adopted in this study. Participants were selected based on their ability to give accurate and valuable information on the socioeconomic status of their household as well as behaviours and practices in seeking malaria treatment for themselves and/or members of their household. The inclusion criteria for participants in this study were:

- Participants must be at least 18 years of age
- Participants must be resident in Nigeria
- Participants must be household heads who bear the financial cost of malaria treatment for themselves and members of their household. The reason for this criterion is to ensure that those who can provide accurate information on the financial cost of malaria treatment, as well as the socioeconomic status of their household, are recruited
- Must have sought malaria treatment for themselves or a member of their household within the last six months to reduce the recall bias.
- Must not have severe malaria infection at the time of the study

In addition to the above, a drug vendor and a pharmacy assistant from the study sites were interviewed to help interpret the findings from the participants.

Furthermore, as qualitative and quantitative studies aim at achieving different outcomes, the number of participants or sample size used in each of the study designs differ. With the qualitative studies more concerned about achieving an in-depth understanding of phenomena, a smaller number of participants are recruited unlike in the quantitative. Quantitative studies tend to investigate the issue under study using a larger number of participants, hence the term 'breadth' used by Patton (2002) to describe these types of studies. Determination of sample size in qualitative studies depend on several factors like the qualitative approach guiding the study, the aim or purpose of the study, and also the available time and resources.

The sample size for the qualitative strand of this study was not determined prior to the conduct of the interview as the aim of the qualitative strand was to explore people's experiences and behaviours until saturation is achieved (Guest et al., 2011). This involved continuous sampling and data collection until saturation was achieved; that is, the point when no new information or category, in relation to the issue under study, was emerging from subsequent interviews (Glaser & Strauss, 2009).

Consequently, the data collection and analysis were simultaneously conducted with each interview transcribed and analyzed before the next interview. With this strategy, emerging codes were considered and incorporated into subsequent interviews. This allowed for validation of data by enabling the researcher to confirm, probe or elicit further explanations on some behaviours or experiences identified in previous interviews. This strategy was also

important in determining when saturation was achieved in this study. Glaser & Strauss, (2009) described this process of concurrent collection and analysis of data as 'theoretical sampling'.

In all, 15 individual in-depth interviews were conducted with 15 participants. Thirteen of these participants were household heads; while the remaining two were pharmacy attendant and chemist. The household heads were the main participants in this study. The recruitment of the pharmacy attendant and chemist as earlier stated was based on the need to clarify some of the findings on drug use behaviours reported by the household heads.

6.4 Development of the Interview Guide

Interviews as a method of qualitative inquiry provide an in-depth account of participants' experiences of issues or subjects under study (Turner, 2010). In designing an interview session, there are three main formats used in terms of the construct of the interview subject and the line of questioning. These include informal conversational interview, general interview guide approach, and standardized open-ended interview. The informal conversational approach is sometimes referred to as unstructured and the most open-ended interview design (Patton, 2002). Here the flow and direction of the interview are not predetermined, as such, it allows the interviewee and the data to lead (Patton, 2002). With the level of flexibility this format offers, the data collected from interviews using the informal conversational interview are usually different for each interviewee, hence largely heterogeneous. As a result, the collection and analysis processes are usually complex and time-consuming (Patton, 2002).

The interview guide approach is similar to the informal conversational approach in that they both allow for some level of flexibility in asking questions during the interview. However, the interview guide differs in that it addresses the weakness of the informal conversational approach by using a guide or schedule that specifies important questions or issues that the interviewer wants to focus on (Patton, 2002). It offers a more focused, systematic and better-managed interview session with the interviewer directing the flow. Although it works with a list of predetermined questions, the use of an interview guide allows for flexibility in exploring and probing for more information from the interviewees (Gall, Gall, & Borg, 2003). The structure and sequence of the questions do not have to be as outlined in the guide, but the interviewer ensures that all questions or issues predetermined are covered (Patton, 2002). This is, however, different in the standardized open-ended interview format.

The basic difference between the interview guide format and the standardized open-ended interview is that the later requires a well-structured and worded question predetermine before the interview (Patton, 2002). In a standardized open-ended interview, the questions are asked as they are outlined on the schedule; hence it ensures uniformity in the questions asked and, to some degree, the variety of responses. Although the participants are usually asked identical questions, the questions are structured to elicit open-ended responses (Gall et al., 2003). Data from interviews using this format usually have fewer variations regarding generated codes or categories.

Amongst all methods, the interview guide approach was the most appropriate for this study in identifying behaviours, practices, and experiences of participants in seeking malaria treatment. This format ensured that information that will help answer the research questions are collected by providing a more focused guide that allows for follow ups and probes when necessary. The interview questions were constructed in an open-ended format. Open-ended questions are questions designed to fully explore detailed information from interviewees on a particular issue without putting restrictions to their responses (Creswell & Clark, 2007).

As stated in the introduction of this chapter, the rationale behind using mixed research design in this study was to identify antimalarial drug use behaviours promoting the development and spread of drug resistance, and the influence of socioeconomic measures in the adoption of these behaviours. As there was no existing detailed study that has looked at the interaction of these variables both in the Nigerian population and in similar populations, there was a need to start from scratch in exploring people's experiences and behaviours in treating malaria and how these are affected by their socioeconomic status. Hence, this study started up with a systematic review to mop up all the scarcely reported relationships. The systematic review was important in giving a holistic picture of what is already known. The results of the systematic review (Anyanwu et al., 2016) were subsequently used in designing the interview guide.

In structuring the interview guide and the issues/questions to be covered in the interview, the choice of words and how the questions will be constructed were considered to ensure they do not come out as ambiguous, assumptive or judgmental. The categories of issues outlined in the interview guide include knowledge of malaria, decisions in seeking malaria treatment, practices, and behaviour in using antimalarial drugs and malaria treatment in children. The questions on participants' sociodemographic background were asked using a short questionnaire administered at the end of each interview. Before the conduct of the main

interviews, the interview guide was piloted with participants with similar characteristics and who met the inclusion criteria as the main participants.

6.5 Pilot interview

According to Kvale (2007), pilot tests prior to the main interviews help to refine the interview design by identifying flaws, limitations or weaknesses that can, otherwise, affect the outcome of the interviews. It helps to ensure the interview questions are unambiguous and that the design and style of questioning are very clear to the interviewees (Plowright, 2011). In addition to this, the conduct of the pilot interviews was important in ensuring the structure and wordings of the interview guide as well as the sequence of the questions/issues to be explored were well organized to achieve a better conversational flow with the interviewees in this study.

The analysis of the pilot interviews helped in further restructuring the guide in relation to the meaning of some terms as used in the population context. Examples: the words used to refer to malaria locally, the terms used for the locally-made insecticides, local names for the herbs used for malaria treatment, among others.

In the conduct of the interview sessions (both the pilots and main interviews), the eight principles to the preparation of interview sessions as outlined by McNamara (1999 pp. 2) were used. These principles severed as a checklist to ensure the interview session is well organized and that all participants get the same basic line of inquiry. These principles include

1. Choose a setting with little distraction
2. Explain the purpose of the interview
3. Address terms of confidentiality
4. Explain the format of the interview
5. Indicate how long the interview usually takes
6. Tell them how to get in touch with you later if they want to
7. Ask them if they have any questions before you both get started with the interview; and
8. Don't count on your memory to recall their answers.

Prior to the conduct of each interview, the researcher met with potential participants for a chat about the research and to give them the participant information sheet as well as address any concerns. Also, the interview date and venue were discussed in these meetings and agreed on.

This initial meeting before the interviews was an effective form of icebreaker as it ensured that on the day of the main interview, the interviewer and interviewee were not total strangers. This icebreaker helped to increase acceptability of the interviewer by the interviewees which is evident in the in-depth accounts from the participants. Also, this strategy of initial meeting was important in making sure the participants had enough time to go through the information sheet and process the information about the study before consenting to participate.

The participant information sheet contained details of the study which include: the purpose of the study; what they need to do to take part; whether they have to take part; what will happen to them if they take part (possible advantages and disadvantages); what to do if something goes wrong during the interview; confidentiality and anonymity of their participation; how the results of the study will be used; who is organizing and funding the study; who has reviewed the study; and contact for further information.

In deciding on where to conduct the interview, each of the participants was asked to choose a venue for the interview in order to ensure a comfortable environment where they will not feel restricted, distracted or threatened to share their information and experiences is provided.

With the consent of all participants individually, all the interview sessions were audio recorded.

Confidentiality was maintained by assigning identification codes to each participant. The identification code was made up of three parts: (1) three words abbreviation of the name of the town/community (2) one word abbreviation indicating type of settlement with U for Urban and R for rural, and (3) a serial number starting with the first interviewer for each site as number one. An example of a participant code is *ABJ/R/01*. This code was useful in the data processing and analysis for linking individual interview transcripts to the respective interview observation note and a sociodemographic questionnaire.

The position of the researcher was also recognized in this study. The researcher having lived in Nigeria for more than two decades have experienced malaria infection, as such had a good understanding of the system and context in which malaria treatment is sought. Nevertheless, in the conduct of the interviews, the researcher identified his position and ensured interview questions were not leading or presumptive to enable the study capture the unique experiences of the participants.

6.6 Interview materials

Materials used in conducting the interviews include:

Sony digital Audio-recorder

Batteries for audio-recorder

Notepad

Pen

Participant information sheet

Participant consent form

Interview guide

Ethical Considerations

The qualitative study was approved by the University of Sunderland Research Ethics Committee (see approval letter in appendix).

6.7 Data Processing and Analysis

6.7.1 Data Processing

The data collected from the interview sessions, which include the audio record of each interview, interview notes and socio-demography questionnaire completed by participants, were processed to prepare them for analysis.

The data processing stage involves refining the collected data to a form that makes its analysis and subsequent interpretation easier. For this study, the data processing involved the

- Saving of the electronic data (interview records) in a password protected storage device
- Transcription of the audio records to written form
- Translation of the transcripts of interviews on local language to English language
- Entering the sociodemographic questionnaire into Microsoft Excel
- Linking each interview transcript with its respective interview observation note and sociodemographic data using the assigned identification code

The interviews were recorded using a digital audio recorder. Digital audio record is a preferred choice to the tape recorder as they offer sophisticated functions like background noise cut and easy transfer and maintenance of the audio files as soft copies. At the end of each interview, the audio record was saved on two password-protected storage devices –a flash drive and drop box. The idea of keeping two copies of each interview record in separate devices is to ensure the interview data are not completely lost if one copy got lost or corrupted. To maintain the confidentiality assured to the participants, access to the devices was strictly on a need to know basis; hence only the researcher and the Director of the study had access to the devices.

Furthermore, all the interview records were transcribed verbatim from audio to a written form by the researcher on the same day they were conducted. The transcriptions were done manually by the researcher. Where necessary, the interview transcripts were translated from local language to English. The transcripts were then analyzed using the thematic analysis method for qualitative research.

6.7.2 Data analysis

As with other types of research designs, there are different methods of analyzing data in qualitative research. The choice of data analysis method is usually determined by the theoretical underpinning guiding the study and the method that will best answer the research question. As this study adopted a pragmatic stance, the latter was the guiding principle in deciding how to analyze the interview data.

With regards to the method of data analysis, there are two broad categories of data analysis methods. The first category comprises of methods that are underpinned by a theoretical or epistemological framework. Qualitative analysis methods such as phenomenology, conversational analysis, discourse analysis, grounded theory among others come under this category (Glaser, 1992; Smith, 2007; Wooffitt, 1998). The second category, however, includes qualitative analysis methods that are not necessarily tied to a theoretical or epistemological framework. With its theoretical freedom, methods of analysis in this category, for example, thematic analysis can be applied to different theoretical and epistemological frameworks. The thematic analysis method, as outlined by Braun and Clarke (2006) was used in this study in analyzing the interview data.

Thematic analysis is a method of analyzing qualitative data through identification, organization, analyzing and interpreting trends or themes in a data set (Braun & Clarke, 2006).

The identification stage in thematic analysis goes beyond counting explicit words or quantifying codes or themes. It involves both implicit and explicit searching of the entire data set to identify and describe trends or patterns (Guest et al., 2011).

Thematic analysis has been described as the "foundational" method of analyzing qualitative data (Holloway & Todres, 2003). Guest et al. (2011) described it as the most useful method in reflecting the richness and complexities of meanings in a data set. As a result of its wide use across other methods of qualitative analysis, some qualitative researchers do not see thematic analysis as a method of qualitative data analysis in its own right; but rather as a set of tools to be used as basis for qualitative analysis across different methods (Boyatzis, 1998; Ryan & Bernard, 2011).

In other instances, thematic analysis method has been described or referred to as grounded theory (Kellchear, 1993). Some have suggested that thematic analysis is just steps within grounded theory method of qualitative data analysis (Douglas, 2002). Nevertheless, some qualitative research experts, like Braun & Clarke (2006), have maintained that thematic analysis is a method in its right and hence should be accorded due attention as a method of qualitative data analysis rather than a set of tools.

The main tools used in the process of thematic analysis are coding, categorization, and development of themes. In summarizing the thematic analysis process, Braun and Clarke (2006) described it as a detailed search across a data set for repeated trends and themes. It is worth mentioning that these tools in the thematic analysis are also used in other methods of analysis like grounded theory.

Certainly, thematic analysis method and grounded theory are methodologically related and adopt similar tools in data analysis. However, both differ in many regards -like the end goal of the analysis, and how codes, categories, and themes are managed. For grounded theory, the overall goal of the analysis is to develop a cogent theory, grounded in the data, which explains the phenomena under study (McLeod, 2011). In other words, it is a theory-generation driven analysis. Thematic analysis, however, does not confer to the theoretical commitment of grounded theory method (Braun & Clarke, (2006)

In using a thematic analysis method, there is need for researchers to establish the type of analysis they are conducting. This is in relation to whether they are conducting a detailed, in-depth description of one particular theme from the data set, or a rich thematic description of

the entire data set (Braun & Clarke, 2006). Conducting a rich thematic description of the entire data set involves identifying themes through coding and analysis of the entire dataset rather than an in-depth description of individual data units (Braun & Clarke, 2006). This analysis involves identifying codes and further analysis to develop themes that reflect the content of the whole data set. This method is ideal for studies aimed at exploring a phenomenon that is not well studied or has limited evidence (Braun & Clarke, 2006). As such, description of the entire data set was used in this study to analyze participants' behaviours in seeking malaria treatment.

In conducting the thematic analysis in this study, the themes were developed in an exploratory inductive manner rather than a deductive one. Inductive and deductive approaches are terms also used to refer to how the themes in a thematic analysis were generated (Boyatzis, 1998; Frith & Gleeson, 2004). In an inductive approach, the generation of the theme is independent of the researcher's theoretical epistemological stance (Braun & Clarke, 2006). The codes are said to emerge from the data rather than been pre-determined; hence the codes in inductive approaches are usually strongly related to the data set (Patton, 2002). Patton (2015) described this approach as useful in generating new ideas, concepts and/or theories from the content of the data set.

On the contrary, the codes in the deductive approach are usually predetermined and influenced by the researcher's theoretical and epistemological stance (Braun & Clarke, 2006). They are used to determine the extent to which the data set and its content support an already existing theory (Patton, 2015). This type of approach will fail to identify new phenomenon or concepts that may be outside the parameters of the predetermined codes or theories.

Furthermore, the analyses of all the interview data were done manually. The decision to conduct a manual analysis as against the use of computer-assisted qualitative data analysis software is that it offers a higher level of engagement with the data as the researcher, in using manual analysis, becomes very familiar with the data and its contents.

6.7.2.1 Coding

Data collected using qualitative methods like interviewing are usually large and complex, therefore not easily manageable at the transcript level. The first step in analyzing qualitative data is to make the data manageable by reducing the volume while retaining the rich content of the data. This process is referred to in qualitative studies as coding. Coding involves the classification of the dataset to produce a creative framework for further organization,

description, and interpretation of the data (Patton, 2015). This creative framework helps to link the entire dataset by building a connection from each unit of data to the ideas they represent and back to other units of data in the set.

Coding is usually the initial step in the analysis of qualitative data (Braun & Clarke, 2006). Although coding in different methods of analysis involves the same activity of labeling relevant pieces and expressions of the transcript, the type or concept of coding can be different for different analysis methods. There are different types or concepts of coding; these include descriptive coding, process coding, in-vivo coding (using participants' own words), pattern coding and multiple coding. Coding, in this study, was conducted at a descriptive level with the aim of summarizing the main concept of each statement from the interview thereby retaining the information from the statement.

The first step in coding (irrespective of what type of coding one is doing) is the researcher reading through the transcript to familiarize themselves with the data (Braun & Clarke, 2006). This was done in this study through a comprehensive read of each data unit (individual interview transcripts and notes) that constitute the set. This was done without making notes or marking on the transcript so as to give the researcher a holistic picture of the data.

The second step was to read through the data set again, but this time, notes and comments were made on the transcripts. This stage involved constructing topics or labels for different parts of the data. The parts labeled can range from few words to sentences. Each data unit (one interview transcript) was read through more than once to ensure that the entire content of the data, that is all keywords, trends or ideas contained in the data set, are represented (Guest et al., 2011). The codes that emerged from the coding process facilitated the development of categories.

6.7.2.2 Categorization

According to Saldaña (2015), categorization involves the clustering together of codes according to their similarities and regularities. This is done by reviewing codes for patterns and linking related codes together to form categories. The process of categorization basically involves sorting the codes to determine those that fit together. By so doing, the researcher looks for relationships between codes in relation to reference (identifying codes that are associated with a particular idea), sequence (identifying codes that inform other codes) and essence (identifying codes that share particular underlying meaning) (Saldaña, 2015).

In developing categories in this study, a comprehensive scan through the coded manuscripts for recurring regularities in the data set was done. According to Patton (2015), two underlying criteria to consider in clustering codes to form categories are the internal homogeneity and external heterogeneity. Internal homogeneity is about considering how similar the codes that will build a category are to each other; while external heterogeneity is concerned with the extent to which each category is distinct to others. Nevertheless, the set of all categories when considered together should produce a whole picture that represents the phenomena under study.

Although the categorization in this study was done by the researcher, the supervisors were actively involved in discussions on what code fits into a category. Suggestions were made by the supervisors and taken on board in the final draft of the categories.

6.7.2.3 Development of themes

The final step in the thematic analysis was on developing key themes from the categories. Mogashoa described a theme as "a cluster of linked categories conveying similar meanings and usually emerges through the inductive analytic process which characterizes the qualitative paradigm" (2014, p. 109). The themes were developed around reported practices and behaviours in seeking malaria treatment that are connected. To achieve this, the categories were considered for relevance and how they connect and interact with one another. Categories that were similar or informed others were combined to build up a key theme.

The interpretation of the data from this study was done at different levels: both within and between individual interviews (data units). These include comparison of frequencies of categories, consideration of distribution of codes across participants of different socioeconomic positions among others. To enhance the data synthesis and interpretation, emerging themes were frequently discussed among the research team.

The results of the qualitative interviews were converted to variables and used in developing a questionnaire which was used as the measurement instrument for the quantitative phase of this study.

6.8 Issues of reliability and validity

Lincoln and Guba (1985) argued that approaches to the validity and reliability of quantitative research are not appropriate for qualitative studies and they suggested credibility, transferability, dependability, and confirmability as more appropriate criteria.

Credibility deals with ensuring that the findings of a qualitative study are credible and reflect the situation under investigation. Merriam and Tisdell (2015) posed the question 'How congruent are the findings with reality?' This was addressed using the respondent's own words to back up claims and by ensuring the outline of the categories was reflective of the interview transcripts. Shenton (2004) also suggests that a wider range of respondents can add to the credibility of the study. Respondents were chosen from a range of socio-economic groups and rural and urban settings. A range of views was, therefore, represented and differences and similarities among the respondents were highlighted in the results section. Another approach employed was the validation of the data from the participants themselves (by summarizing their accounts during the interview and asking them for a validation of this) and of other participants (through constant comparative method to validate the experiences of other participants). Furthermore, the researcher's familiarity with the study setting was very important in establishing a good communication with the participants, and understanding the social context of the study population –language, culture, social structure, and healthcare system.

Furthermore, dependability refers to the internal consistency. It is recognized that in qualitative research, the theoretical position of the researcher can affect the direction of the analysis. This factor is recognized, but this study was an exploration of relatively concrete behaviour, and the dependability largely was achieved through the quality of the data analysis. Thematic analysis as outlined by Braun and Clarke (2006) was used as the method of analysis, and a clear process was followed, open to scrutiny. The process of analysis was carried out by the researcher and then reviewed by the three supervisors. The researcher and supervisors were involved in the discussions and decisions on the analysis of the data -for example, in deciding which categories constitute a key theme from the analysis.

Indeed, confirmability, which refers to the objectivity of the study, can be complex in qualitative research as the researcher will bring his or her particular theoretical position. The key issue here is whether the data analysis was logical and consistent and if the researcher was transparent in all processes; this was a guiding principle in the study design.

Finally, transferability equates to external validity, and again in qualitative research, this can be difficult as samples are small and often not representative. Generalization is about whether the findings can be transferred to another setting or is the presentation of the data clear enough to allow the reader to do this? The sample was small and examined inhabitants of only two

Nigerian areas. However, it did identify strategies and behaviours which allow comparison, and in this sense, transferability was achieved.

6.9 Socio-demographic description of participants

The socio-demographic characteristics of the participants are shown in Table 6.1. Overall, 53.3% of the participants were females. The mean age of the participants was 40 years. The most common occupation of the participants was farming. Almost half (46.7%) of the participants reported they earn below the current Nigerian minimum wage of eighteen thousand Naira (₦18,000) (about £64) per month. Seventy three percent (73%) of the participants had at least some secondary education. Urban dweller constituted 53.3% of the participants. For the meaning of some key terms used in this study see table 6.2.

Table 6.1: Socio-demographic description of participants

Characteristics	**Number (%)**
Total No. of participants: Household heads [13] Drug vendor [1] Pharmacy attendant [1]	15 (100)
Sex:	
Males	7 (46.7)
Females	8 (53.3)
Age:	
Mean age	40
Mode age	31
Relationship status:	
Single	3 (20)
Married	6 (40)
Widowed	6 (40)
Educational level:	
No formal education	1 (6.7)
Some primary school education	3 (20)
Some secondary school education	2 (13.3)
O'level/SSCE holder	2 (13.3)

Tertiary Education/degree	4 (26.7)
Post graduate degree	3 (20)
Income level:	
Below ₦18,000 (£63)	7 (46.7)
₦18,000 to ₦50,000 (£64 to £177)	1 (6.7)
₦50,001 to ₦100,000 (£178 to £355)	2 (13.3)
₦100,001 to ₦300,000 (£356 to £1065)	3 (20)
Above ₦300,000 (£1065)	2 (13.3)
Type of settlement:	
Urban:	7 (46.7)
Owerri, Imo state [2]	
Abuja Municipal City [5]	
Rural:	8 (53.3)
Ihitte-Uboma, Imo state [4]	
Zuba community in Abuja [4]	

Table 6.2: Key terms used and their meaning in the context of this study

Terms	Meanings
Pharmacy	Used to refer to the registered pharmacy shops that are usually found in the cities. These shops are usually owned or run by a trained pharmacist. Some pharmacies in Nigeria are however run by pharmacy attendants or nurses.
Chemist/drug vendors	Used to refer to drug vendors or patent medicine vendors in the study setting. These are usually traders with little or no pharmaceutical trainings who either hawk or sell drugs in a small shop. They are mostly common in the rural and suburban areas in Nigeria. The terms chemist and drug vendors were used interchangeably in this study.

6.10 Thematic Analysis

The social structures existing within societies and their socioeconomic indicators are usually based on characteristics that are valued in the society –educational level, income level, type of settlement, occupation, employment status, among others. As indicators of socio-structural position within the society, an individual's level of socioeconomic measures can determine the

likelihood of healthy or unhealthy exposures, behaviours and outcomes (Lynch, Kaplan, & Salonen, 1997).

Several key themes emerged from the analysis of the interview data. The themes were developed around the antimalarial drug use behaviours reported, and their associated socioeconomic factors. The socioeconomic factors identified in this study -income level, type of settlement, educational level and occupational/job type- are all related to one another with some (for example, educational and income levels) acting as determinants to the others. The significant malaria treatment behaviours influenced by socioeconomic factors in this study were 'mixing', presumptive treatment of malaria, source of treatment, non-adherence behaviours like sharing of drugs, stopping treatment to save drugs for future use, and the use of anti-malaria monotherapies. In interpreting the role of socioeconomic factors in these treatment behaviours, the Donabedian model was adapted and used in this study.

The Donabedian model (Donabedian, 2005), which was initially developed to serve as an evaluative framework for quality of healthcare, has been widely used in studying other aspects of healthcare (Ancker, Kern, Abramson, & Kaushal, 2012). The model assumes three main components in studying health outcomes: Structure, Process and Outcomes (Ammenwerth, Ehlers, Hirsch, & Gratl, 2007; Ancker et al., 2012; E. Kelley & Hurst, 2006). These three domains work in unidirectional way with each domain influencing the next. This was an appropriate model in organizing the categories established through the analysis of the interviews conducted in this study.

In applying the Donabedian model to this study (see Figure 6.1 of an adapted Donabedian model showing study findings), the 'structure' represents the factors that affect the context in which malarial treatment is sought. These factors control how patients and providers act in seeking and providing malaria treatment respectively. The structure include background characteristics of the patient like socioeconomic factors (measures of educational level, level of income, type of settlement and occupational type) as well as socio-cultural factors (like beliefs, norms, and constructions). The structures in this study were identified from the participants' interview accounts as well as the socio-demographic questionnaires completed by all the participants. These structural factors influence the 'process'.

The 'process' represents practices and behaviours of the participants in treating malaria, which are products of the interaction with the structures. This includes reported behaviours like drug

'mixing' for malaria treatment, presumptive treatment, non-adherence to treatment guideline, use of monotherapies, among others. These behaviours were influenced by the structural factors which have the ability to limit people's choices, how they seek malaria treatment and how they use antimalarial drugs.

Importantly, the process subsequently determines the 'outcome' which can be in the form of treatment failure, drug resistance, effective treatment or death. Most of the behaviours that constitute the 'process' have the tendency to encourage the development and/or spread of antimalarial drug resistance.

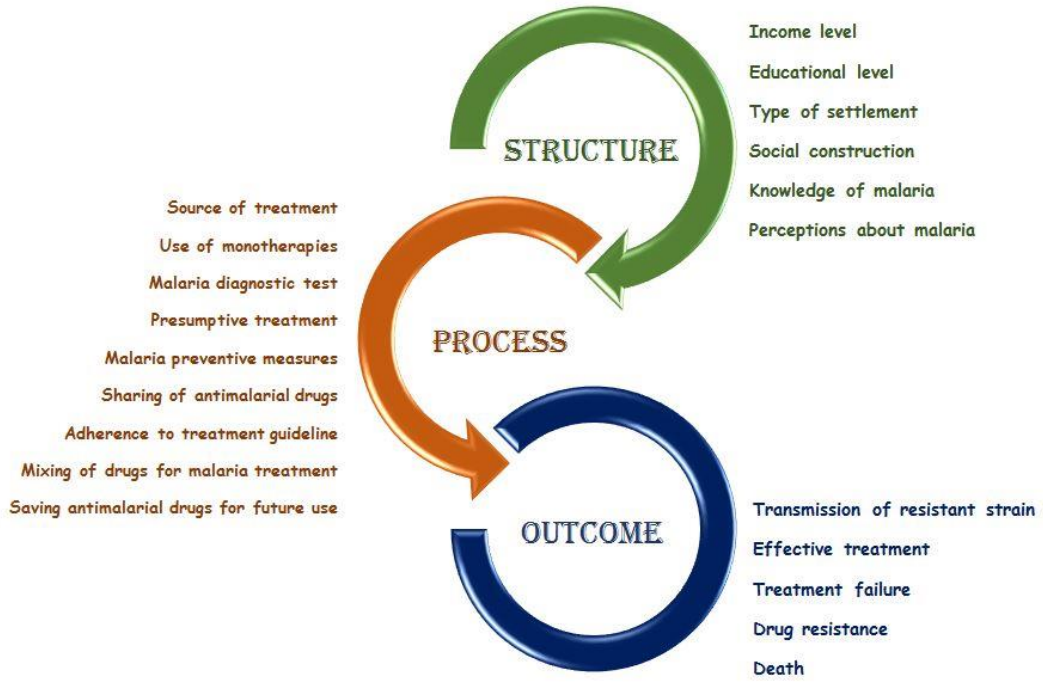

Figure 6.1: Presentation of interview results using the Donabedian Model

6.10.1 Structure

6.10.1.1 Socioeconomic factors

As earlier stated, socioeconomic factors like income level, type of settlement and educational levels constitute structures that can enhance or endanger a population's health. These factors were reported to affect the way malaria treatment are sought and how antimalarial drugs are

used. For instance, educational level affects one's ability to read and understand written instructions on how to administer antimalarial drugs.

> *Yes. But even if they write it, did I go to school? What I know is that way they have shown me to take it, that's the way I follow* ***(Female, age not known, rural area).***

> *Let me say the poor condition that some of us we are living in because we don't have access to eh this eh hospital –the so-called hospitals they are talking about because we don't have money* ***(Male, 32 years old, rural area).***

6.10.1.2 Knowledge and perception on malaria

A key structural issue was the level of knowledge of malaria, which influences preventive and treatment-seeking behaviours. Malaria was described by the participants as a very common disease in Africa. The high burden of malaria in Africa was attributed to physical environment as well as some supernatural powers that made the African climate tropical and very conducive for mosquitoes to breed.

> *Malaria, the little I know is that it is a very very -eh its an endemic disease that Nigeria and Africa, in general, is suffering from, you know. And it is the number one killer among ehm people here in Nigeria* ***(Female, 44 years, Urban area).***

Some of the perceptions about the cause of malaria demonstrated by the participants (like the perception that consumption of fatty diets as well as spiritual attacks as a cause of malaria) were products of social construction from the different communities. All the participants identified the link between mosquitoes and malaria and they also were aware of some indirect causal factors, such as dirty environment, living in dilapidated housing condition, stagnant waters around the house, among others. However, these indirect predisposing factors were perceived as direct causes of malaria by many of the participants.

> *What I know about malaria is that some people say taking too much of oil -oil is one of the causes of malaria, palm oil. Another thing I know that causes it is like, for example, some people might be asked not to eat something like 'egusi', 'egusi' causes malaria too* ***(Female, 49 years old, rural area).***

As malaria is a common disease which all the participants had experienced, knowledge of malaria symptoms was satisfactory among the participants. There were, however, some cultural

and superstitious constructs and explanations for malaria infection; three participants said they believed some evil spiritual powers can cause malaria. This perception was reported in relation to the cause of malaria as well as the manifestation of the disease.

> *Some people say it's a spiritual attack. You understand. Because it was very mysterious -my mouth was very bitter, but the symptoms were malaria symptoms. I don't know if anything passed through the malaria* ***(Female, 33 years old, urban area).***

At one end of the continuum many of the participants perceive malaria infection as life threatening; however, others saw it as a very common disease which is easy to treat hence not a life threatening or serious infection.

> *Well, maybe because I am a Nigerian, I don't see it as a life-threatening disease. But I know that eh, when you travel abroad, they don't want to even hear that you have malaria. Malaria to us or to me personally, is like having headache. Am serious about that* ***(Female, 40 years old, urban area).***

Another important perception reported in relation to knowledge about malaria is about the treatability of malaria. Some rural participants were of the view that malaria cannot be cured. They described antimalarial drugs as a palliative rather than a curative treatment.

> *You know malaria never goes. Whoever says it goes is a thief [liar]. What am telling you is the truth. Whoever says malaria can go finally is a thief; he does not know what he is doing. He is a liar* ***(Female, age unknown, rural area).***

6.10.2 Process

6.10.2.1 Malaria preventive behaviours

Several malaria preventive measures were reported by the participants in the study. They include keeping the environment clean, the use of insecticide-treated bed nets, putting nets in the doors and windows, the use of herbal remedies to prevent malaria, the use of insecticides - both the locally made ones and the factory-manufactured ones. Some of these measures were used in combination while some were reportedly used alone.

There was a disparity in the type of insecticide used by participants from different levels of the socioeconomic measures identified in this study. The use of factor-manufactured insecticides was reported more by those residing in the urban areas. In addition, all the participants who

reportedly used the locally made insecticides were from the rural areas, and their monthly income was below the minimum wage. Some terms like "Otapiapia" and 'Tusatusa" were used to refer to the locally made insecticides. Of all rural participants, only one reported that she does not use the locally made insecticides as they pose high health risks.

> *Ehm malaria- to me like I keep saying. I am not a fan of malaria, so I don't even allow malaria to get into me. What I do basically is I make sure, every week I make sure I fumigate my house with ehh, there is one ehh insecticide they call it 'Sniper' [factory manufactured insecticide]* ***(Female, 44 years, Urban area).***

> *Mosq -to kills mosquitoes. Like the time I have not received the net. I use one 'otapiapia' they call it 'Silver'. So I will buy that one. When I spray it at the four corners of the room. So I may do like three days, and there will be no mosquitoes* ***(Female, years, rural area).***

Among all preventive measures, keeping the environment clean and the use of insecticide-treated nets (ITNs) were the most commonly reported preventive measures in this study. It was adopted by participants of different level of the socioeconomic measures in this study. However, some participants also reported either not having the ITNs or having it but not using it. The most reported reason for not using the ITNs was excessive sweating when sleeping under ITNs. This was reported widely across participants of different levels of the socioeconomic measures. Other reasons given for not using the ITNs include discomfort as a result of the insecticide embedded in the nets, the net not fitting the bed, no pole to fix/tie the net amongst others.

> *Aah, the heat makes us not to use it often. It gets so hot while using it. That's why we rarely use it because when you sleep inside it the heat, especially in this area. Anytime you go to bed it gets hot even in the harmattan [dry season]. The heat doesn't let us use it well* ***(Male, 55 years, rural area).***

6.10.2.2 Malaria treatment-seeking behaviours

When symptoms were experienced, socioeconomic factors, like the type of settlement, income level, and type of job, tended to determine the treatment behaviours and therefore informed and determined the experience of the illness. This was in terms of the first point of contact for treatment, choice of antimalarial drugs, and how antimalarial drugs are used. Conversely,

behaviours, like presumptive treatment, were reported across all socioeconomic groups in this study.

On experiencing malaria-like symptoms, there are several facilities one can seek treatment in Nigeria: hospitals/clinics, health centres, chemists/drug vendors, pharmacies and herbal healers. These facilities usually offer different treatment options ranging from a laboratory diagnostic test prior to treatment, to presumptive treatment based on presenting symptoms. Those living in urban areas mostly use the pharmacy or hospital as the first point of contact whereas in the rural areas pharmacies and hospitals were less common as "chemists" were easier to access hence more used.

With a large proportion (53%) of the Nigerian population living in rural areas, the chemists/drug vendors serve as the first point of contact for malaria treatment for many. The pharmacies provide more professional and expensive services whereas the drug vendors often lack the knowledge and skill which was reflected in both advice and cost of services in these facilities.

Cost was an important factor in malaria treatment seeking for those of low socioeconomic level. For instance, decisions on which health facility to seek malaria treatment from was influenced by the cost of treatment. The chemist/drug vendor was the most reported first point of seeking malaria treatment among participants whose monthly income was below the ₦18,000 (£64) minimum wage. Even when other sources were closely located, the chemists/drug vendors remained the most commonly used source for malaria treatment by those of low socioeconomic status. The seeming trust in the chemist/drug vendors by the rural dwellers was not based on their ability to offer more effective treatment than the hospitals, health center or pharmacies. Rather, it was because, unlike the other sources, the chemist/drug vendors are more available and accessible through the provision of credit payment options, cheaper alternatives, convenient locations and out-of-hours services. Most importantly, the chemists were usually owned and/or managed by a member of the community.

> *Eh hospital is not far from me, from where I leave… why I don't go there is that those two chemists, they 'help' me. eh. That's why I go to theirs. So if I don't have money, they help me. If it's the government hospital, everybody comes from different places to work. They will say pay us before we give you the drugs* ***(Female, 31 years old, rural area).***

'If I don't have money, she [the chemist] will just look for one that is -she will give me the one that I will -that will work for me. She will say I should go and take it' ***(Female, 31 years old, rural area).***

The participants were fully aware of the difference in standard between the pharmacies and the chemists, but both availability and low cost determined the use of the chemists

The way we look at chemist in Nigeria is that chemist is meant for, you know, people that are in the villages, you know that cannot afford (laughs) because in that chemist you see all sort of, manner of drugs. You see fake drugs there ***(Female, 44 years old, urban area).***

Furthermore, when symptoms were severe or when seeking malaria treatment for children, most of the participants would use hospital or pharmacies as the first point of treatment. Some of the reasons given for use of formal facility for malaria treatment for a child were that, firstly, malaria in children was considered a serious issue. Secondly, the inability of a child to communicate their symptoms precisely, which is important in seeking treatment in informal health facilities like the chemist.

So that kind of case, if someone does not notice it on time, you just keep the child and say it's a minor thing, before you know the child will 'go'[die] ***(Female, 31 years old, rural area).***

Most of the participants reported that when malaria is suspected, their first source of treatment is usually the informal health facilities (that is, pharmacy and chemists). The formal health facilities were mostly used when treatment with drugs from informal health facilities, which is usually presumptive, fails.

If that woman gives me and it doesn't work, I will rush to one eh hospital that is there. That one is a doctor ***(Female, 31 years old, rural area).***

6.10.2.3 Presumptive diagnosis and treatment of malaria

Presumptive treatment of malaria, which involves treating suspected malaria cases based on presenting symptoms rather than a confirmatory diagnostic test (World Health Organization, 2000) was the most common approach to malaria treatment and was found in all socioeconomic groups. Those who mostly use the hospital for treatment, who were also the highest earners with the highest educational levels, reported the use of laboratory testing to confirm diagnosis

more than those who use the chemist/drug vendors or pharmacies. The pharmacies tended to implement treatment on the basis of presumptive diagnosis, while the chemist/drug vendors almost entirely implemented treatment on the basis of presumptive diagnosis.

An example of this is with the three participants who reported they had never gone for a malaria diagnostic test before (neither microscopy nor Rapid Diagnostic Testing) as they all used the chemist for most malaria treatments. The most common reasons given by these participants for this practice were their inability to afford diagnostic cost, lack of access to hospitals and cultural factors. These three participants were rural dwellers and earned below the minimum wage of ₦18,000 (£64) per month.

> *…I don't know whether some of the sicknesses I experience sometimes are malaria. Eh, I may –I might have had it, but I may not know it was malaria –I think I have told you that I have never gone for any malaria lab test to test me, to justify what is really my problem* ***(Male, 32 years old, rural area).***

Another reported behaviour with regards to presumptive treatment and the use of malaria diagnostic test prior to treatment was the practice of using previous results of malaria diagnostic test and the prescription received to treat subsequent episodes with similar symptoms. This was reported by two participants from the rural areas.

> *Sometimes, I go to the health centre. There was a time I went there and they ran a test and said its malaria and typhoid. They treated and gave me some drugs and also directed me to a nearby pharmacy to buy more drugs and add to the ones they gave me and take them all. After the treatment, when next I have malaria, I go to the pharmacy and buy the same drugs. It's not all the times that I have the money to run a test* ***(Male, 55 years old, rural area).***

Only one participant said she always used a diagnostic test to confirm she has malaria prior to her use of antimalarial drugs (household income level of above ₦300,000). The other participants who also use laboratory diagnostic test prior to malaria treatment were not consistent as they also reported they practiced presumptive treatment. These were mostly participants who earned more than ₦100,000 per month. For the high-income earners in this study who practice presumptive treatment, affordability was not reported as a reason for this behaviour. The main reasons for this practice include: confident they can diagnose malaria and the perception of presumptive treatment as a time-saving route to malaria treatment.

Similarly, affordability was not always the key issue in decisions on the type of antimalarial drug to get among different socioeconomic groups. The pharmacy attendant reported that most of the customers at the urban area are not really concerned about price, but on the effectiveness of the drug, hence ACTs were reported as the most sold class of antimalarial drugs by the pharmacy attendant. This was, however, different in the rural areas and among the low socio-economic groups; as would be expected, affordability was an important issue for these groups. The cost of ACTs was reported as out of reach by many rural and urban dwellers who earned below the national minimum wage. As a result, monotherapies and non-ACTs like SP (which are cheaper but less effective in parasite clearance) were reportedly the most used antimalarial drugs by low-income earners and rural dwellers.

> *Like if severe, most of the people do not have enough money to treat themselves. They may tell you they need drugs of two hundred naira or one hundred and fifty naira. At times I have to use Laridox (Sulfadoxine-Pyrimethamine)* ***(Male Drug Vendor, rural area).***

6.10.2.4 Adherence to treatment guidelines

As an important factor in the development of drug resistance, adherence (in terms of completion of treatment course and administration of the proper dose at the correct time, in accordance with the World Health Organization Guidelines for the Treatment of Malaria (World Health Organization, 2015a) was considered in this study. Many participants reported non-adherence at least once in the last six months. Reports of poor adherence were more common among participants of lower level of education and income level of below ₦50,000 (£177). However, some low-income participants, who reported a moderate level of adherence, saw antimalarial drugs as expensive, so when they do buy them, they tend to complete the treatment as they do not want to waste their (expensive) treatment, and so want value for their money.

> *There are times they will give me and I will take it and take it and take it, if the thing (malaria) clears, I will throw away the remaining. Even if its injection, I will not go to complete it. Because the thing [malaria] has cleared* ***(Male, 55 years old, rural area).***

> *Yes. If they give me drugs, I finish them. I don't leave them because I used my money to buy them. Any drug they give me in the hospital I must take all of them. I don't*

miss it. I don't miss it as -am I not the one that will bear the pains? How can I miss it? If I don't take it I will feel the sign in my body of course ***(Female, 35 years old, rural area).***

While ideas of cost effectiveness encouraged adherence in some low-income earners, less commonly (mentioned only by two participants), it contributed to some non-adherence practices like stopping the treatment to save the drug for future use. The practice of stopping to save drugs for future use was not common as most of the participants were wary of this practice as it was seen as risky and there was a fear of taking expired drugs.

When I buy and give him and he takes and gets better and says he will not take any more, I throw the rest away. Because when you keep it, do you know the day the sickness will come? By the time the sickness come, and u give it to him, it might bring another sickness for him because you don't know if the drug has expired ***(Female, 31 years old, rural area).***

Sharing of antimalarial course among two or more people was also reported. One of the three participants who reported this behaviour was of high income (above ₦300,000 (£1065) per month) and high educational level (postgraduate education). The difference between this participant's behaviour and that of the other two (of income level below ₦18,000 (£64) and some primary school education) is that for the former, it was a one-off act because she could not buy a new course for a member of her household who got ill in the middle of the night; while for the later, it was reported as a recurrent behaviour. In most cases of sharing of antimalarial drugs with others, all parties involved end up not getting a complete treatment course.

6.10.2.5 Use of monotherapies

Generally, the knowledge of the names of antimalarial drugs used was poor among the participants. Nevertheless, most of those who could identify the names of the antimalarial drugs they use reported that Artesunate was the most used antimalarial drug, (five from the rural area reported using this drug compared to two from urban sites). Additionally, the drug vendor and pharmacy shop assistant that were interviewed also reported the sale of monotherapies (like Artesunate) and non-artemisinin-based combinations (like SP). The drug vendor in the rural area described a higher rate of monotherapy sale than the pharmacy attendant in the urban area. The major reason given for this by the drug vendor was the inability of some customers in the

rural areas to afford the price for the artemisinin-based combination therapies, which is the first line treatment for malaria in Nigeria.

6.10.2.6 Use of mixed drugs for malaria treatment

The concept and practice of 'mixing' were first mentioned in the initial interviews with participants from Zuba (rural area) in Abuja, and then subsequently in most of the interviews from other rural areas. To clearly understand the practice of mixing and how it is done, a drug vendor from one of the communities in the rural areas and a pharmacy attendant from an urban area were interviewed. They described mixing as the practice of combining different drugs to treat malaria. It is done by including, for example, a dose from each of the included drugs to form a mixed dose. There was no standard in terms of the number or types of drugs used in the mixture for malaria treatment.

> *Almost all the people here normally mix drugs. They may come and say I need a malaria drug of fifty naira or hundred naira. ehm I don't have much money to buy a complete one* ***(Male Drug Vendor, from rural area).***

Mixing was described as a very handy and flexible coping strategy by the low-income earners. Also, all the participants from the rural areas reported they mixed. The highest level of education attained by most of those who mixed was some primary education.

> *No I haven't taken those packaged as complete course. The ones they mix, that's the ones they buy for me. That's the one our hand can get to. We only buy the ones we can afford* ***(Female, age not known, rural area).***
>
> *The problem that will make me not to get the treatment that I want is that 'my hand no go reach am' [cannot afford it]. Because when you have money, you get the better treatment* ***(Female, 31 years old, rural area).***
>
> *If you have up to five hundred naira or more, we can even mix Artesunate or Paracetamol or any analgesic, Panadol, ehm Amoxil or Septrin* ***(Male Drug Vendor, from a rural area).***

In describing their experience in using mixed drugs, some of the participants from the rural areas reported that sometimes they use mixed drugs as palliative measure in situations where they cannot afford the complete treatment, pending when they can. For one of them, the use of mixed drugs as an initial measure helped him to reduce the malaria symptoms for a while.,

Nevertheless, the antimalarial drugs bought from the pharmacies were mostly sold as a complete course in their original packets. As the mixed drugs are sold in units of 'one mixed dose', a very important factor in determining how many doses of the mixture a customer gets is the amount they can afford. The customers can decide to buy a day's dose or two days' dose and so on. While the complete course of antimalarial drugs like Artemether-Lumefantrine was reported to be about ₦800 (£2.84); ₦100 (£0.35p) will get you a day dose of mixed antimalarial drugs if you cannot afford ₦800. Another important issue on the 'mixing' practice is that these drugs are not sold in their original packets as they are either cut up into bits or removed from the blister pack while being dispensed. Hence the customers/patients have little or no information about the individual drugs that constitute the mixture nor their expiry dates.

> *The last time I used antimalarial drugs, I bought it from the chemist. They mixed the drugs for me. They mixed that of two days. How they mix is, it depends on how many days' dose you want them to mix for you* ***(Male, 55 years old, rural area)***

6.10.2.7 Use of herbal medicine for malaria treatment

The use of herbal medicine for malaria treatment was also reported in this study. Apart from one, all participants from the rural area reported that they have used herbal medicines for malaria treatment. The reasons given by the participant from the rural area who said she does not use the herbal medicine was the time it takes to prepare the medication. She reported that due to the nature of her job as a labourer and nanny in a nursery school, she does not have the time to source for the herbs and to prepare them. In addition, of the participants from the urban area, only one reported that she has used herbal medicine for malaria treatment in the past while growing up.

> *Up till now, yes. Malaria is in my body till now (laughs), up till now. Even as we are discussing now I have the herbs now that I am taking. Yes, I have herbs that I boiled that I am taking now for malaria* ***(Male, 55 years, rural area).***

Importantly, several factors influencing the wide use of herbal medicines were reported by the participants. One key factor reported was the fact that the herbal medicines are free of charge. The participants reported that they prepared the medicines themselves and that the leaves and herbs they use for it are readily available in the bush. Other factors that encouraged the use of herbal medicine include: the perceived higher effectiveness of herbal drugs in treating malaria than orthodox antimalarial drugs and the adverse effects from orthodox antimalarial drugs

We don't pay for them (the herbs) because majority of -in those days majority of us know about it. Majority know -even if its not your own father, your father will consult his friend, they will just give you. But the orthodox drugs for malaria, you must pay. It is so expensive ***(Female, 35 years, rural area).***

Despite the well reported use of herbal drugs, the preparation and ingredients (leaves and herbs) used in them differ. There is no particular recipe for the preparation and administration of the herbal antimalarial drugs. When asked about how they prepare the herbal medicines, some of the participants were initially reluctant to share this because it was like a trade secret and was handed down to them by their father or their ancestor.

The final analysis of the entire dataset revealed that most of the herbal medicines had a common ingredient, the *Dogwonyaro* leaves. Similarly, they all shared a basic preparation procedure of boiling the leaves and herbs in water at high temperature for about three hours. Administration of the drug (the extract from the boiled herbs) is usually by drinking the extract when it is cool, showering with the extract, or sitting by the pot while the extract is still boiling and covering yourself with a blanket to ensure the steam penetrates the skin.

To understand how much factors like affordability affects the decision to use herbal medicine for malaria treatment; we compared the response of the participants who use herbal medicines to the question on how they will seek malaria treatment if money or cost was not an issue. Most of them said if money was not an issue, they will use the hospital and orthodox antimalarial drugs, after a proper diagnostic test.

6.10.3 Outcome

As earlier stated there are four likely outcomes from the reported practices and behaviours indicated under the 'process'. These include:

- recovery which can be an indicator of an effective malaria treatment;
- treatment failure in the form of lack of response or worsening of the clinical manifestation of the infection after administering an antimalarial course;
- development of resistance to antimalarial drugs by the *Plasmodium parasite;* or
- death.

Some participants in this study discussed the outcomes of their malaria treatment. Through the interview data, outcomes like death could not be explored since most participants were

interviewed based on their malaria treatment seeking behaviour. Although drug resistance was not directly measured in this study, it is worth mentioning that malaria treatment failure can be an indicator of drug resistance as well as other factors like inappropriate treatment dosage or regimen (Huijben, 2010).

Participants' experiences of the outcomes were different depending on reported practices and behaviours like the type of antimalarial drug used, adherence to the recommendation on how to administer the drugs, amongst others. On their last malaria treatment experience, treatment failure was reported by three participants who used the mixed antimalarial drugs. Only one of the participants who used a formal health facility during her last malaria episode reported treatment failure.

> *… you just go to the chemist. Because the way I used to even treat my own when it happens like that, there's one chemist that is near our house, I will meet the woman and she will just mix drugs and give me. When she gives me I will just give them. They will take. Their body will be ok. When it is ok for like two days, before three days again, they will still complain again. Before you know it, you carry them to the hospital* ***(Female, 31 years old, rural area).***

> *The difficulty I encounter sometimes is that there are sometimes that malaria will hold me down, and if I go and tell the chemists that malaria is disturbing me, they will mix medicine for me and tell me how I will take them. Even after taking them, it will be like I didn't take any medicine* ***(Male, 55 years old, rural area).***

Nevertheless, at their last malaria episode, recovery or effective treatment was mostly reported in line with the practices of seeking treatment from a formal health facility and adhering to the recommended dose and completing the course. As the formal health facilities were reportedly used last time by mostly those from urban areas, many of those who reported effective treatment, without prior failure, were urban dwellers. However, one participant from rural area who used a hospital last time reported an outcome of effective treatment with no prior treatment failure.

> *So I rushed to meet that doctor… he said its malaria oo. Eh he started giving me treatment. I didn't even go to the farm for one week. I stayed home and took all the drugs when I took all the treatments I got myself* ***(Female, 31 years old, rural area).***

As there is no detailed antimalarial drug resistance surveillance program in Nigeria, some of the reported cases of treatment failure, which can be drug resistance cases, go unreported and not recorded or followed up. The lack of adequate care and surveillance for these potential cases of drug resistance can encourage further spread of resistant *Plasmodium* parasites in the population.

CHAPTER SEVEN

QUANTITATIVE SURVEY

7.1 Introduction

The methodology adopted in the survey as well as the results of the data analysis are presented in this chapter. The methodology details the process of participants recruitment, design of the survey instrument, data collection as well as types of analysis conducted. The descriptive statistics results are first presented, followed by the inferential statistics. The results of the statistical test for each hypothesis was presented as a subsection under this chapter.

7.2 Overview

Several designs exist within the quantitative method (Bowling, 2014a; Creswell, 2013). The choice of a survey design in this study as against other quantitative methods is underpinned by the need to investigate the behavioural trends of the population and its associated factors. With this aim, the use of other quantitative designs, like an experimental design which involves testing the impact of an intervention on an outcome (Creswell, 2013), will be inappropriate as this study had no interventions implemented.

A survey is a quantitative research design used in collecting information on a whole population by studying a sample of the population of interest, then draw inferences on the general population using the results from the samples (Bowling, 2014a; Creswell, 2013). A survey can be designed to measure certain behaviours, attitudes, phenomena or trends in a population. It is one of the most commonly used designs in quantitative research. The survey design is different from census studies. While a census study is targeted at including all the members of the population, a survey study focuses on a sample of the population.

Furthermore, there are different types of survey: descriptive, analytic longitudinal and cross-sectional surveys. These designs differ regarding the number of times data is collected. The cross-sectional survey as used in this study involved a retrospective approach (asking participants of past behaviours, practices, and experiences (Bowling, 2014a)) whereby data is collected from a sample of the population at a particular point in time. The cross-sectional survey design gives a snapshot of the population from the lenses of the sample. In using this method, there is no follow-up or subsequent surveys as with a longitudinal survey. In addition,

the use of a cross-sectional design, as against the longitudinal, is more practical in this study considering the financial cost and the time required to conduct a longitudinal study.

7.3 Sampling Technique

Generally, the overall aim of quantitative studies is to test out how common a behaviour, attitude, issue or relationship is in a population. In reality, it is difficult to study an entire population as this will require a lot of financial resources and time. Consequently, most quantitative studies are conducted using a sample drawn from the population and making inferences about the population based on the results from the sample. The representativeness of the sample becomes important in such scenario. The representativeness depends on the sample size and how the sample was drawn; this will also affect the generalizability of the finding to the entire or similar populations. In other words, the sampling is a very important aspect of the quantitative study; hence the decision on what sampling technique to adopt is crucial to the outcome of the study.

In general, there are two broad sampling methods, probability/ random and non-probability/non-random sampling. The basic difference between these two sampling methods is that unlike non-probability sampling, probability sampling offers all members of the population an opportunity to be selected. As a result, probability sampling is more likely to produce a representative sample and generalizable findings than the non-probability method.

Generally, different types of techniques exist under probability/random sampling. These include simple random sampling, systematic sampling, stratified sampling, and cluster sampling (Cochran, 2007; Jaeger, 1984; Kish, 1965; Pedhazur & Schmelkin, 2013). In choosing which of the techniques to use in this study, the objective of the research, as well as the population characteristics, were considered. Subsequently, a simple random sampling was used in the selection of facilities to recruit participants from, while a systematic probability sampling method was used in selecting participants from each healthcare facility.

7.3.1 Selection of Health Facilities and Participants

7.3.1.1 Selection of Health Facilities

Prior to the systematic sampling for study sample, we selected the health facilities to recruit participants from. As this study was conducted in two states in Nigeria, we selected health facilities in rural and urban areas in these states. Using simple random sampling technique, we selected two local government areas in the rural and urban areas in each state.

From each of the local governments, a list of all government and private hospitals were made, and using a random number table; we selected two private and two government hospitals from each area. As there was no comprehensive list of pharmacies and chemists in these areas, we randomly selected two chemist and pharmacies from the rural and urban areas respectively, by listing the names of the chemists and pharmacies identified in the areas and randomly picking two from each area.

In all, eight hospitals, two chemists, and two pharmacies were approached for this study. Letters were sent to these facilities seeking approval to recruit study participants from the facilities. Included in the letters were the study protocol and sample of the questionnaire. Seven facilities (two private hospitals, two government hospitals, one pharmacy, one chemist and one health center) consented to be part of this study.

7.3.1.2 Selection of participants

According to Rodriguez (1997), systematic sampling is a sampling technique that involves selecting every kth element from a population into the sample. This selection usually starts with a random first number or starting point, and then every kth (this can be, for instance, every 5^{th}, 9^{th} or 15^{th} element) is selected into the sample. Of all probability sampling techniques, the systematic sampling is the most suitable in selecting participants for this study considering the population characteristics.

As most of those visiting the outpatient clinics in all the facilities require no appointment prior to the visit, there were no published lists of the patients who have an appointment in the outpatient clinics at the start of each day. Hence a simple randomization using a list of patients was impractical given the system in the facilities in the study area. Therefore, prior to the day data was collected from each facility, a meeting was held with the chief medical directors (CMDs) or managers of each facility to ascertain the average number of patients that seek malaria treatment from their facility and also to get some information on the attendance pattern with regards to peak periods and days in the facilities.

From the meeting with the CMDs and health facility managers, most of the patients seeking treatment at the outpatient clinics or from the pharmacy and chemists were treated for malaria. There were also differences in peak days and time of the day for different types of facility and locations. For instance, the pharmacies tended to have higher sales at lunch time (between 12 – 1 pm) and evenings when people are on break from work and are back from work

respectively. For the hospitals, Mondays were the usual peak days, with most patients seen in the morning hours.

Interestingly, in the rural settings, additional factors affected the attendance pattern of patients in the outpatient clinics in the hospitals. The most prominent were local market days and religious worship days. Fewer people were seen in the formal health facilities on market days as locals usually go to the market. Hence the market days were off-peak periods here. This was, however, the reverse for the chemists in the rural areas where market days constitutes peak periods for sales as the chemists are usually located around the village squares and markets. So, rural dwellers tend to buy drugs when they come to the market.

In addition to the above, religious worship day was another prominent factor in determining the patients' attendance trend. For instance, the facilities in Abuja identified Fridays as their off-peak day as it is the worship day for Muslims (with Islam being the most common religion in Abuja).

All these factors were put into consideration in determining the day to collect data from each facility and how to sample while achieving randomization.

To this effect, in randomly recruiting samples for this study, depending on the average number of patients who seek malaria treatment from the facility in a day, a systematic sampling method was used where for instance, every 5^{th} patient with a malaria prescription was selected. Where the 5^{th} patient declined to participate, the next is approached and the cycle continues.

7.4 Sample size

Sample size estimation is not only important in ensuring a representative sample, is is also useful in ensuring a precise and accurate conclusion. In determining sample size, different approaches, ranging from selecting a fraction of the population, selecting a sample size based on the margin of error the researcher can tolerate, data from similar studies in the population of interest, sample size calculation using statistical formulas, among others exist (Creswell, 2013). Among all, the use of formulas for sample size estimation is the most preferred in determining the appropriate sample size that is enough to make an inference on the population (Fowler, 2013). The Slovin formula is one of such formulas used in calculating sample size. Slovin's formula is usually ideal when there is limited prior information about the population. With the poor level of documentation and record keeping in the Nigerian health sector, relevant

data that could provide more details of the population characteristics, like the number of those who use government hospitals in a state, was not available.

In determining the sample size for this study, Slovin's formula was used in calculating the sample size at 5% (0.05) margin of error. As a malaria holoendemic country, almost all (97%) members of the Nigerian population are at risk of malaria infection (National Population Commission, 2013b). Hence in determining the size of the population (that is, the two states in Nigeria that this study covered), the National Population and Housing Census (National Population Commission, 2006) was used to determine the number of households in these populations.

Using Slovin's formula in determining the sample size

$$n = \frac{N}{1 + Ne^2}$$

Where n is the sample size

N is the population size

e is the margin of error

Population size = 1,164,595

At 95% confidence interval

Margin of error = 0.05

$$n = \frac{1164595}{1 + (1164595)(0.05)} = 399.862660355 \sim 400$$

In all, four hundred and fifteen (415) participants were recruited in this study.

7.5 Materials and Data Collection

7.5.1 Measurement Tool/Instrument

As a research instrument, questionnaires are tools used in collecting and recording data about an issue under study (Patel & Joseph, 2016). When analyzed, questionnaire data are important

in answering survey research questions; as such, a well-designed questionnaire should meet the aims and objectives of the research. In survey research designs, questionnaires can be used in collecting data from a representative sample of a population, and the information obtained from the analysis can be applied in making an inference to the larger population (Patel & Joseph, 2016; Rattray & Jones, 2007a).

Questionnaires are the most widely used measurement tool in quantitative research. Unlike other data collection methods, questionnaires can cover a wider range of participants and are easy to administer and analyze. Hence, they offer a more economical option for data collection than other methods like interviewing or use of equipment (Bowling, 2014a). Although made up of a list of questions and instructions (Patel & Joseph, 2016), when well developed and used, questionnaires have the ability to captures individual's experiences, behaviours, perceptions, and attitudes about the issues or phenomena studied (Rattray & Jones, 2007a). The data collected using questionnaires can be qualitative variables which are then converted to numerical form and analyzed using statistical tests (Rattray & Jones, 2007a).

One of the advantages of using a questionnaire in data collection is that standardization is achieved (Kelley, Clark, Brown, & Sitzia, 2003). In using questionnaires, all participants are asked the same set of questions, and the responses are usually within the options set, which leads to consistency in the responses (Burns, 2000).

Despite their acceptance and use in academic and non-academic research inquiries, questionnaires have been criticized as an inadequate method for an in-depth study of behaviours, practices, perceptions or attitudes of people. One of the reasons for this criticism is based on the type of question most commonly used in questionnaires: close-ended questions (Bowling, 2014a). In addition to this, questionnaires are based on certain assumptions, for instance, that a common underlying assumption exists between the researcher(s) and respondents in relation to language and interpretation of words (Rattray & Jones, 2007a). In addition to the above, another disadvantage of this tool of data collection is that it requires the researcher to have a grounded knowledge of the issue under study so as to enable him/her to develop exhaustive response options for each close-ended question. These disadvantages of questionnaire were resolved with the researcher's knowledge of the subject area and the study population context, as well as the qualitative interviews that informed the development and design of the questionnaire.

7.5.2 Development of Questionnaire

In conducting a survey using a questionnaire, researchers are faced with two main options of either using an already validated/developed questionnaire or developing their questionnaire. Although the use of already developed and validated questionnaire is much easier than developing a new one, however, there are situations that will require the design of a new questionnaire instrument. Such situations, for example, are when the existing questionnaires cannot be tailored to the research aim or cannot be used to measure the variables of interest; and when there is no existing questionnaire. The latter is more common when the research subject or issue is not well represented in literature. A new questionnaire was developed for the survey as there was no existing questionnaire for assessing the association between socioeconomic factors and drug resistance promoting behaviours.

The design and development of a good survey questionnaire is a rigorous and time-consuming process. Considerations are given to the items and contents of the questionnaire, the types of questions to ask, the language to use, the length and number of questions, the order and arrangement of items, amongst others (Rattray & Jones, 2007a). All these factors play important roles is developing an efficient questionnaire.

7.5.2.1 Questionnaire content/items

Deciding what items or questions to include in a questionnaire is one of the most important tasks in questionnaire development. Questions used in survey questionnaires are usually developed based on evidence from existing literature. This was the guiding principle in the development of the questionnaire for this study. The questions were rooted in the findings of the systematic review (Anyanwu et al., 2016) and the qualitative interview (Anyanwu et al., 2017) which were both conducted with the primary goal of generating findings to inform the design of the questionnaire for the survey. In addition to this, the existing literature on malaria treatment and drug use, as well as consultation with experts in the field, informed the construct of the questions and the response options.

7.5.2.2 Question types

In designing the questions to be used in a questionnaire, researchers are faced with the decision of what types of questions to ask. In making such decisions, consideration is given to the conceptual framework and the variables to test, available resources to collect and analyze the question, among others.

For the purpose of questionnaire design, questions are usually classified based on the structure of the question and response style (open ended or close ended questions), the nature of the options available (ranking or rating scales), and the number of options to be selected for each question (single or multiple response). In addition to these, other question types, like filter or contingency questions, exist.

Open and close-ended questions

As shown above, questions can be said to be open or close-ended. This classification is based on the expected response style from the question, hence they both differ in question structure. For open-ended questions, respondents are allowed to articulate the response/answer and to represent this in their own words and language (Patel & Joseph, 2016). As such, the open-ended questions are good in eliciting in-depth information from participants. They are very useful in asking questions that the researcher is not sure of the possible response options.

Nevertheless, with the unrestrictive nature of the open-ended questions, respondents may not be sure of the extent to go in answering or giving their response to a question (Patel & Joseph, 2016), hence a mixture of detailed and non-detailed responses can be gathered from open-ended questions. In addition to this, repeatedly, evidence from existing studies on the use of questionnaire has shown that open-ended questions are difficult to analyze. The analysis of open-ended questions involves, firstly, coding the responses before statistical analysis. The process of inputting the responses (that is typing them in a computer device), development of coding scheme and analysis of the coded responses require more time, financial resources and skilled labour. Also, the issue of being able to understand people's individual handwriting can be a challenge in using open-ended questions in a questionnaire (Krosnick & Presser, 2010). These disadvantages of open-ended questions are main contributors to the widespread use of close-ended questions in questionnaires (Krosnick & Presser, 2010).

At the far end of the continuum are closed or close-ended questions. With close-ended questions, respondents are provided with response options to the question. For a researcher to effectively construct a close-ended question, there is a need for him/her to have a good knowledge of the subject area or issue the question covers as this is needed to ensure an exhaustive list of response options is provided. There have been suggestions that the provision of response options in a close-ended question is important in reducing recall bias as this helps prompt the participants on the possible response options that represents their experience (Krosnick & Presser, 2010). Nevertheless, close-ended questions are more likely to have issues

of correct guessing than open-ended questions (Krosnick & Presser, 2010). Also, the restrictive nature of the questions can be frustrating to respondents especially when the response options are not comprehensive.

Furthermore, as with most questionnaires, a mixture of the open and close- ended questions were used in the questionnaire design for the survey in this study. Mixing was important in ensuring that participants are not easily bored with the questionnaire and that a changing pace is maintained to keep the respondents engaged all through the completion process. Altogether, close-ended questions were used more (85%) in the questionnaire for this study.

The responses to the close-ended questions in the questionnaire were drawn from existing literature (especially the systematic review conducted for this study), the results and responses from the qualitative interviews, researcher's knowledge of the subject area and experience in the study population, as well as the type of variable the question is measuring. Moreover, many of the closed questions had an 'other, please specify' option which was analyzed and treated as an open-ended question (that is, they were coded using collective words or terms that represent related opinions and responses. The frequency of these codes was then analyzed across the data set. These codes were subsequently treated as response options in the further statistical analysis).

Furthermore, questions can also be classified based on the nature of options available. Therefore, this classification –single and multiple responses- is sometimes considered to be sub-classes of close-ended questions (as open-ended questions usually have no response options). Single response questions are questions where participants are required to choose one option from the list of response options; while for multiple response options, participants can choose more than one option from the list. In some cases where multiple answers are offered, a ranking or rating scale can be used to explore how important or frequent the reported attitude, behaviours or practices are to the respondent. The most used rating scale in questionnaire design is Likert scale.

Contingency questions

In addition to the above mentioned types of questions, contingency or filter questions were also used in the questionnaire. Contingency questions usually involve more than one question asked progressively together; where the first question asks if a respondent has an opinion on a particular issue, then the next question(s) asks for the opinion of those who responded they

have (Krosnick & Presser, 2010). In other words, the first question serves as a filter to ensure only those who have the opinion needed for the next question are directed to it. The use of contingency questions is useful in ensuring respondents are only asked questions they have an opinion or experience of, making the questionnaire more tailored and efficient.

7.5.2.3 Questionnaire language

The questionnaire was developed in the English, which is the official language in Nigeria. Nevertheless, not all the members of the population are English-language literate. Hence, the questionnaires were translated into local languages that are prominent in the areas that this study covered -Igbo language, Hausa language, and Pidgin-English).

For translation to each language, two translators who speak both the local language of interest and the English language were used. In validating the questionnaire, the researcher, who also speaks the local languages, compares the individual translations by each translator in drafting an appropriate version of each question.

According to Patel (2016), a translated version of a validated questionnaire is not assumed to retain the validity of the original version as the validity of any questionnaire instrument is specific and not transferable from one instrument version to another. Consequently, the translated questionnaires were further piloted and test-retested to ensure the content was valid and also that the translated and English versions collected the same data as intended. This was done by testing the different questionnaire versions (for example, English language and Igbo language versions) with participants who can read and write both languages. The results of the English and local versions completed by each participant were compared for similarities. The response from the English and translated versions from all seven individuals who participated in the retest exercise for the translated versions of the questionnaire were 100% similar.

7.5.2.4 Structure of the questions

The questions were structured to be simple and easy to understand with correct tenses used to ensure viable communication. Jargons and words with unclear meaning were avoided in constructing the questions for this survey. Also, double-barreled and double negative questions, which can be confusing to participants, were avoided. A double-barrel question is a single question that inquiries about more than one issue, but allows for a response to only one issue. With double-barreled questions, respondents are unsure which issue to respond to or which

issue the researcher is interested in (Bowling, 2014a). Double-barreled questions were avoided in this study by splitting such questions into two contingency or normal individual questions.

The layout of the questions -and the responses for the close-ended ones- was very clear, neat and well-spaced. Questions were printed with black ink on a good quality white paper that allowed for easy absorption of ink when written on. Caution was taken in ensuring the finished hard copy of the questionnaire appears neat and attractive. Instructions were given on how to answer the questions at the beginning of each session. The instructions were printed in italics to draw attention to them so respondents do not miss them when going through the questionnaire. In all, the questionnaire contained seventy-two questions. Some of the questions were contingency/filter questions; hence not all questions applied to all participants.

In ordering the questions, questions that were on the same or similar variables were grouped together. This helps maintain a logical flow while ensuring participants are asked about one topic or issue at a particular stage (Krosnick & Presser, 2010). The 'funneling approach' (Krosnick & Presser, 2010) was used in the ordering by starting with general questions and then gradually narrow the questions down to treatment behaviours and practices. In using this approach, the questions were divided into different groups. The first group of questions was on socio-demography. This was followed by questions to test participants' level of knowledge and perceptions about malaria causes and prevention. The third group of questions was on malaria treatment seeking and drug use behaviours for the current malaria episode as well as previous cases of malaria. The fourth group was on malaria treatment for children while the last group of questions was on perceptions about some practices in using antimalarial drugs and participants' frequency of their use. Each question had a unique serial number assigned to it

As with other measurement instruments, the final questionnaire draft was subjected to further processes to ensure its validity and reliability as a measurement tool. Some of the processes adopted in this study to ensure validity are piloting and Test-retest.

7.6 Piloting

Prior to the psychometric validation exercises and the main dissemination, the questionnaire was piloted using 20 participants who met the inclusion criteria. These participants were similar to the target participants for the main survey. The pilot study tested the:

- reactions of respondents to the research procedures and questions related to sensitive issues like their socioeconomic status, treatment seeking behaviour, drug use among others
- appropriateness of study type and research tools selected for the purpose of the study
- appropriateness of the format and wording of questionnaires (Mostafa, 2009)
- the effectiveness of the questionnaire in collecting the necessary data.

During the piloting of the questionnaire, some participants were uncomfortable with giving their names and signing a consent form. This was a likely barrier to participation and response in the main survey. Hence, in the main survey, participants after reading through the information sheet and having any question or concern addressed, were informed that by completing the questionnaire, they are giving an informed consent to participate in the survey

7.7 Psychometric validation

According to Bowling (2014a, p. 170), 'Psychometric validation is the process by which an instrument is assessed for reliability and validity through mounting of a series of defined tests of the population group for whom the instrument is intended'. Most survey instruments undergo psychometric validation prior to their use in data collection. There are different avenues or tests for psychometric validation of the measurement instrument. These tests are geared towards ensuring the reliability and validity of the instrument.

7.7.1 Reliability

Quantitative researchers are usually interested in proving that the measurement instrument used in their study is stable. Ascertaining the stability of the measurement instrument will help assure the users of the result or the instrument of its trustworthiness. This interest forms the concept of reliability. Reliability deals with how consistent the measurement instrument is in collecting the desired information (Bryman, 2015). In order words, it refers to the homogeneity and repeatability of the measurement instrument (Bowling, 2014b). The methods of assessing the reliability of an instrument used in this study include internal consistency, test-retest, and interrater.

Internal consistency: Internal consistency is an important feature of a good research tool. It is used to determine the consistency of information from a respondent by comparing to know whether their responses on any one indicator corresponds or relates to their response to other indicators (Bryman, 2015). In order words, it is concerned with the relationship between all the

results gotten from one respondent (Roberts, Priest, & Traynor, 2006). In assessing internal consistency in this study, during the test-retest exercise, participants' responses to some of the questions (like in contingency questions where indicating the absence of an opinion in the first question discredits any opinion reported in the second question) were compared for consistency. In all the individual responses to the questions on the instrument were highly related and consistent.

Test-retest: Furthermore, a test-retest exercise was conducted in this study to assess the stability of the instrument over time. This was carried out to ascertain the reliability of the questionnaire in providing the same information if used on same participants at different periods (Bowling, 2014a; Bryman, 2015). It involved administering the questionnaire to ten 10 participants, who fall into the sample inclusion criteria, in two different occasions -one week apart from each other-, under the same conditions (Patel & Joseph, 2016). Their responses were then compared for correlation level. 93% similarity was achieved from the test-retest exercise with 10 participants.

Inter-rater reliability: In addition to the test-retest exercise, an inter-rater exercise was also conducted to assess the reliability of the exercise further. The difference between the test-retest and the inter-rater exercise is that in the latter, a different person administers the questionnaire the second time (Bowling, 2014a). Hence, inter-rater deals more on assessing whether different outcomes can be achieved when the instrument is administered to the participant by different people. It assesses the objectivity of the instrument. As the inter-rater process of assessing instrument reliability is not applicable to the self-administered questionnaire, we only conducted this with participants who cannot administer the questionnaire themselves because of their literacy level. A piloted version of the questionnaire was administered to ten (10) people who are similar to the participants in this study and then re-administering the same questionnaire on a later date on the same people by a different research assistant. Each participant's responses to the two tests were compared to determine correlation level. The Kappa test was used in analyzing the results from the inter-rater exercise. A kappa result of 0.96, showing high inter-rater reliability, was recorded.

7.7.2 Validity

Validity deals with the ability of the measurement instrument to precisely measure the particular concept it sets out to measure (Bryman, 2015). Validity is broadly categorized into internal and external validity. While internal validity is concerned with the reasons for the

inferences or outcome of the study and helps to minimize systematic errors and other factors that could have facilitated the outcome; external validity is about the generalizability of the findings to a larger population (Bowling, 2014a).

Internal validity was assessed in this study using face validity, construct validity, and content validity approaches.

Face validity: Although sometimes considered as a subjective and less scientific assessment of validity (Bowling, 2014a), face validity is important in ascertaining whether the measurement instrument or questions appears to be assessing the issue of interesting. In assessing face validity in this study, experts in the field were consulted to review the instrument to ensure the questions are relevant, demonstrate the content of the concept in question (Bryman, 2015), and that the presentation of the questions in the questionnaire is logical, clear and easy to understand.

Content validity: Although similar to face validity, content validity deals more with the construct and logical appearance of the instrument. Although not the strongest of the internal validity approaches, content validity is specifically important in studies investigating participants' attitude, behaviours, opinions or knowledge on a specific concept (Roberts et al., 2006). As such, content validity is very important to this study; and was assessed through the conduct of the pilot study. The piloting of the questionnaire was a very important aspect of this research as it was used to test and demonstrate the questionnaire's validity as the best instrument in answering the research question. Corrections were made on the content and construct of the questionnaire based on the findings from the piloting.

Construct validity: Construct validity is a process adopted in research to ascertain that an instrument measures up to its claim. This deals with whether the measurement instrument designed to measure a particular event or concept reflects the event or concept it is measuring (Bowling, 2014a). In order words, this deals with the ability of the instruments to serve as an indicator of the variable it is testing. In ascertaining construct validity in this study, an extensive review of the literature on the subject area was conducted to identify the indicators used in measuring concepts like adherence to treatment, perceptions about malaria severity, treatment seeking behaviours amongst others. Also, other measurement instruments previously used by experts in the field (like Professor Obinna Onwujekwe of University of Nigeria Nsukka) were

sourced and compared to the developed instrument to ensure the indicators used for measuring concepts are appropriate.

External validity: External validity is about ensuring the conditions under which the study is carried out are representative of the situations and times to which the findings are to be applied (Black, 1999; Roberts et al., 2006). As external validity is concerned with the issue of generalizability of the findings to a larger population, a representative sample with reference to relevant characteristics in the study is important in this regard. The most important factors in assessing external validity of a study are the sampling method and sample size. Random sampling techniques, like simple random and systematic sampling used in this study, help to ensure the external validity of the study by selecting a sample representative of the population. Similarly, the sample size adds to external validity as the number of participants recruited is large enough to make an inference to the general population.

In line with the above, there was a need to ensure representativeness regarding participants characteristics. In achieving this, participants were recruited from both genders, different age brackets and different types of settlement.

7.8 Data Collection

In survey studies, several data collection methods exist. These methods are based on how the research instrument is disseminated to the target population. The commonly used dissemination methods in survey studies include post or mail, email, telephone, the Internet, personal interviews, group administration, face-to-face among others (Fink, 2012; Fowler, 2013). The response rate from each of these methods differs. For instance, while the post or mail might seem a convenient way to disseminate survey instruments, however, this method has repeatedly been reported to have low response rate (Hikmet & Chen, 2003; Yu & Cooper, 1983) and follow up is usually not easy. When response rate is low, non-response bias is increased; and this, in turn, will limit or reduce the generalizability of the findings. For other methods like telephone and the internet, the cost of owning the devices needed for these media of communication can limit those reachable with these to a particular class of people. Although the oldest way of disseminating questionnaire, face-to-face dissemination still offers a lot of advantages especially in technological resources-limited areas.

A face-to-face dissemination method was used in this study. In choosing this method, the cost of the dissemination process, the convenience of the method, prompt response, the response

rate, as well as population characteristics were considered and compared in relation to this method and other methods. Dissemination methods like, postal, email and internet were not feasible or practical in this study given the low popularity of the technologies and system needed for their use in Nigeria. The participants from the low socioeconomic level are less likely to have access to internet or email. Also, the postal address and code system in Nigeria is not as well established as that of countries like the UK and so will not be a good route to disseminate questionnaires to participants.

The questionnaires were designed to be administered by the participants themselves. The anonymity of self-administered questionnaires allows for more honest responses from participants, and the researcher is less likely to affect the outcome of the survey. The independence of the results/findings from questionnaire-use increased the reliability of information from the study (Nardi, 2015).

Nevertheless, as most of the participants from low socioeconomic class were not literate enough to read and answer the questionnaires themselves, the researcher or one of the research assistants helped in administering the questionnaire to such participant by reading out each question and response option (when available) to the participant and recording their response. When appropriate or required, translated versions of the questionnaire were used in asking the survey questions in a local language.

The option of disseminating the questionnaires translated into local languages to participants who are not English language literate and allowing them to complete the questionnaire themselves was also considered. But given the fact that fluency in the local languages does not necessarily mean the participants can read and write the languages, this option was deemed unfeasible in administering the questionnaires properly in this study.

Research assistants recruited for the dissemination of the questionnaire were positioned outside the consultation rooms/areas and/or at the pharmacy.

Prior to the start of the survey in each of the formal health facilities (hospitals and health centers) the CMD or a senior administrative staff member made an announcement in the outpatients' clinic waiting area, introducing the researchers and the study to the waiting patients and informing them of the stage during their consultation at which they will be approached. This strategy was useful in improving acceptance, collaboration and the willingness of the patients to partake in this study.

Also, the healthcare practitioner/chemist/pharmacists seeing the patients first spoke to those who were receiving malaria treatment about the study, and if they indicated interest, they are flagged up, and a research assistant approached them with the participant information sheet and details of the research.

Furthermore, before completing the questionnaire, participants were given the information sheet that explained the aim of the research, role of participants, risk involved in participation, and also participation advantage. Participants were required to give their consent and also assured of confidentiality and anonymity of their identities and responses.

7.9 Data Analysis

Quantitative data analysis involves several processes (such as data cleaning, transformation, and modeling) aimed at transforming the data into useful information. All the processes of data analysis for the survey data were conducted using the IBM SPSS Statistics 23.

Depending on the research design and type of data collected, different methods exist for analysis of research data. For quantitative research designs, statistical methods are used in analyzing the data. Prior to the main analysis of the data in this study, the data were cleaned and inspected by ensuring data is accurately transferred from the individual questionnaires to the analysis SPSS Statistics 23 packages, and by considering how to manage the missing data.

7.9.1 Missing data imputation

According to Allison (2002), a typical data set usually will have some missing data on some variables for some cases. Different reasons can lead to missing data on some variables or some cases in a data set. Some of the reasons for missing data include the intentional refusal of participants to answer the question; forgetfulness or overlook of some questions; lack of information or opinion needed to answer the question –for instance in cases of contingency questions that might not apply to all participants.

Indeed missing data is a long-standing issue in social, health and epidemiological research (Allison, 2002; Wood, White, & Thompson, 2004). The general assumption with regards to missing data is that cases who have missing values on a particular variable are not significantly different from those with observed measurements in terms of the value of the response on the variable.

Before the decision on how to treat the missing data, a detailed inspection of the data set and each case with a missing value in the data set is essential in determining whether or not the data is missing at random. According to Tabachnick and Fidell (2013), the amount of missing is not as important as the pattern of missing. In achieving this in this study, within and between cases inspections were conducted to see if missing data on one particular variable is related to the value of that variable or the value of another variable (Allision, 2002). Also, the results of descriptive analysis on each of the variables with missing data were evaluated to ensure that missingness is random rather than concentrated on the values of some other variables. For instance, the researcher considered the descriptive statistics on participants' type of settlement and the variables with missing data to ensure missing values in the variables are not occurring mostly among those in rural areas than urban. At the end, of the evaluation exercise, the missing data in the dataset for this survey were confirmed to be missing completely at random (MCAR).

There are different methods available to quantitative researchers for handling missing data prior to data analysis. These include listwise deletion, pairwise deletion, and imputation methods. In handling missing data using the listwise deletion method, any case with a missing value for any of the variables to be used in the analysis model is dropped from the analysis. Simply put, it means any case with a missing value on at least one of the specific variables to be used is removed from the analysis model, and only cases with a complete set of data on the specific variables are used. Although an easy way to treat missing data as it required no imputation, listwise deletion constitutes bias and can lead to a high standard error as less information is entered in the analysis (Allison, 2002).

A pairwise deletion differs from a listwise deletion in that the former does not completely drop a case with missing values on one specific variable from the model; instead it takes into account those with missing values by adopting an analysis by analysis basis thereby utilizing all the available data (Allison, 2002; Tabachnick & Fidell, 2013). Simply put, a pairwise method will only include the complete data in a variable A, but it can use the excluded cases (cases with missing data on variable A but not missing data in variable B) when analyzing other variables in the model.

On the other hand, in handling missing data, some quantitative researchers substitute the missing data with new values based on reasonable guess and then use the data set as a complete set with no missing data (Allison, 2002). Although the imputation method might seem subjective, there are different ways to impute missing values, and the contemporary imputation

methods utilize more objective statistics in doing so. Some of the missing data imputation methods include: marginal mean imputation (where missing values on a specific variable are substituted with the mean score of the observed values); conventional mean imputation method (use complete data on the other variables for the case by a way of multiple regression), maximum likelihood method, and multiple imputation (both single random and multiple random imputation). One of the advantages of using imputation method in handling missing data is that it reduces the standard error estimates.

In handling the missing data in this study, the multiple imputations method was used. Multiple imputation is a method of addressing missing data by creating different multiple probable imputed/complete data set and then integrating the results from each of the imputation to form a pooled value for each missing data (Sterne et al., 2009). As such, multiple imputation method accommodates the uncertainty about the missing data by devising several different likely data sets in place of the missing data; and then integrating these (Sterne et al., 2009). The choice of this method for this survey is based on its ability to be used for any data and in conducting any statistical analysis or model (Allison, 2002). Also, as the multiple imputation method utilizes statistical estimation, the outcome of the imputation is usually statistically valid.

In using the multiple imputation method, the imputation process was repeated five (5) times thereby generating five complete data sets. The imputed values for each of the missing values in each imputation were slightly different as this method uses random component (Allison, 2002). A pooled mean of the randomly generated values for all five was used in replacing the missing values. The use of multiple random imputation as against single random imputation helps to ensure the standard error is not too small (Sterne et al., 2009).

7.9.2 Data preparation

Further efforts were made to ensure the data set was prepared and in a form appropriate for the statistical test to be conducted. Some of the preparatory activities conducted before data analysis were centered around ensuring the variables were at the appropriate measurement level needed for any specific statistical test that it is to be used in. In relation to this, the processes of discretization and dummy coding of data were conducted in the preparation of the data for analysis.

7.9.3 Discretization

Simply put, discretization is the transformation of a variable from a continuous data measurement form to a discrete form. This process is important especially when the researcher

needs to use a variable measured at a continuous level in the form of categories or groups. For instance, there was a need to discretize the household income, which was originally collected as a continuous variable, into household income groups to enable its use in some statistical tests like contingency table using Pearson chi-square test.

7.9.4 Dummy variable coding

In some instance, some important predictor variable that a researcher might be interested in adding to a statistical model, like regression analysis, might have been collected in the form of a qualitative or nominal data. At this level of measurement, the variable cannot be entered into such analysis. One of the ways to deal with such issues is to dummy code the variable by treating each of the responses as a variable with a response of 1 indicating present and 0 indicating absence. Dummy coding was described by Tabachnick and Fidell, (2013) as 're-categorization of a discrete variable into a series of dichotomous ones'. For instance, the variable on the type of settlement collected qualitative data with three responses: urban, rural and suburban. In preparing this variable for logistic regression, there was a need to dummy code as logistic regression does not permit the use of nominal variables as predictors, however, it does permit the use of dichotomous variables. So, the three responses were each treated as a separate variable, as such three variables were formed: urban dweller, rural dweller, and suburban dweller. For each of the variables, two responses of yes=1 and no=0 were used to indicate participant's original response on their type of settlement.

In all instances where a variable was discretized or dummy coded, a copy of the original measurement level of the data was kept as some other analysis might require their use in this form.

7.9.5 Factor analysis

In most survey studies, some questions/variables can be used as indicators or measurements of a particular phenomenon or factor. Prior to the use of these questions as indicators of a factor or theory, a factor analysis can be performed to assess how inter-correlated the variables constituting the structures are (Pallant, 2013). Factor analysis is a statistical method used for detection or assessment of assumed underlying structure or theory between some variables in a data set (Pallant, 2013; Tabachnick & Fidell, 2013). It is sometimes described as a technique for reducing the number of variables in a data set as the result of the analysis can indicate the need to drop a variable in a *factor*, especially when the intercorrelation of the variable with other variables is poor (correlation matrix of below 0.30 are considered poor) or too high

(correlation matrix of 0.8 and above is considered high as this indicated the two variables are too related or can explain the same thing). It is important in determining whether the responses on a group of variables/questions are underpinned by the specific underlying structure. These structures are usually referred to as 'factors'.

Factor analysis was conducted in this study to assess the intercorrelation of variables that were used as indicator or structures for a factor. For instance, a factor analysis was conducted using the variables that the researcher recognized as indicators of socioeconomic position. The result of this analysis showed that among the socioeconomic variables, (that is educational level, household monthly income, occupational type, type of settlement, and employment status) occupational type had a poor intercorrelation with the other variables. All other variables constituting the socioeconomic *factor* were interrelated to each other at correlation matrix of more than 0.3. Hence occupational type was not considered a good indicator of socioeconomic position in this study. Based on this finding, occupational type was dropped as a socioeconomic indicator in all the inferential analysis that assessed the relationship between socioeconomic position and antimalarial drug use behaviours. Factor analysis was also performed for other *factors*, adherence level among others.

7.9.6 Statistical tests used in data analysis

In analyzing quantitative data, statistical tests are employed for different roles like an evaluation of the frequency of responses on specific variables, assessing the relationship between variables, exploring the direction of the relationship between variables amongst others. To conduct any of the above analysis, different statistical tests can be carried out. The types of statistical tests can be broadly categorized into descriptive and inferential statistics.

Descriptive statistics is used to describe the characteristics of the sample regarding their response on specific variables or combination of variables (Pallant, 2013; Tabachnick & Fidell, 2013). In addition to this, descriptive statistics play important role in inspecting the variables in the data set for outliers or violation of the assumptions of some inferential statistical tests (Pallant, 2013). Although they do not consist of vigorous statistical techniques, descriptive statistics when used alone can provide rich descriptions of patterns in a data set. Therefore, descriptive statistics can be used alone in addressing particular research questions (Pallant, 2013). In this study, descriptive statistics was conducted on the frequency of each of the variables in the survey instrument.

As descriptive statistics lack statistical vigor, they are usually not able to test relationships between variables to determine whether existing differences are by chance or dependable (statistically significant). To test the relationships between variables in the study, and to explore differences in the study population based on the study sample, inferential statistics are used. Inferential statistical tests are used in making inference on the population based on the findings from the sample, hence the word "inferential". They are important in survey studies for testing the hypotheses (Tabachnick & Fidell, 2013).

In testing the hypotheses in this study, different inferential statistical techniques were used. These include:

- Analysis of variance (ANOVA)
- Multiple analysis of variance (MANOVA)
- Logistic regression technique
- Multiple regression technique
- Correlation and
- Contingency table using Pearson chi-square.

The decision on which statistical technique to use in testing each hypothesis was guided by

- the specific hypothesis to be test (for instance whether a relationship exists and/or the direction of the relationship)
- The number of dependent variables and independent variables available for each specific hypothesis
- The level of measurement for each of the variables that are important in testing the hypothesis. For instance, the level of measurement used for a specific dependent or independent variable (continuous scale or categorical) was considered in deciding the type of statistical test that can be conducted using the variable

Analysis of Likert Scale Variables

The debate over the use of parametric test in the analysis of Likert scale has been on-going for more than half a century now. The underlying factor in this debate is whether Likert scales are to be treated as ordinal or interval variables. Many statisticians have found the use of Likert scale in parametric tests effective in producing unbiased results (Carifio & Perla, 2008, 2007; Glass, Peckham, & Sanders, 1972; Lubke & Muthén, 2004; Norman, 2010; Pell, 2005; Piepho,

1996). Nevertheless, this stance has been criticized by some statisticians. The critics of the use of Likert scale for a parametric test like ANOVA describe Likert scale as ordinal in character; as such do not satisfy the assumption of the normality of distribution (Jamieson, 2004; Stevens, 1946, 1951). For this reason, they recommend Likert scale should not be analyzed using parametric tests.

However, several studies have shown that the above reason does not invalidate or bias the results of parametric tests using a Likert scale. For instance, looking at ANOVA, the assumption of normality (which is one of the key arguments that those who hold the ordinalist view of Likert scale present against the use of parametric tests in its analysis) is of the distribution of means and not of the data (Norman, 2010). The central limit theorem shows that as the sample size gets larger (greater than 5 or 10 per group), the distribution of the sampling means approaches a normal distribution regardless of the shape of the original distribution of the population (Lee, Lee, Chang, & Tai, 2016; Norman, 2010).

In addition, one of the misconceptions underpinning the argument made by ordinalists in Likert scale is that they fail to make a distinction between a Likert response format, a Likert question, and a Likert scale (collection of items). Whereas Likert questions or items may be ordinal, Likert scale, which comprises of a collection of many items, is interval (Carifio & Perla, 2008; Pell, 2005). In further simplifying this using everyday events, Norman (2010) likened this to the practice of treating the total of correct responses in a multiple choice exam, each of which is binary, as an interval scale. Also, in contextualising this issue, Carifio & Perla (2008) used the disparity between atoms and molecules to demonstrate the difference between a Likert question and Likert scale. Although molecules (in this case Likert scales) are made up of a collection of atoms (individual Likert items), the molecules usually differ in properties with the individual atoms that constitute them. The treatment of the Likert scale in this study as interval variables enabled their use in conducting sophisticated parametric analysis to test hypotheses that had such variables.

A rigorous process was adopted in deciding what variables to use in testing each hypothesis, what relationships to test and what appropriate statistical test can be conducted using the variables. This process was strictly overseen by one of the supervisors to ensure the validity of the results by establishing that the assumptions of each statistical test are not violated. All statistical tests were significant at p-value of 0.05 or less at a 95% confidence interval.

To justify the decisions on statistical techniques used in this survey, each of the techniques used has been briefly explained below.

Analysis of variance (ANOVA)

Analysis of variance is a statistical technique used to explore the relationship between two variables by comparing the mean scores for both variables to see if there are statistically significant differences among the variables (Pallant, 2013; Tabachnick & Fidell, 2013). In other words, the basic function of ANOVA is to compare two estimates of variance (Tabachnick & Fidell, 2013). This can be done in two ways: by using a one-way ANOVA or by using a two-way ANOVA.

A one-way analysis of variance is used to compare the means score on a continuous dependent variable across two or more groups in a categorical independent variable (Pallant, 2013). The name one-way is derived from the fact that only one independent variable is used, that is, the analysis is testing the mean score on a continuous dependent variable across groups/categories under one independent variable. A one-way ANOVA alone will be able to assess whether the groups under the independent variable differ regarding mean score on the continuous dependent variable, but it is unable to indicate among which of the groups the difference occurs (Pallant, 2013)

A two-way ANOVA, on the other hand, permits the assessment of the impact of two independent variables on the dependent variable (Pallant, 2013). That is, it tests whether a statistically significant relationship exists between the groups in each of the independent variables on the continuous dependent variable (this is referred to as the main effect of each independent variables); as well as the interaction effect of the two independent variables on the continuous variable when combined (Pallant, 2013). All ANOVA tests conducted in this study were two-way.

As ANOVA test alone are unable to indicate where the difference occurred, a post hoc test was added to the ANOVA analysis to achieve this. A post hoc test is used as an additional test when an ANOVA result is statistically significant, to indicate which specific group differed.

As with all inferential statistical tests, there are assumptions that needed to be met before a good ANOVA model can be achieved. The assumptions of ANOVA, according to Pallant (2013) include:

- The dependent variable must be measured in a continuous scale level while the independent variable must be at the categorical level.
- Random sampling methods should be used in recruiting the sample who the scores are obtained from
- Each measurement must be independent of the influence of the other measures
- Study population should be normally distributed especially in relation to the dependent variable. Normality of distribution is usually achieved easier with a larger sample size than a small sample size.
- Homogeneity of variance. ANOVA assumes that all the groups in the model have common or similar variance. This assumption is tested by running a Levene's (*F*) test. An alpha value under Levene's test of more than the level of significance indicates the assumption of homogeneity has been violated and the null hypothesis is being falsely rejected (Pallant, 2013; Tabachnick & Fidell, 2013).

These assumptions were met prior to the use of ANOVA for each hypothesis that it was used in testing.

Multiple analysis of variance (MANOVA)

In some instances, there might be need to assess the mean score of two or more groups on more than one dependent variable. In using MANOVA, you can assess the significance of the mean difference between the groups on each of the dependent variables and the combined of the dependent variables (Pallant, 2013). Importantly, the dependent variables in MANOVA need to be related or have some form of similarity among them.

As in ANOVA, there are two types of MANOVA, one-way MANOVA, and two-way MANOVA. The difference still lies in the number of independent variables used in the model. For a one-way MANOVA, one categorical independent variable and two or more continuous dependent variables that are similar are used (Pallant, 2013). While for a two-way MANOVA, two categorical independent variables and two or more continuous dependent variables that are similar are used (Pallant, 2013). In addition to these, a higher-order MANOVA design consisting of two or more categorical independent variables can be used.

According to Pallant (2013), the assumptions for MANOVA are similar to that of ANOVA in terms of

- Measurement level
- Normal distribution, and
- Homogeneity of variance

Additional assumptions required for a good MANOVA model include:

- Sample size: MANOVA required that the number of cases in each cell is more than the number of dependent variables used in the model.
- Outliers: outliers come in the form of extreme scores that are different from the rest of the scores. Prior to the conduct of each MANOVA model, outliers were checked for each dependent variable individually, and for the dependent variables in combination to identify participants with extreme scores. None of the dependent variable used in MANOVA in this study had outliers as almost all were measured using Likert scale hence the possibility of extreme outliers was reduced.
- Linearity: a linear relationship is expected between each pair of the dependent variables to be used in MANOVA. To assess whether linearity exists, a scatter plot using each pair of the dependent variable was generated and observed for any evidence of non-linearity which will be dots that are scattered about rather than concentrated to form a line.
- Multicollinearity: as stated earlier, for a good MANOVA design to be achieved, the dependent variables need to have some relationship between them. This relationship is referred to as multicollinearity; and was assessed in this study by conducting a correlation test using the dependent variables to check the strength of the correlation between them. This was conducted prior each MANOVA test in this study. Although linearity is desired among the dependent variables, having two dependent variables with a high level of correlation, for example, of above 0.7 is, however, a concern. This is an indication that the two dependent variables are too correlated that they might as well be measuring the same factor; hence the best way to handle such situation is to drop one of the highly correlated variables from the model. The desired level of correlation is usually between 3.0 (medium) to 7.0 (high).

In using MANOVA in this study, care was taken in ensuring these assumptions were not violated.

Regression

Regression analysis is a statistical analysis used to estimate the relationship between a dependent variable and one or more independent variables. The independent variables in regression analysis are referred to as the predictor or explanatory variables, while the dependent variables are referred to as outcome or response variables (Hosmer, Lemeshow, & Sturdivant, 2013).

As with other types of analysis, regression analysis has its assumptions; violation of which can lead to building an unfit regression model. These assumptions include

- Sample size: requires a large sample size with the number of cases expected to be larger than the number of predictor variables to be used in the model
- Multicollinearity of predictor variables. Again, this was assessed using correlation test.
- Outliers (Pallant, 2013).

Two common types of regression analysis used in quantitative data analysis are binary or logistic regression and linear regression (Hosmer et al., 2013). These two differ in the measurement level of the dependent or outcome variable (Hosmer et al., 2013).

Binary regression

Binary or Logistic regression is a type of regression that analyzes the relationship between two or more continuous and/or categorical predictor variables and one categorical outcome variable with a binary response (Pallant, 2013; Tabachnick & Fidell, 2013). The binary categorical variable usually tests the presence or absence of a phenomenon, for instance between those who used malaria diagnostic test and those who did not. In using logistic regression in this study, the researcher aimed to explore the effect of the predictor variables in explaining the categorical outcome/dependent variables. It does this by assessing the main effects of each predictor variable on the categorical outcome variable, as well as the interaction effect of the combined predictor variables on the categorical outcome variable (Pallant, 2013).

In building a logistic regression model, different methods can be used depending on how the analyst wants the predictor variables to be added in the model. The most common methods used in logistic regression are the ‘enter’ method and the ‘stepwise’ procedure (forward and backward methods) (Pallant, 2013). The enter method, which involves forcing all the predictor variables into one block to assess their individual and collective predictive ability (Pallant, 2013), was used in this study.

Additionally, the Hosmer-Lemeshow goodness of fit test was used in the logistic regression analysis to test the how good the model is. The Cox & Snell R-squared and the Nagel Kerke R-squared values were used as indicators of the proportion of the variance in the outcome variable explained by the model using the predictor variables. While The Wald test was used to assess the contribution of each predictor variable in the model (Pallant, 2013).

Multiple regression

Multiple regression, on the other hand, is a form of linear regression. Unlike the logistic regression that requires a binary categorical outcome variable, the multiple regression uses a continuous outcome variable. It tests the predictive effect of more than one continuous predictor variable on one continuous outcome variable (Pallant, 2013). As in logistic regression, there are different types of multiple regression based on how the predictor variables were entered into the model: standard, hierarchical and stepwise. In the standard method, which was used in this study, all the predictor variables were entered into the model simultaneously while evaluating the predictor effect of each in relation to the other predictor variables (Pallant, 2013). This is different from the hierarchical method where the researcher/analyst determines the order by which the variables will be entered into the model. For the stepwise method, the program is provided with a set of predictor variable and allowed to order these in terms of how they are entered into the model, based on a set of statistical criteria (Pallant, 2013; Tabachnick & Fidell, 2013)

Contingency table using Pearson Chi-square

Contingency tables, also known as crosstabulation, plays an important role in the analysis of survey data collected at qualitative level (Everitt, 1992). It is used when the dependent and independent variables are either categorical or nominal. A crosstabulation output usually shows the frequency and percentage distributions of the variables, with one variable displayed in the row while the other variable is displayed in the column. In using contingency tables in this study, the independent variables were the column variable while the dependent were the row variables. Also, the adjusted residual was also represented in the contingency table to help indicate cells with interesting interactions. According to Agresti (2011), cells in the contingency table with adjusted residuals of more than 2 indicates that the number of cases in that particular cell is significantly higher than the expected number if the variables tested were statistically independent. Also, an adjusted residual of less than -2 indicates that the number of cases in that particular cell is significantly lower than the expected number if the variables

tested were statistically independent. This means some interesting interaction exists within that cell.

Furthermore, Pearson chi-square test of independence was used in the contingency table to determine whether a statistically significant relationship exists between the variables. The chi-square test compares the observed percentage of the cases that occur in each of the categories with the expected values if no relationship exists between the two variables crossed (Pallant, 2013). In interpreting the direction of the relationship, the adjusted residual and inspection of the frequency distribution of each cell in the contingency table, were used.

7.10 Sociodemographic characteristics of study participants

Four hundred and thirty-two participants who met the inclusion criteria were recruited for this study. Seventeen participants were later excluded from this study as they left the facility before they could complete the questionnaire. In all, data from the 415 participants who completed the questionnaires were used in this analysis. Participants were recruited from formal (73%) and informal healthcare facilities (27%). The types of healthcare facility recruited from include private hospitals (23.4%); government/public hospitals (49.6%); chemists (9.6%); and pharmacies (17.1%).

The recruited participants were seeking malaria treatment for themselves (59.4%), for a member of their household (19.1%) or both -themselves and a member of their household- (10.6%). 10.8% did not specify who the patient was, however, as part of the inclusion criteria, all participants in this study were seeking malaria treatment at the time of the study.

Furthermore, 63.4% of the participants were females. The main reason for the higher proportion of females as against males is related to the health seeking behaviour in this population where women tend to have better health seeking behaviour than men. Also, women are more likely to be the ones to seek treatment for a child when he/she gets ill -even though the men, in most cases, provide the financial resources for this. Of the 79 participants who were seeking treatment for a member of their household, 62% were females while 38% were males. Also, of the 44 participants who were seeking treatment for both themselves and a member of their household, 81.8% were females (see figure 7.10).

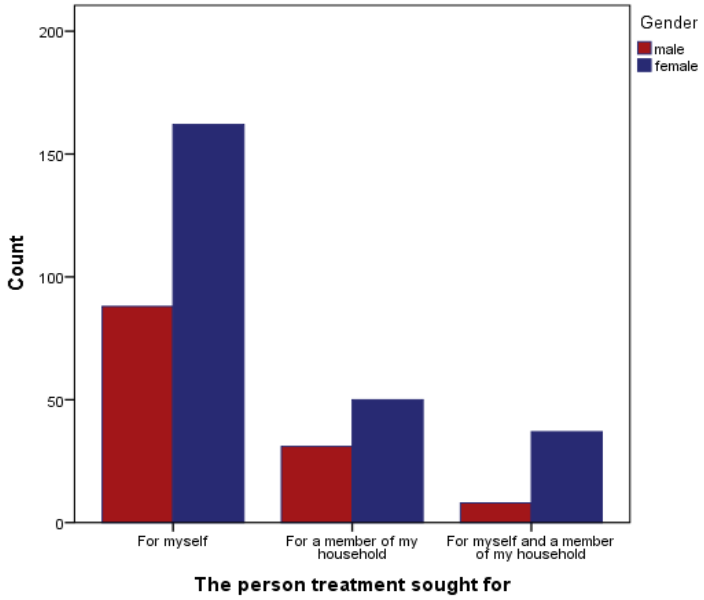

Figure 7.10: Chart of crosstabulation of variables Gender and who treatment was sought for

7.11 Socioeconomic Measures

As indicators of levels of socioeconomic measures, data were collected on participants' educational level, household income, occupation, type of settlement and employment status, and used in the statistical analysis.

In using these measures for statistical analysis, each of the socioeconomic factors was used as an independent variable rather than combining the data on the different socioeconomic factors for each participant to form single variable/measure of socioeconomic status. The reason for this is that by fusing the factors to form a single variable/indicator of socioeconomic status, the statistical analysis will be unable to indicate which particular socioeconomic measure (for instance, educational level) has a more predictive effect on particular outcomes than the others (Lynch et al., 1997; Svedberg, Nygren, Staland-Nyman, & Nyholm, 2016). Also, knowing the predictive effect of each socioeconomic factor in determining the variance in a particular outcome will be important in targeting campaigns and strategies to address the particular outcome.

Descriptive analysis of participants' educational level showed that 2.7% had no formal education; 6.7% attained a primary education; 23.6% attained secondary education; 36.4% attained tertiary education; while 30.6% attained postgraduate education (see figure 7.11.1). The high proportion of participants with tertiary education and above in this study (67.2%) is as a result of the location that participants were recruited from. With half of the study participants recruited from urban areas (50.1%) (compared to 29.9% from suburban and 20% from rural areas), it is expected that the overall educational level of the study participants will be high as urban areas accommodate more of the highly educated than the suburban and rural areas.

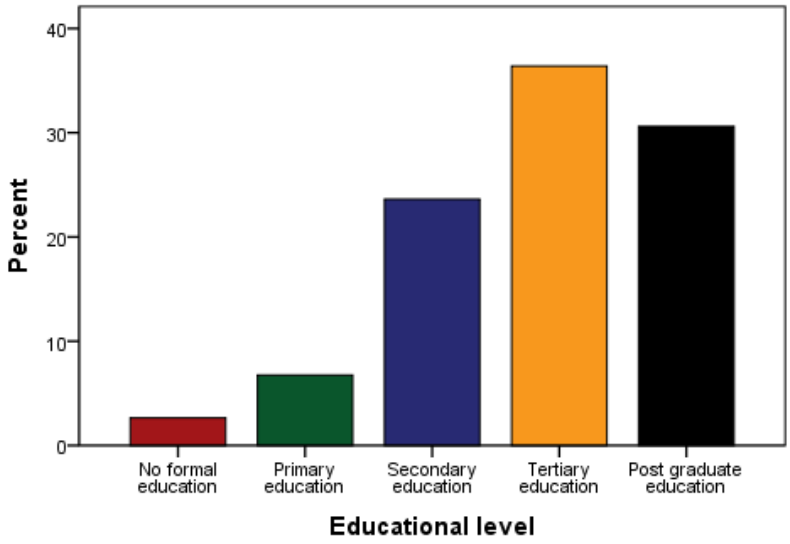

Figure 7.11.1: Educational level of participants

Participants' monthly household income was accessed in Naira, which is the Nigerian currency. At the time of this study, the official exchange rate of naira to pounds was at ₦412.39 (Nigerian Naira) for £1 (British Pounds). Participants' monthly household (household) income ranged from ₦3000 (£7.3) to ₦1,500,000 (£3637.4); with a mean household monthly income of ₦121,217 (£293.9). It should be noted that the mean monthly income recorded was offset by a few very high-income earning participants in this study. The median income was ₦72,182 (£175). As a continuous variable, there was a need to discretise the household monthly income into categories to enable its use as an independent variable in some statistical analysis like contingency table and multiple analysis of variance. To this effect, the household monthly income was categorized into six groups. Figure 7.11.2 below shows the groups and their

frequencies. The income group of ₦18,000 to ₦50,000 had the highest frequency with the household income of 115 (27.7%) participants falling under this category.

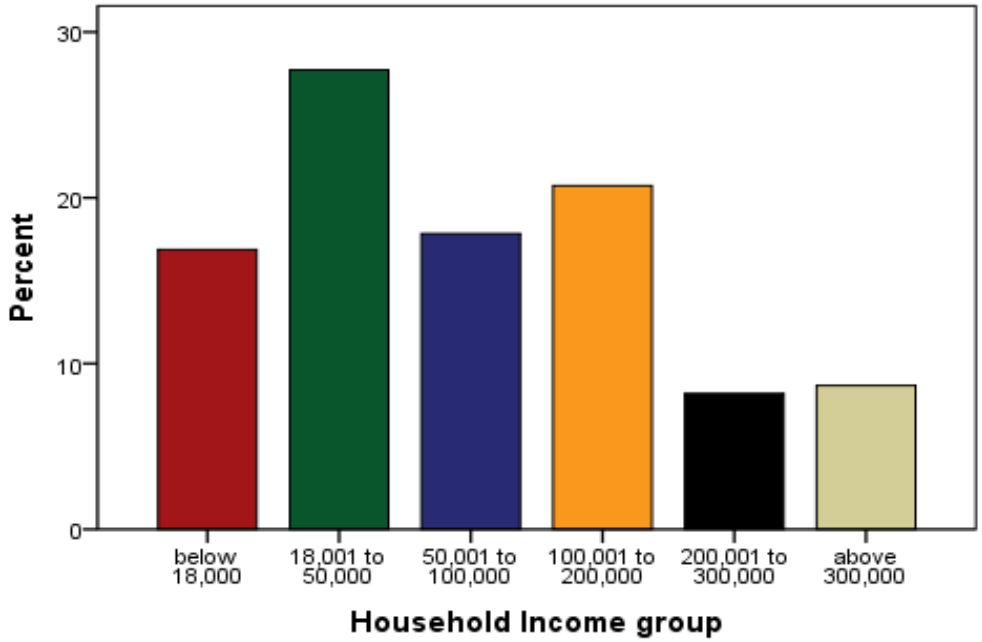

Figure 7.11.2: Income level Groups

At the time of this study, 83.9% of the participants were employed. Of those who were not in employment, 2.2% were retired, 4.6% in education, and 9.4% were unemployed.

Participants were also asked to indicate the occupation which is the main source of income for their household. To this 10.8% indicated farming, 18.3% indicated Civil service, 16.1% indicated business, 16.6% indicated professional jobs, 14.9% indicated corporate work, 20.7% indicated unskilled labour, while 2.4% indicated gifts/aids. The factor analysis performed as a preliminary test prior to analysis for relationships showed that type of occupation was not a strong indicator of socioeconomic position in this study (see section on Factor Analysis in chapter three for more on factor analysis in this study).

Another socioeconomic factor reported in this survey was the type of settlement. As shown in Table 7.2.4 in the appendix, urban settlement was the most popular type of settlement in this study with half (50%) of survey participants living in urban areas. The other two types of settlements, suburban and rural, had 30% and 20% respective. Among the 83 participants from rural areas in this study, 72% had secondary education as the highest level of education and

were of household income of below ₦50,000 (£121), with almost half of these of household income level below the minimum wage of ₦18,000.

Among all the socioeconomic factors reported, education and household income levels stand out as key indicators of socioeconomic position (Solar & Irwin, 2007). Nevertheless, education and household income levels are related to other measures of socioeconomic position like the type of settlement, employment status, and occupational type. household income can affect the type of settlement one will reside in. Likewise, an individual's educational level can affect his/her employment status as well as occupation. When analysed using a contingency table with a chi-square test, the relationship between participants' household monthly income level and type of settlement was statistically significant ($p<0.001$); with those of the lowest household income group (below ₦18,000) more likely to live in rural areas than those of other household income groups; and those of the highest income group (above ₦300,000) more likely to live in urban areas than other household income groups.

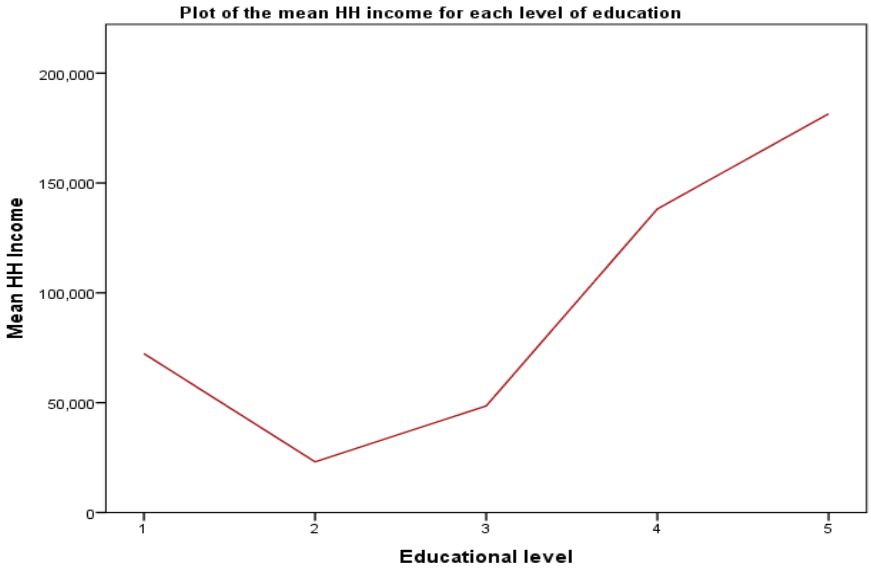

Figure 7.11.3: Plot of the mean of household income for each educational level

Furthermore, as expected, the comparison of mean household income for all levels of education shows that, from primary education, the higher the educational level of participants, the higher their mean household monthly income (see figure 7.11.3).

The descriptive statistics of all the variables used in this survey are shown in Table 7.2.4 in the appendix.

7.12 Research Hypotheses Testing

As stated in the introduction chapter, eleven hypotheses were made based on the results of the qualitative study. The survey instrument was subsequently used in testing these hypotheses with a larger sample size.

In testing the research hypotheses in this study, specific variables related to each hypothesis were used in conducting an analysis to determine whether or not the null hypothesis was to be accepted or rejected. In relation to this, subsequent results of the survey were structured around the different hypothesis and the statistical tests conducted in testing them.

The decision on the statistical test to use in testing each hypothesis was based on the type of variable (dependent or independent), and the nature of the variable (categorical, scale or continuous).

7.13 Hypothesis One

H0: Socioeconomic position is not related to adherence to malaria treatment course

H1: Socioeconomic position is related to adherence to treatment course

The hypothesis on the relationship between measures of socioeconomic status and adherence behaviours was tested using multiple analysis of variance (MANOVA). The variables used in testing this hypothesis include:

- Independent variables: Socioeconomic measures (educational level, household income, type of settlement, and employment status). See Table 7.2.4 in the appendix for measurement levels for the socioeconomic factors
- Dependent variables: administering antimalarial drugs at recommended time, administering the recommended dose, stopping malaria treatment to save drugs for future use and sharing of an antimalarial drug with others.

Multiple analyses of variance test was used in exploring the adherence levels for people at different levels of socioeconomic factors. To ensure clarity in interpretation of the results from MANOVA, only two independent variables were entered into each MANOVA model in this study. The first MANOVA in testing hypothesis one was conducted using educational level and household income as the independent variables; while a second MANOVA used type of settlement and employment status as the independent variables. There was a statistically

significant difference among the educational levels/groups on the combined dependent variables on adherence to malaria treatment (Wilks' Lambda value=0.873, F=3.342, p<0.001, partial eta squared=0.33 (large effect size)). Each of the dependent variables was considered separately with each independent variable, the results of this are shown in table 7.13.1. In considering the relationship with educational level/groups, there was a statistically significant difference among educational levels/groups on the behaviours of taking antimalarial drugs at recommended time, stopping antimalarial treatment to save drugs for future use and sharing an antimalarial course with others (see Table 7.13.1). There was no statistically significant difference among the educational levels/groups on the behaviour of taking the recommended dose of antimalarial. An evaluation of the mean scores for the significant results on educational level indicated that, on the behaviours of taking antimalarial drugs at recommended time, those with primary education and those of no formal education had the lowest means (mean scores of 3.4 and 3.7 respectively) while those of secondary and tertiary education had the highest means (mean scores of 4.5 and 4.2 respectively). For stopping antimalarial treatment to save drugs for future use, the mean score decreased as educational level increased, with those of no formal education having the highest mean score (mean=2.4). Also, for sharing an antimalarial course with others, generally the mean score reduced as educational level increased; with those with no formal education having the highest mean score (mean=2.6).

Furthermore, there was a statistically significant difference among the household income groups on the combined dependent variables on adherence to malaria treatment (Wilks' Lambda value=0.916, F=1.722, p=0.025, partial eta squared=0.022). In considering household income and each dependent variable, there was a statistically significant difference among household income groups on the behaviours of taking antimalarial drugs at the recommended time, stopping treatment to save antimalarial drug for future use, and on sharing an antimalarial course with others (see Table 7.13.1). However, household income groups were not significantly different in terms of the behaviour of taking the recommended dose of antimalarial. An inspection of the mean score for the different household income groups showed that, for taking antimalarial drugs at the recommended time, the lowest income group (below ₦18,000) had the lowest mean (3.6) while the high-income group of ₦200,001 to ₦300,000 had the highest mean score (Mean=4.6). However, for sharing of antimalarial drugs with others, the household income group of ₦100,001 to ₦200,000 had the highest mean score (2.0). Nevertheless, dichotomizing the variable into those who have shared and those who have never done so shows that as the household income level increases, so does the adoption of the

practice of saving (see figure 7.13). On stopping to save, the lowest household income group had the highest mean score and percentage of stopping to save. More than half 57.1% of those in the lowest income group of below ₦18,000 reported they do this. The two lowest income groups (below ₦18,000, and ₦18,001 to ₦50,000) accounted for 57.7% of the total number of those (137) who stop to save.

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Educational level	Take at recommended time	15.117	4	3.779	3.239	.012	.032
	Take the recommended dose	6.556	4	1.639	1.769	.134	.018
	Stop malaria treatment to save drugs for future use	13.384	4	3.346	6.052	.000	.059
	Shared antimalarial drug with others	14.727	4	3.682	6.937	.000	.067
HH Income group	Take at recommended time	13.977	5	2.795	2.396	.037	.030
	Take the recommended dose	6.390	5	1.278	1.379	.231	.017
	Stop malaria treatment to save drugs for future use	6.026	5	1.205	2.180	.050	.027
	Shared antimalarial drug with others	9.544	5	1.909	3.596	.003	.044

Table 7.13.1: Tests of Between-Subjects Effects for Educational level and household income

The combined effect of educational level and household income groups on the combined dependent variables on adherence to malaria treatment was not statistically significant (Wilks' Lambda value=0.839, F=1.084, p<0.306).

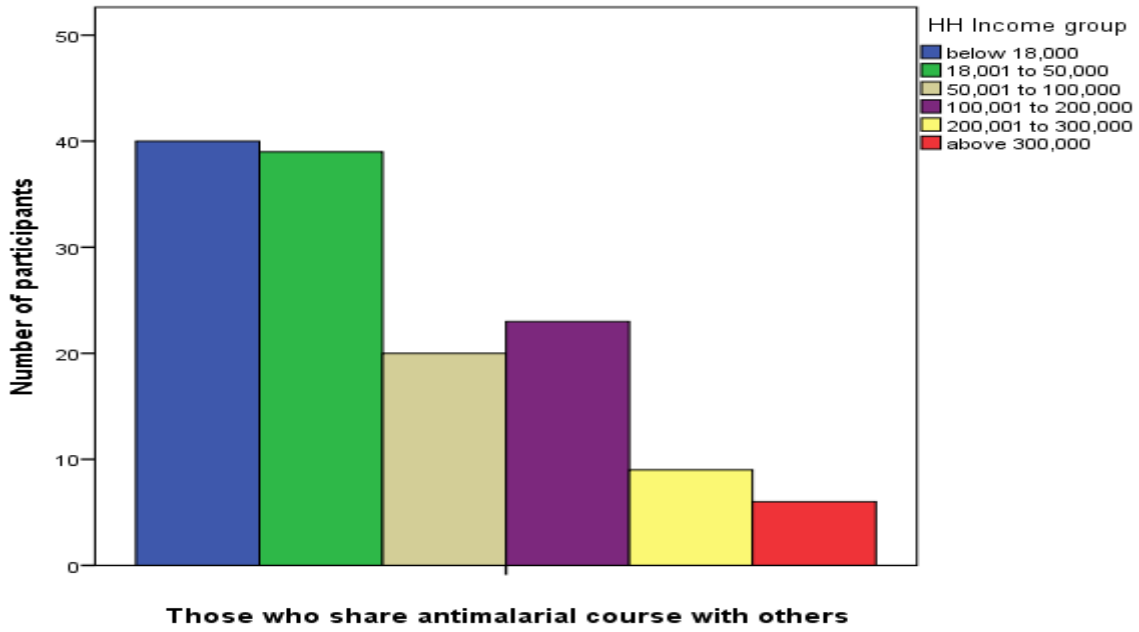

Figure 7.13 showing plot of dichotomized variable on sharing a course with others and household income

The second MANOVA was conducted using type of settlement and employment status as the independent variables. There was no statistically significant difference among the employed and unemployed groups on the combined dependent variables on adherence to malaria treatment (Wilks' Lambda value=0.995, F=0.53, p=0.714).

Nevertheless, there was a statistically significant difference among the types of settlement on the combined dependent variables on adherence to malaria treatment (Wilks' Lambda value=0.926, F=3.99, p<0.001, partial eta squared=0.038). Further evaluation of the differences among the types of settlement on each separate dependent variable showed a statistically significant difference on each of the four dependent variables on adherence (see Table 7.13.2). Table 7.13.3 shows the mean score of the types of settlement for each dependent variable on adherence. The results on the table generally indicate that the urban dwellers reported the best adherence behaviours among the three types of settlement, with the rural dwellers having the poorest.

The combined effect of type of settlement and employment status on adherence to malaria treatment showed a statistically significant relationship (Wilks' Lambda value=0.946, F=2.87, p=0.004, partial eta squared=0.028). The results on the combined effect of type of settlement

and employment status on each dependent variable indicated that on all four variables under adherence to treatment, statistically significant difference existed for only one of the variables, taking the recommended dose of an antimalarial drug (F=7.99, p <0.001, partial eta squared=0.04).

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Type of settlement	Take at recommended time	10.475	2	5.237	4.399	.013	.021
	Take the recommended dose	8.731	2	4.365	4.868	.008	.023
	Stop malaria treatment to save drugs for future use	5.076	2	2.538	4.386	.013	.021
	Shared antimalarial drug with others	4.771	2	2.385	4.176	.016	.020

Table 7.13.2: Tests of Between-Subjects Effects for type of settlement

Dependent Variable	Type of Settlement	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Take at recommended time	urban	4.371	.108	4.159	4.582
	suburban	4.212	.119	3.979	4.446
	rural	3.738	.184	3.377	4.100
Take the recommended dose	urban	4.636	.093	4.452	4.820
	suburban	4.206	.103	4.004	4.409
	rural	4.366	.160	4.053	4.680
Stop malaria treatment to save drugs for future use	urban	1.399	.075	1.251	1.547
	suburban	1.530	.083	1.367	1.693
	rural	1.838	.128	1.586	2.090
Shared antimalarial drug with others	urban	1.357	.075	1.211	1.504
	suburban	1.450	.082	1.288	1.612
	rural	1.784	.127	1.533	2.034

Table 7.13.3: Estimated Marginal Mean for Type of settlement

Summary of Results for Hypothesis One

There was a statistically significant difference among educational levels/groups on the behaviours of taking antimalarial drugs at recommended time, stopping antimalarial treatment to save drugs for future use and sharing an antimalarial course with others. There was no statistically significant difference by education on the behaviour of taking the recommended dose of antimalarial drugs.

There was a statistically significant difference among household income groups on the behaviours of taking antimalarial drugs at recommended time, stopping treatment to save antimalarial drug for future use, and on sharing an antimalarial course with others. However, household income groups were not significantly different in terms of the behaviour of taking the recommended dose of antimalarial.

Also, type of settlement had a statistically significant relationship with all the four variables on adherence (taking antimalarial drugs at the recommended time, taking the recommended dose of antimalarial, stopping treatment to save antimalarial drug for future use, and sharing an antimalarial course with others).

Based on the results of the statistical analysis, the null hypothesis is rejected as the results show that a significant relationship exists between socioeconomic measures of educational level, household income and type of settlement, and adherence to malaria treatment course.

7.14 Hypothesis Two

H0: Socioeconomic position is not related to the use of the recommended antimalarial drugs

H1: Socioeconomic position is related to the use of the recommended antimalarial drugs

Hypothesis two was used to test the relationship between socioeconomic status and the use of recommended type of drug for malaria treatment. Three statistical tests were performed in testing this hypothesis: logistic regression, contingency table, and multiple regression. Variables on the type of antimalarial drugs used last as well as socioeconomic variables were used. This include:

- Predictor/independent variables: educational level, household income, type of settlement, and employment status, perception of antimalarial drugs sold as a complete course as the best for malaria treatment, perception of mixed antimalarial drugs as the best for malaria treatment, and the type of health facility used for malaria treatment (private hospital, government hospital, chemist, and pharmacy)

- Outcome/Dependent variables: getting the complete malaria treatment course, the name of the antimalarial drug used last time, and use of herbal medicine for malaria treatment.

The logistic regression statistics was used in testing the predictive effect of socioeconomic factors on getting the complete malaria treatment course. The result of the model with all the predictor variables was statistically significant, indicating the model was good for differentiating between those who got the complete treatment course last time they used antimalarial drugs and those who did not χ^2 (df 6, N=415) = 66.537, p<0.001. Generally, between 14.8% (Cox & Snell R square) and 21% (Nagelkerke R squared) of the variance in the use of complete treatment course was explained by the model. In addition, the model was able to correctly predict 70.1% of the cases. Results of the predictive effects, represented in Table 7.14.1, shows that among the predictor variables (measures of socioeconomic factors) used in this model, only household income group, employment status and urban settlement made a statistically significant contribution to the model. Educational level and other types of settlement made no significant contribution to the model. Amongst the significant contributors, the strongest predictor of getting the complete treatment course was household income (OR=1.5, 95% C.I=1.2, 1.8) (see Table 7.14.1).

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	-.086	.136	.397	1	.529	.918	.703	1.199
Income group	.375	.098	14.782	1	.000	1.455	1.202	1.762
Employment status	-1.200	.288	17.297	1	.000	.301	.171	.530
Settlement Urban	-1.128	.364	9.600	1	.002	.324	.159	.661
Settlement Suburban	-.588	.331	3.159	1	.075	.555	.290	1.062
Constant	1.253	.812	2.384	1	.123	3.502		

Table 7.14.1: Logistic Regression predicting the likelihood of getting the complete malaria treatment course

Additionally, a logistic regression was conducted to explore the predictive effect of other non-socioeconomic factors -like the perception of antimalarial drugs sold as a complete course as

the best for malaria treatment, perception of mixed antimalarial drugs as the best for malaria treatment, and the type of health facility used for malaria treatment (private hospital, government hospital, chemist, and pharmacy)- on whether or not a malaria patient gets the complete course of antimalarial drugs. The logistic regression model produced was statistically significant in differentiating between those who got the complete treatment course last time they used antimalarial drugs and those who did not χ^2 (df 5, N=415) = 71.906, p<0.001. The model summary showed that overall, between 15.9% (Cox & Snell R square) and 22.2% (Nagelkerke R squared) of the variance in the use of complete treatment course was explained by the model. In addition, the model was able to correctly classify 73.5% of the cases. Results of the predictive effects shows that among all the predictor variables in this model, only two types of health facilities -private (Wald=6.76, p=0.009, OR=3.09, 95% C.I=1.32, 7.25) and chemist (Wald=24.31, p<0.001, OR=0.1, 95% C.I=0.04, 0.24)- made a statistically significant contribution to the model. With private hospital having the highest predictive effect in the model, those who got their antimalarial drug from a private hospital were three times more likely to get the complete course of antimalarial treatment than those who did not. As such, the use of private hospital was important in getting the complete treatment course. For those who used the chemist, getting the complete treatment course has an odds ratio of less than 1 indicating the odds of getting the complete treatment course by those using the chemist decreases by a factor of 0.1, all other factors being equal.

The next statistical analysis conducted in testing this hypothesis was a contingency table with a chi-square test of the relationship between the name of the antimalarial drug used last and socioeconomic factors. For the variable of the name of the antimalarial drug used last, participants' responses were recoded into three groups: those who used ACT, those who used Non-ACT, and those who cannot remember. These were tested using a contingency table with the four measure of socioeconomic position.

The relationship between educational level and the type of antimalarial drugs used last was statistically significant (Pearson chi-square 48.523, p<0.001, Cramer's V=0.169). Those with a higher level of education were more likely to use ACT (with those of postgraduate education having the highest percentage). None of those with no formal education reported they used an ACT.

Household income was also statistically related to the antimalarial drug used (Pearson chi-square 23.573, p=0.009, Cramer's V=0.031). The percentage of those who used ACT within

each household income level/group increased as the income level progressed. The lowest within group percentage of ACT users was among those at the lowest income group of below ₦18,000 (24.3%); while the highest was among those at the highest income level of above ₦300,000 (58.3%).

Type of settlement was also statistically related to the antimalarial drug used (Pearson chi-square 30.337, p<0.001, Cramer's V=0.191). Those in urban areas were the most likely to use ACT, while those from the rural areas were the least likely. 45.7% and 44.4% of the urban and suburban dwellers, respectively, used ACT; each of these were three times higher than the 15.7% of ACT users from rural areas.

Employment status was, however, not statistically significant to the antimalarial drug used last (Pearson chi-square =0.389, p=0.823).

Furthermore, the use of herbal medicine for malaria was explored across different levels of the socioeconomic measures. A standard multiple regression was used to assess how much of the variance in the use of herbal medicine for malaria treatment (dependent variable) was explained by socioeconomic factors (predictor variables). The 'enter' method was used in the multiple regression. Preliminary analyses were conducted to ensure the assumptions of multiple regression with regards to normality, linearity, homoscedasticity and multicollinearity were not violated.

Overall, the multiple regression model was statistically significant and explains 18.2% of the variance in the use of herbal medicine for malaria treatment (R squared = 0.182, F (5,409) =18.143, p<0.001). Evaluation of each of the predictor variables shows that, apart from the urban settlement, other measures of socioeconomic position used in the model (educational level, household income, rural settlement, suburban settlement, and employment status) made a statistically significant contribution to the model (see Table 7.14.2). Furthermore, comparison of the contribution of each predictor variable using the beta values indicates that rural settlement made the strongest contribution (0.264) in explaining the dependent variable when all other variables in the model are controlled for.

Variable	Unstandardized coefficients		Standardized Coefficient Beta	t	Sig.	95% Confidence Interval for B		Part correlation
	B	Std. Error				Lower bound	Upper Bound	
(Constant)	1.914	.269		7.107	.000	1.385	2.444	
Educational level	-.128	.057	-.127	-2.265	.024	-.239	-.017	-.101
household Income	-9.344E-7	.000	-.141	-2.896	.004	.000	.000	-.130
Employment Status	.313	.126	.112	2.479	.014	.065	.561	.111
Suburban settlement	.286	.113	.128	2.528	.012	.064	.508	.113
Rural settlement	.676	.151	.264	4.476	.000	.379	.973	.200

Table 7.14.2: Multiple regression coefficient output showing unique contributions of predictor variables used in the model

Summary of Results for Hypothesis Two

These analyses tested the relationship between the measures of socioeconomic position and the use of recommended antimalarial drugs for malaria treatment. Among the measures of socioeconomic position used in this study, household income group, employment status, and urban settlement were statistically significant predictors of getting the complete malaria treatment course by participants. Therefore, the null hypothesis was rejected. In addition to these socioeconomic factors, the type of facility visited contributed significantly to the decision on getting the complete malaria treatment course. The type of antimalarial drug used last was statistically associated with educational level, household income, and type of settlement. Employment status was however statistically independent from the type of antimalarial drug used last. Among the socioeconomic factors that significantly contributed to the use of herbal medicine for malaria treatment, rural settlement was the strongest contributor.

7.15 Hypothesis Three

H0: The practice of mixing drugs for malaria treatment does not vary according to socioeconomic position

H1: The practice of mixing drugs for malaria treatment varies according to socioeconomic position

The practice of mixing drugs for malaria treatment, which was picked up during the interviews for the qualitative phase of this study, has never been reported in malaria literature. Although reported during the interview by those at lower levels of the socioeconomic gradient, there was need to assess the relationship between this important antimalarial drug use behaviour and measures of socioeconomic factors using a larger sample size as in this survey. The hypothesis three, therefore, looks at how well the measures of socioeconomic factors can predict the practice of mixing drugs for malaria treatment.

Two types of test were conducted in testing this hypothesis, a logistic regression and a multiple analysis of variance. Variables used in the tests include:

- Predictor/independent variables: educational level, household income, type of settlement, and employment status
- Outcome/Dependent variable: use of mixed drugs for malaria treatment and perception of mixed drugs as the best for malaria treatment

The logistic regression test was used in assessing the predictive ability of socioeconomic factors in the practice of mixing drugs for malaria treatment. The full model containing all the predictor variables was statistically significant, χ^2 (df 5, N=415) =93.266, p<0.001, indicating the model can distinguish between those who use mixed drugs for malaria treatment and those who do not. The model summary also showed it explained between 20.1% (Cox & Snell R square) and 26.9% (Nagelkerke R squared) of the variance in the dependent variable with 68.4% of the cases correctly classified. Also, as shown in the output table 7.15.1, three predictor variables significantly contributed to this model (household income, urban settlement, and suburban settlement).

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	-.134	.139	.932	1	.334	.875	.666	1.148
Income group	-.331	.085	15.039	1	.000	.718	.608	.849
Employment status	-.526	.295	3.174	1	.075	.591	.331	1.054
Settlement Urban	1.931	.432	19.998	1	.000	6.894	2.958	16.068
Settlement Suburban	1.535	.418	13.503	1	.000	4.644	2.047	10.533
Constant	-.243	.835	.085	1	.771	.784		

Table 7.15.1: Logistic Regression predicting the likelihood of using mixed drugs for malaria treatment

Of these three, urban settlement was the strongest predictor (OR=6.9, 95% C.I=3.0, 16.1) with those living in urban areas 6.9 times less likely to mix than those who are not. Tables 7.15.2 and 7.15.3 show the results of a cross-tabulation of the frequency of mixing among the different types of settlement and household income groups respectively.

The second test conducted in testing this hypothesis was a multiple analysis of variance used in assessing the differences in perception of mixed drugs as the best drug for malaria treatment among different groups or levels of socioeconomic measures. The multiple analysis of variance showed that among the socioeconomic measures/factors used as independent variables in this hypothesis, only educational levels/groups had a statistically significant relationship with the perception of mixed antimalarial drugs as the best for malaria treatment (F=2.39, p =0.05, partial eta squared=0.02).

			Have used mixed drugs before		Total
			No	Yes	
Settlement type	**Urban**	Count	131	77	208
		% within settlement	63.0%	37.0%	100%
		% within mixing	66.2%	35.5%	50.1%
		% of total	31.6%	18.6%	50.1%
	Suburban	Count	58	66	124
		% within settlement	46.8%	53.2%	100%
		% within mixing	29.3%	30.4%	29.9%
		% of total	14.0%	15.9%	29.9%
	Rural	Count	9	74	83
		% within settlement	10.8%	89.2%	100%
		% within mixing	4.5%	34.1%	20.0%
		% of total	2.2%	17.8%	20.0%
Total		Count	198	217	415
		% within settlement	47.7%	52.3%	100%
		% within mixing	100%	100%	100%
		% of total	47.7%	52.3%	100%
Settlement type	**Urban**	Count	131.2	76.4	207.6
	Suburban	Count	59.2	65.6	124.8
	Rural	Count	9.2	73.4	82.6
Total		Count	199.6	215.4	415

Table 7.15.2: Crosstabulation of Type of settlement and use of mixed drugs for malaria treatment

			Have used mixed drugs before		Total
			No	Yes	
Household Income group (₦)	**below 18,000**	Count % within household income group % within mixing % of Total	9 12.9% 4.5% 2.2%	61 87.1% 28.1% 14.7%	70 100% 16.9% 16.9%
	18,001 to 50,000	Count % within household income group % within mixing % of Total	46 40.0% 23.2% 11.1%	69 60.0% 31.8% 16.6%	115 100.0% 27.7% 27.7%
	50,001 to 100,000	Count % within household income group % within mixing % of Total	37 50.0% 18.7% 8.9%	37 50.0% 17.1% 8.9%	74 100.0% 17.8% 17.8%
	100,001 to 300,000	Count % within household income group % within mixing % of Total	61 70.9% 30.8% 14.7%	25 29.1% 11.5% 6.0%	86 100.0% 20.7% 20.7%
	Above 300,000	Count % within household income group % within mixing % of Total	26 72.2% 13.1% 6.3%	10 27.8% 4.6% 2.4%	36 100.0% 8.7% 8.7%
Total		Count % within household income group % within mixing % of Total	198 47.7% 100.0% 47.7%	217 52.3% 100.0% 52.3%	415 100.0% 100.0% 100.0%

Table 7.15.3: Crosstabulation of household income and use of mixed drugs for malaria treatment

Summary of Results for Hypothesis Three

These analyses tested the predictive effects of the measures of socioeconomic position in the practice of using mixed drugs for malaria treatment. household income, urban settlement, and

suburban settlement were significant predictors of the use of mixed drugs for malaria treatment. Also, of all measures of socioeconomic position, only educational level had a statistically significant relationship with the perception of mixed antimalarial drugs as the best for malaria treatment.

7.16 Hypothesis Four

H0: The use of malaria diagnostic test prior to treatment does not vary according to the level of measures of socioeconomic position

H1: The use of malaria diagnostic test prior to treatment varies according to the level of measures of socioeconomic position

As an important aspect of malaria treatment, the use of malaria diagnostic test prior to treatment plays a key role in the quality of treatment received and in the development and spread of antimalarial drug resistance as its use helps reduce antimalarial drug pressure. Not using a parasite-based diagnostic test prior to treatment was used in this study as an indication of presumptive treatment of malaria. In terms of malaria diagnostic test prior to treatment, the questionnaire investigated participants' perception on the importance of going for a diagnostic test prior to treatment, their reported behaviours in terms of frequency of use, and their use of malaria diagnostic test prior to their current malaria treatment. These variables were further tested for relationships with different socioeconomic factors.

Hypothesis Four, which considers the practice of diagnostic testing prior to malaria treatment across different socioeconomic levels, was tested using logistic regression. In testing the hypothesis, three models were built using three variables that are indicators of the practice of diagnostic testing prior to malaria treatment, and the variables on measures of socioeconomic level. These variables include:

- Predictor/independent variables: educational level, household income, type of settlement, and employment status, perception on the importance of diagnostic testing and type of facility used for current malaria episode.
- Outcome/Dependent variables: malaria diagnostic test prior to the current treatment, malaria diagnostic test for previous treatments, use of malaria diagnostic test for children

Using the dependent variable on malaria diagnostic test prior to treatment, we conducted a logistic regression to assess how well the above-listed predictor variables are in explaining the use of malaria diagnostic test. The full model containing all the predictors was statistically significant, χ^2 (df 9, N=415) =136.879, p<0.001, indicating the fitness of the model to distinguish between those who had malaria diagnostic test prior to treatment of current malaria episode and those who did not. Overall, the model explained between 28.1% (Cox & Snell R square) and 37.7% (Nagelkerke R squared) of the variance in use of malaria diagnostic test prior to current malaria treatment. Also, the model correctly classified 73% of cases, this is a large difference from the 56.1% when the predictor variables were not entered into the model.

As shown in table 7.16.1, only three of the independent variables made a statistically significant contribution to the model (employment status, used the private hospital for current malaria treatment, and the use of chemist for current malaria treatment). Amongst these, the strongest predictor of use of malaria diagnostic test for the current episode was the variable on the use of chemist for the current treatment from a chemist with an odds ratio (OR) of 5.6 (1.15, 27.47). This indicates that the odds of a person who received current malaria treatment from the chemist using malaria diagnostic test prior to treatment is 5.6 times lower than that of those who did not. This was followed by the only direct measure of socioeconomic factor that was significant in this model, employment status, with those in employment 2.8 times more likely to use diagnostic test than those who are not.

In addition to the variable on using diagnostic tests for current malaria episodes, participants were also asked to report on their overall behaviour in terms of using malaria diagnostic test prior to treatment. The essence of this is to assess how consistent they were in the use of malaria diagnostic test prior to treatment.

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	.100	.141	.500	1	.479	1.105	.838	1.458
Income group	.005	.099	.003	1	.957	1.005	.828	1.221
Employment status	1.021	.316	10.461	1	.001	2.777	1.496	5.157
Settlement Urban	-.712	.390	3.330	1	.068	.491	.229	1.054
Settlement Suburban	-.680	.360	3.572	1	.059	.507	.250	1.026
Perception on importance of diagnostic test	.271	.159	2.897	1	.089	1.312	.960	1.792
Used private facility for current malaria treatment	-2.840	.458	38.523	1	.000	.058	.024	.143
Used government facility for current malaria treatment	-.586	.310	3.572	1	.059	.557	.303	1.022
Used the chemist for current malaria treatment	-1.726	.810	4.546	1	.033	5.619	1.150	27.470
Constant	.799	1.322	.365	1	.546	2.223		

Table 7.16.1: Logistic Regression predicting the likelihood of using malaria diagnostic test prior to treatment

For the next analysis, the response on the variable on consistency in use of diagnostic test prior to treatment was dichotomized into those who always use diagnostic test and those who do not use this always. A logistic regression was conducted on this dependent variable using all predictor variable listed under this hypothesis excluding that of the type of facility used for current malaria episode as this was not important in this model. The overall result of the logistic regression model with all the predictor variables was statistically significant, indicating the model was good for differentiating between those who always use malaria diagnostic test prior to treatment and those who do not χ^2 (df 6, N=415) =52.986, p<0.001. Generally, between 12% (Cox & Snell R square) and 21% (Nagelkerke R squared) of the variance in the consistent use of malaria diagnostic test prior to treatment was explained by the model. In addition, 87.7% of the cases were correctly classified by the model. Among the predictor variables used in this model, only three made a statistically significant contribution to the model (educational level, household income level and perception on the importance of diagnostic testing). Employment status and types of settlement made no significant contribution to the model. Amongst the significant contributors, the strongest predictor of consistency in the use malaria diagnostic test

is the perception on the importance of malaria diagnostic test (OR=2.5, 95% C.I=1.4, 4.3) (see Table 7.16.2). The odds of always using malaria diagnostic test prior to treatment is 2.5 times higher for one unit increase in perception of malaria diagnostic test as important (according to the scale used in this study). The next in line regarding strength of contribution to the model is educational level with a positive relationship at odds ratio of 1.835.

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	.607	.219	7.645	1	.006	1.835	1.193	2.821
Income group	.450	.113	15.750	1	.000	1.569	1.256	1.959
Employment status	-.124	.434	.082	1	.774	.883	.377	2.068
Settlement Urban	.494	.600	.676	1	.411	1.638	.505	5.312
Settlement Suburban	.110	.588	.035	1	.852	1.116	.352	3.533
Perception on importance of diagnostic test	.910	.278	10.735	1	.001	2.484	1.441	4.281
Constant	-8.503	1.596	28.394	1	.000	.000		

Table 7.16.2: Logistic Regression predicting the likelihood of always using malaria diagnostic test prior to treatment

The last test for the hypothesis 4 involved the use of malaria diagnostic test prior to treatment in children. As this did not apply to all participants, only responses from participants who reported having at least a child in their household were used in this model. All predictor variables listed under this hypothesis, excluding that of the type of facility used for current malaria episode, were used in this model.

The result of the full model containing all the predictor variables was statistically significant, χ^2 (df 6, N=271) =96.696, p<0.001, indicating the model is able to distinguish between those who use malaria diagnostic test prior to treatment for a child and those who do not. Overall, the model explained between 28.3% (Cox & Snell R square) and 37.8% (Nagelkerke R squared) of the variance in use of malaria diagnostic test prior to malaria treatment in children. In addition, the model correctly classified 74.9% of cases. Furthermore, the only significant predictor of this behaviour was the perception on the importance of diagnostic test (p<0.001,

OR=3.5, 95% C.I=2.4, 5.2). The odds of using malaria diagnostic test prior to treatment for a child is 3.5 times higher for one unit increase in perception of malaria diagnostic test as important level (according to the scale used in this study).

Summary of Results for Hypothesis Four

These analyses tested the effect of the measures of socioeconomic position and other important factors in predicting the use of malaria diagnostic tests prior to current malaria treatment. Employment status was the only socioeconomic measure that significantly predicted the use of malaria diagnostic test prior to current malaria treatment. Other predictors of this behaviour were the use of private hospitals for current malaria treatment, and use of chemist for current malaria treatment.

On the consistency/frequency of the use of parasite-based diagnostic test prior to malaria treatment, educational level and household income level were significant predictors of this behaviour; the other significant predictor was participants' perception on the importance of diagnostic testing. None of the measures of socioeconomic position was a significant predictor of the use of malaria diagnostic test prior to treatment in children; participants' perception on the importance of diagnostic test was the only predictor of this behaviour.

The null hypothesis is rejected on the basis that employment level as a socioeconomic measure, was a significant predictor of the use of parasite-based diagnostic test prior to malaria treatment; and also on the basis that educational level and household income level were significant predictors of consistency in the use of parasite-based diagnostic test prior to malaria treatment.

7.17 Hypothesis Five

H0: The experience of treatment failure is not statistically associated with the measures of socioeconomic position

H1: The experience of treatment failure is statistically associated with the measures of socioeconomic position

The indicators of treatment failure were having previously sought malaria treatment for the current malaria episode, having taken an antimalarial drug for the current episode, and having taken an antimalarial drug within the last 14 days (based on evidence that the reappearance of

the *Plasmodium* parasites within 14 days of treatment with antimalarial drugs is more likely a case of treatment failure than reinfection (Bloland, 2001)).

Descriptive statistics of the variables used as indicators of likely treatment failure cases showed that of the 415 participants in this study, 33% (135 participants) reported they were seeking malaria treatment for the current episode for the first time, while 67% (280 participants) reported they have previously sought malaria treatment for the current episode. Within these 280 participants who had previously sought treatment, 25% (69 participants) reported they have not taken an antimalarial drug for the current episode prior to their visit to the health facility, while 75% (211 participants) reported they have. Of the 211 participants who have previously sought treatment and taken an antimalarial drug for the current malaria episode, 57% (120 participants) had the last malaria treatment more than 14 days to the day they visited the facility, while 43% (91 participants, and 22% of the study participants) had the malaria treatment within the last 14 days. These 91 participants represent the likely cases of treatment failure and drugs resistance.

As this group of likely cases of treatment failure is important to this study, there was a need for further analysis to investigate the differences between participants under this group and those who are not. In line with this, a new variable labeled 'likely case of resistance' was created with a dichotomous response of yes and no. The 'yes' response represented participants who reported they have previously sought treatment for the current malaria episode, taken an antimalarial drug for the current malaria episode, and reported they had taken the last antimalarial drug within 14 days prior to their visit to the health facility. All other participants outside this group were represented by the 'no' response.

This hypothesis was tested using logistic regression with the variables on

- Predictor variables: Measures of socioeconomic position (education, income, type of settlement and employment status)
- outcome/dependent variable: The variable indicating likely treatment failure experience

The result of the model with all the predictor variables was statistically significant, indicating the model was adequate in distinguishing between those who were likely cases of treatment failure and those who were not χ^2 (df 5, N=415) = 36.020, $p<0.001$. Generally, between 8.3% (Cox & Snell R square) and 12.8% (Nagelkerke R squared) of the variance in the experience of likely treatment failure was explained by the model. In addition, the model was able to

correctly classified 80.4% of the cases. The result of the predictive effects, represented in Table 7.8.1, shows that only educational level and suburban settlement contributed significantly to the model. The odds of experiencing suspected treatment failure was 3.1 times higher for suburban dwellers than non-suburban dwellers (OR=3.1, 95% C.I=1.5, 6.4). For educational level, the odds of experiencing suspected treatment failure is 0.6 as one progresses from one level of education to another (OR=0.6, 95% C.I=0.5, 0.9).

Further analysis on this hypothesis involved the use of contingency tables with a chi-square test to assess the relationship between each measure of socioeconomic position and the likely treatment failure experience for statistical significance. As shown in Table 7.8.2, apart from

	B	S.E	Wald	df	p	Odds ratio	95% C.I for Odds Ratio	
							Lower	Upper
Education	-.457	.151	9.130	1	.003	.633	.471	.852
Income	.022	.100	.050	1	.823	1.023	.841	1.243
Urban Settlement	.660	.388	2.894	1	.089	1.935	.904	4.139
Suburban Settlement	1.132	.369	9.434	1	.002	3.102	1.506	6.389
Employment status	-.008	.346	.001	1	.981	.992	.503	1.954
Constant	-.810	.882	.844	1	.358	.445		

Table 7.17.1: Logistic Regression predicting the likelihood being a likely case of treatment failure

Variable	Pearson Chi-square Value	df	P value
Educational level	26.715	4	<0.001
Income group	27.400	5	0.001
Type of settlement	29.070	2	<0.001
Employment status	0.50	1	0.824

Table 7.17.2: chi-squared result of the association between socioeconomic measures and likely treatment failure experience

employment status, all other measures of socioeconomic factor had a statistically significant relationship with the experience of likely treatment failure.

The contingency table with educational level showed that postgraduate education had the highest adjusted residual for those who are likely cases of treatment failure (3.8) and the lowest adjusted residual for those who are not likely cases of treatment failure (-3.8). 90% of those with postgraduate education were not likely cases of treatment failure, only 10% were. Other cells with an adjusted residual of more than 2 were the cells on no formal education (2.6 and -2.6) and the cells on primary education (2.8 and -2.8).

For income level, those whose household income was below ₦18,000 had the highest adjusted residual (3.4 for the cell on likely cases of treatment failure, and -3.4 for the cell on cases who are not likely treatment failure). Of the 91 participants who are likely cases of treatment failure in this study, 27.5% were of household income below ₦18,000 while 33% were of household income ₦18,000 to ₦50,000. Other higher income groups had contributed from 7.7% to 11% each to the 91 likely cases of treatment failure.

Furthermore, for the type of settlement, rural dwellers had the highest adjusted residual (5.4 for the cell on likely cases of treatment failure, and -5.4 for the cell on cases who are not likely treatment failure). Rural dwellers contributed the highest percentage of the 91 likely cases of treatment failure. Also, the comparison of the within group percentage for all types of settlement showed that the rural dwellers had the highest within the types of settlement percentage, with 43% of the rural dwellers in this study among the likely cases of treatment failure.

Summary of Results for Hypothesis Five

Of the 415 participants in this study, 91 were classified as likely cases of treatment failure based on the criteria that they have previously sought treatment for the current malaria episode, already used an antimalarial drug for the current episode, and reported the antimalarial drug was used within the last 14 days to the study. Educational level, household income, and type of settlement were all statistically associated with the experience of likely treatment failure. However, employment status was not. As such, the null hypothesis was rejected.

7.18 Hypothesis Six

H0: The type of facility malaria treatment is sought is not associated with the outcome of treatment failure

H1: The type of facility malaria treatment is sought is associated with the outcome of treatment failure

Hypothesis six focused on exploring whether the type of health facility participants got their last antimalarial drug from and the variable indicating likely treatment failure experience were statistically independent.

In analyzing the relationship between the types of health facility participants received their last antimalarial drug from and the variable on likely treatment failure, a contingency table with a chi-square test was used to check the independence of the two variables as both variables are categorical. The analysis showed a statistically significant association between the type of health facility participants received their last antimalarial drug from and their experience of likely treatment failure (Pearson chi-square = 37.811, df 5, $p<0.001$). The contingency table showed that, with the highest (5.4) and lowest (-5.4) adjusted residuals for the yes and no cells respectively, the chemists contributed most to the significance in this analysis. Of the 91 participants who were in the group of likely cases of treatment failure, 41.8% used the chemist for their last antimalarial drug; this was followed by pharmacy at 34.1% (with participants who got their last antimalarial drug from these two informal health facilities constituting 75.9% of the likely cases of treatment failure).

Summary of Results on Hypothesis Six

There was a statistically significant association between the type of health facility participants received their last antimalarial drug from and their experience of likely treatment failure. The null hypothesis was therefore rejected.

7.19 Hypothesis Seven

H0: Antimalarial drug use practices are not associated with the experience of treatment failure.

H1: Antimalarial drug use practices are associated with the experience of treatment failure.

Hypothesis seven tests the relationship between antimalarial drug use practices, like non-adherence to treatment guideline, and treatment outcome of suspected/likely treatment failure. This was assessed using reports of the last malaria treatment as this will involve less recollection bias than other previous malaria episodes. For this hypothesis, contingency table using chi-square test was used in testing the relationships.

The contingency table included the following variables:

- The use of mixed drugs for malaria treatment; the practice of stopping malaria treatment to save drugs for future use, and sharing of antimalarial course with others.
- The variable indicating likely treatment failure experience

The results of the analysis showed a statistically significant relationship between the practice of mixing and the experience of treatment failure (Pearson chi-square=10.823, df=1, p=0.001). Within the 91 participants who were in the group of likely cases of treatment failure, 67% reported they use mixed drugs for malaria treatment.

Similarly, the crosstabulation of the variable indicating likely treatment failure experience and the practice of stopping malaria treatment to save drugs for future use showed a statistically significant relationship (Pearson chi-square=13.364, df=1, p<0.001). Those who said they stop malaria treatment to save drugs for future use were more likely to have experienced likely treatment failure than those who do not (32.2% of those who stop to save vs. 16.5% of those who do not stop to save)

Like the outcome of the other analysis used in testing this hypothesis, the relationship between the variable indicating likely treatment failure experience and the practice sharing an antimalarial course with others was also statistically significant (Pearson chi-square=17.776, df=1, p<0.001). Within those who reported they share an antimalarial course with others, 34.3% are under the group of likely cases of treatment failure. This was more than double of the within-group percentage for those who do not share antimalarial course (with only 16% reporting likely treatment failure experience).

Summary of Results for Hypothesis Seven

Antimalarial drug use practices like use of mixed drugs for malaria treatment, stopping malaria treatment to save drugs for future use, and sharing an antimalarial course with others were all

statistically related to the experience of likely treatment failure. With this significant relationship, the null hypothesis was rejected.

7.20 Hypothesis Eight

H0: Socioeconomic position does not affect knowledge about malaria infection.

H1: Socioeconomic position affects knowledge about malaria infection.

The variables used in testing this hypothesis were variables on

- Socioeconomic factor (see Table 7.2.4 in the appendix for measurement levels for the socioeconomic factors)
- Knowledge of causes of malaria (using 5 point Likert scale)
- Knowledge of malaria symptoms (using 5 point Likert scale)
- Knowledge of malaria treatment (using 5 point Likert scale).

Two types of statistical analysis were used in testing this hypothesis: two-way between-groups analysis of variance (ANOVA) and multiple analysis of variance (MANOVA).

Knowledge of causes of malaria

Descriptive statistics of the variables on causes of malaria showed that, generally, the study participants' knowledge of the causes of malaria was satisfactory, with 89.1% of the participants indicating they were sure or absolutely sure that mosquito bite can cause malaria. However, other factors with no evidence of a direct causal relationship with malaria infection, like consumption of fatty food and spiritual attack were reported.

Mosquito as a cause of malaria: A two-way between-groups ANOVA was conducted to explore the impact of educational level and type of settlement on the level of knowledge about mosquito bite as a cause of malaria. The interaction effect between educational level and type of settlement was statistically significant ($F = 3.81$, $p < 0.001$) with a medium effect size (partial eta squared = 0.071), that is, 7% of the variance in the knowledge of mosquito as a cause of malaria is accounted for by the interaction effect of educational level and type of settlement. There was a statistically significant main effect for education, ($F = 13.04$, $p < 0.001$), however, the effect size was small (partial eta squared = 0.012). The main effect of type of settlement was not statistically significant (p = 0.090). This means that the knowledge level

of mosquito bite as a cause of malaria does not differ for different types of settlements (rural, suburban and urban); but there is a difference in the level of knowledge of mosquito bite as a cause of malaria for participants of different educational levels. Post-hoc comparisons using the Scheffe test indicated that the mean levels of knowledge for the 'No formal education', 'Primary' and 'Secondary' education groups were each statistically different from that of 'Tertiary' and 'Postgraduate' education groups. See figure 7.20.1 for the profile plot of the analysis.

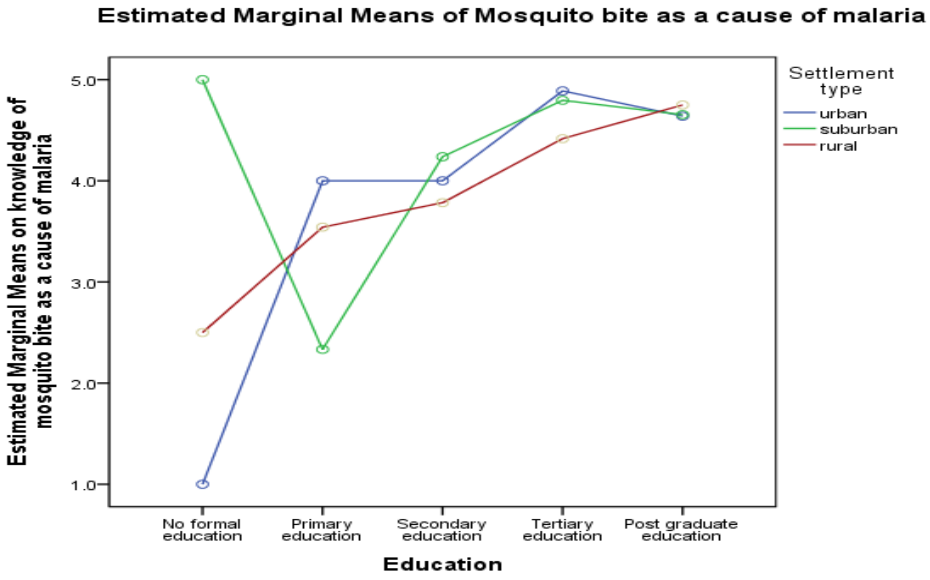

Figure 7.20.1: Profile plot of estimated marginal means for mosquito as a cause of malaria

From the plot, there was no significant difference on knowledge level on mosquito bite as a cause of malaria across all types of settlements within each level of education from secondary education and higher. Nevertheless, there was a difference across the types of settlements for those within the groups with no formal education and those with primary education. Interestingly, for those with no formal education, across the three types of settlements, urban dwellers had the lowest level of knowledge, followed by the rural, while the suburban dwellers had the highest. For those with primary education, the urban dwellers had the highest level of knowledge, followed by the rural dweller, while the suburban dwellers had the lowest level of knowledge on mosquito bite as a cause of malaria.

To explore the interaction between type of settlement alone and the knowledge of mosquito bite as a cause of malaria, the result of the two-way ANOVA was followed up with one-way

ANOVAs with each type of settlements used as a dichotomous independent variable and the knowledge level as the dependent variable. There was a statistically significant difference in the mean level of knowledge on mosquito as a cause of malaria between those living in urban areas and those who are not (p<0.001, F=19.737) with those living in urban areas having a higher mean level of knowledge than those who were not. Similarly, the difference in mean level of knowledge on mosquito as a cause of malaria was statistically significant between those from rural areas and those who were not (p<0.001, F= 48.490), with those living in rural areas having lower level of knowledge than those who were not. The difference in the level of knowledge among those living in suburban areas and those who were not was not statistically significant (p=0.310, F=1.034).

Consumption of fatty/oily food as a cause of malaria: Some participants also attributed the cause of malaria to some other factors with no established direct causal link to malaria, some of these factors include: eating fatty/oily foods, dirty environment, and spiritual attack.

Therefore, this study went further to investigate the impact of educational level and type of settlement on the level of knowledge of fatty/oily food consumption as a cause of malaria. For this, a two-way between-groups ANOVA was conducted. The results show that the interaction effect between educational level and type of settlement was statistically significant (F = 2.62, p = 0.008) (see figure 7.20.2 for profile plot). There was also statistically significant main effect for education (F = 8.60, p < 0.001) and type of settlement (F = 7.58, p = 0.001). The effect size of education alone (partial eta squared = 0.08), which was medium, was more than that of the type of settlement alone (partial eta squared = 0.037), as well as that of the interaction of educational level and type of settlement (0.05). Eight percent (8%) of the variance in the level of knowledge of fatty/oily food consumption as a cause of malaria was accounted for by educational level. Post-hoc comparisons using the Scheffe test indicated that the mean levels of knowledge for the 'No formal education' and 'Secondary' education groups were each statistically different from that of 'Tertiary' and 'Postgraduate' education groups. Within educational levels, those of the highest level of education (postgraduate) had the lowest mean (1.9) on the knowledge of fatty/oily food consumption as a cause of malaria while those of lowest educational level (no formal education) had the highest mean (3.9). The Post-hoc also showed that the mean level of knowledge for rural dwellers was statistically different from that of the urban and suburban dwellers. Within types of settlement, urban dwellers had the lowest mean (2.1) while rural dwellers had the highest mean (3.5).

A follow up with one-way ANOVAs with each type of settlement used as a dichotomous independent variable and the knowledge level as the dependent variable showed a statistically significant difference in the mean level of knowledge of fatty/oily food consumption as a cause of malaria between those living in urban areas and those who are not (p<0.001, F=114.30), with those living in urban areas having a lower mean level of knowledge than the non-urban dwellers. Similarly, the difference between those from rural areas and those from non-rural areas was statistically significant (p<0.001, F= 149.74), with those living in rural areas having a higher level of knowledge than the non-rural dwellers. The difference in the level of knowledge among those living in suburban areas and those who were not was not statistically significant (p=0.240, F=1.384).

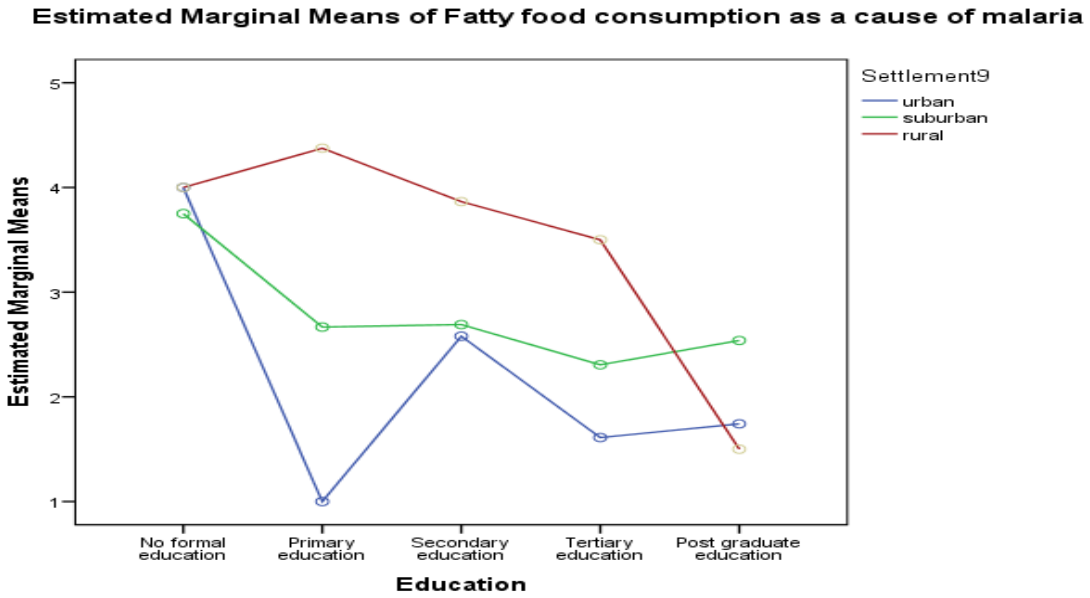

Figure 7.20.2: Profile plot of estimated marginal means for fatty food consumption as a cause of malaria

Dirty environment/surroundings as a cause of malaria: The relationship between educational level and type of settlement on the knowledge or perception of dirty environment as a cause of malaria was also tested using two-way between-groups ANOVA. The results show that the interaction effect between educational level and type of settlement was not statistically significant (p =0.143). There was also not statistically significant main effect for education (p =0.0.826). However, there was a statistically significant main effect for type of settlement (F = 5.50, p = 0.004) with a small effect size of 0.027. The post-hoc comparisons

using the Scheff test indicated the mean difference on the level of knowledge on dirty environment as a cause of malaria was statistically different between rural and urban dwellers (p=0.001), and between rural and suburban dwellers (p=0.003). There was no significant difference between the mean of urban and suburban areas (p=0.989). See figure 7.20.3 for the profile plot of the analysis.

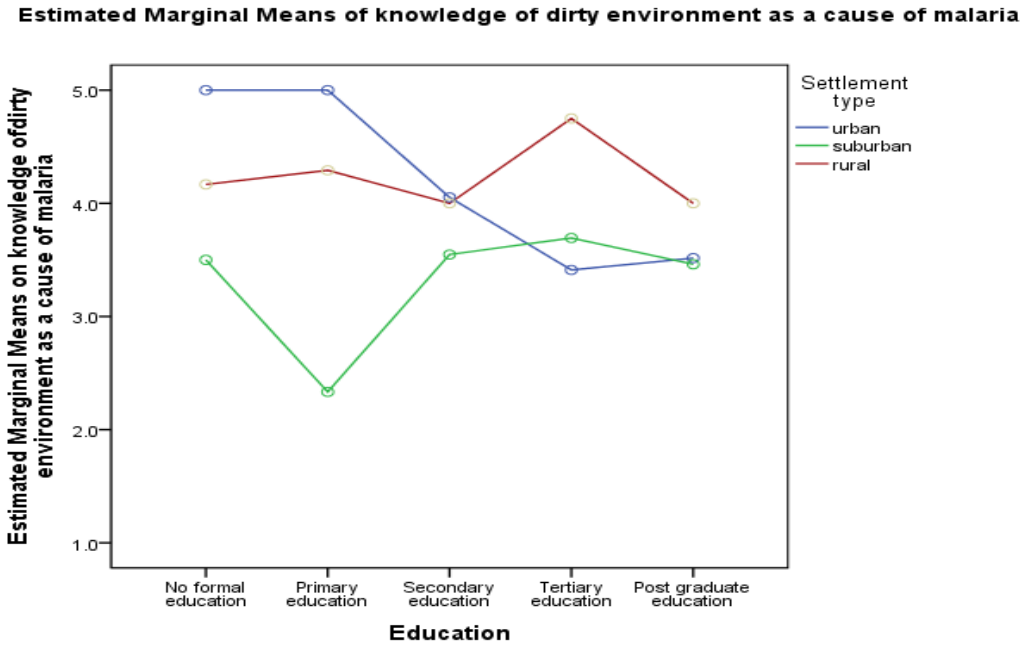

Figure 7.20.3: Profile plot of estimated marginal means for dirty environment as a cause of malaria

Spiritual attack as a cause of malaria: Finally, the effect of educational level and type of settlement on the knowledge of spiritual attack as a cause of malaria was also tested using two-way between-groups ANOVA. The results show that the interaction effect between educational level and type of settlement was statistically significant (F = 3.60, p < 0.001) with a medium effect size (partial eta squared = 0.07). There was also statistically significant main effect for education (F = 3.93, p = 0.004) and type of settlement (F = 6.41, p = 0.002). The individual effect sizes of education and type of settlement were both small at partial eta squared of 0.04 and 0.03 respectively.

Post-hoc comparisons using the Scheffe test indicated that the mean level of knowledge for the 'No formal education' was not statistically different from that of 'Primary education' group. Similarly, the mean level of knowledge for the 'Tertiary education' was not statistically

different from that of 'Postgraduate education' groups. Other combinations of educational groups were all statistically different from each other. Within educational levels, those of the highest level of education (postgraduate) had the lowest mean (2.09) on the knowledge of spiritual attack as a cause of malaria, while those of lowest educational level (no formal education) had the highest mean (4.27).

The Post-hoc also showed that the mean level of knowledge for rural dwellers was statistically different from that of the urban and suburban dwellers. There was no significant difference between the mean of urban and suburban areas. Also, within types of settlement, urban dwellers had the lowest mean (2.482), closely followed by the suburban (2.483), while rural dwellers had the highest mean (3.4). See Figure 7.20.4 for the profile plot of the analysis.

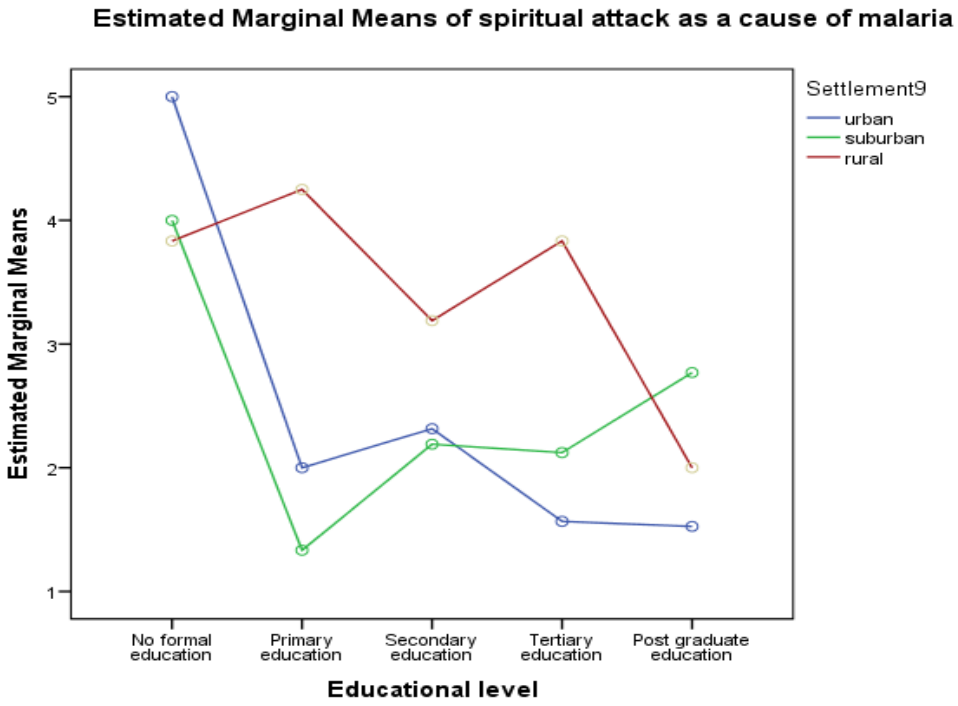

Figure 7.20.4: Profile plot of estimated marginal means for spiritual attack as a cause of malaria

Knowledge of malaria symptoms

Knowledge of malaria symptom was also explored alongside some measures of socioeconomic status. The two-way between-groups ANOVA was used to test the effect of educational and type of settlement in the variance in the level of knowledge on some malaria symptoms like fever and vomiting.

For knowledge of fever as a malaria symptom, the interaction effect between educational level and type of settlement was statistically significant ($F = 3.92$, $p < 0.001$) with a medium effect size (partial eta squared = 0.073), that is, 7.3% of the variance in the knowledge of fever as a symptom of malaria is accounted for by the interaction effect of educational level and type of settlement. There was a statistically significant main effect for education, ($F = 6.75$, $p < 0.001$), with a medium effect size (partial eta squared = 0.063). The main effect for type of settlement was also statistically significant (p = 0.006); however, the effect size was small (partial eta squared = 0.025).

The posthoc comparisons using the Scheffe test indicated that the mean level of knowledge for those with 'No formal education' was statistically different from that of those of 'Tertiary' and 'Postgraduate' education groups. While the level of knowledge for those who had 'primary education' were statistically different from that of those of 'Secondary', Tertiary' and 'Postgraduate' education groups. Within educational level, those who had postgraduate education had the highest mean (4.8) on the knowledge of fever as a malaria symptom while those of primary education had the lowest mean (3.3). The Post-hoc also showed that the mean level of knowledge for rural dwellers was statistically different from that of the urban dwellers. Within types of settlement, urban dwellers had the lowest mean (3.7) while rural dwellers had the highest mean (4.5). This shows that the average level of knowledge of fever as a malaria symptom is highest in the rural areas than in other types of settlements.

Furthermore, the interaction effect between educational level and type of settlement on knowledge of vomiting as a malaria symptom was not statistically significant ($F = 1.05$, $p = 0.401$). Similarly, the main effect of educational level was not statistically significant ($F = 1.76$, $p = 0.137$). However, the main effect of type of settlement was statistically significant ($F = 3.17$, $p = 0.016$, partial eta squared = 0.016). Within the types of settlement, those from rural areas had the highest mean level of knowledge of vomiting as a malaria symptom (4.34) while those from urban areas had the lowest mean level (3.63).

From the qualitative interviews, some symptoms that were associated with malaria by the participants had with no established evidence in literature as symptoms or manifestations of malaria infection. One of such symptoms tested under this hypothesis was bitterness of mouth.

The interaction effect between educational level and type of settlement on knowledge of bitterness of mouth, as a symptom of malaria, was not statistically significant (F=1.57, p=0.133). The main effect of type of settlement was also not statistically significant (F=0.21,

p=0.812). Nevertheless, the main effect of educational level was statistically significant (*F*=3.76, *p*=0.005) with a medium effect size (partial eta squared=0.036). Although the Post hoc test showed no significant difference within groups under educational level, however, those of primary education had the lowest mean level of knowledge of bitterness of the mouth as a malaria symptom (3.72) while those of postgraduate education had the highest mean level (4.41).

Knowledge of best type of medication to treat malaria

In exploring the relationship between participants' socioeconomic status and level of knowledge on the best type of medication to treat malaria, MANOVA test was used. In conducting this analysis, variables on the different malaria treatments reported in this population (mixed drugs for malaria, antimalarial drugs sold as complete course, herbal medicine for malaria) were used as dependent variables while measures of socioeconomic factors.

The first MANOVA tested to see if there is any difference in the level of knowledge on the best type of medication for malaria treatment (dependent variables) between the groups under the education variable and also the household income groups (independent variables). There was a statistically significant difference among the educational levels/groups on the combined dependent variables on best medicine for malaria treatment (Wilks' Lambda value=0.945, *F*=1.849, *p*=0.037, partial eta squared=0.02). When the results for the dependent variables were considered separately for educational groups, there was a statistically significant difference among educational levels/groups on the knowledge of mixed antimalarial drugs as the best medicine for malaria treatment (*F*=2.39, *p* =0.05, partial eta squared=0.02) and on the knowledge of antimalarial drugs sold as complete course as the best medicine for malaria treatment (*F*=2.81, *p*=0.025, partial eta squared=0.03). However, there was no statistically significant difference among the educational groups on the knowledge of herbal medicine for malaria as the best medicine for malaria treatment (*F*=0.41, *p*=0.805). An inspection of the mean scores for the significant results on the separate variables indicated that, for knowledge of mixed antimalarial drugs as the best medicine for malaria treatment, those with no formal education had the highest mean (Mean=3.97); while for knowledge of antimalarial drugs sold as complete course as the best medicine for malaria treatment, those with no formal education had the lowest mean (Mean=3.71).

There was a statistically significant difference among the household income groups on the combined dependent variables on best medicine for malaria treatment (Wilks' Lambda value=0.911, *F*=2.44, *p*=0.002, partial eta squared=0.30). Consideration of differences among the household income groups on the dependent variables individually showed a statistically significant difference in the knowledge of antimalarial drugs sold as complete course as the best medicine for malaria treatment (*F*=3.34, *p* =0.006, partial eta squared=0.04) and knowledge of herbal medicine for malaria as the best medicine for malaria treatment (*F*=3.55, *p*=0.004, partial eta squared=0.04). There was no statistically significant difference on knowledge of mixed antimalarial drugs as the best medicine for malaria treatment (*F*=0.41, *p* =0.845, partial eta squared=0.005). Further consideration of the mean scores for the significant results on the separate variables indicated that, for knowledge of antimalarial drugs sold as a complete course as the best medicine for malaria treatment, those of the highest income level (above ₦300,000) had the highest mean (Mean=4.75) while those of middle income (₦50,001 to 100,000) had the lowest mean (Mean=3.67). For knowledge of herbal medicine for malaria as the best medicine for malaria treatment, those of high-income group of ₦100,001 to ₦200,000 had the lowest mean (Mean=3.71) while those of the lowest income group (below 18,000) had the highest mean (Mean=3.35).

The combined effect of educational level and household income groups on the combined dependent variables on best medicine for malaria treatment showed a statistically significant relationship (Wilks' Lambda value=0.804, *F*=1.83, *p*=0.001, partial eta squared=0.07). When the results for the dependent variables were considered separately for educational groups and household income (combined independent variables), there was no statistically significant difference between the groups on the knowledge of mixed antimalarial drugs as the best medicine for malaria treatment (*F*=1.55, *p* =0.080) and knowledge of herbal medicine for malaria as the best medicine for malaria treatment (*F*=1.53, *p*=0.086). However, there was a statistically significant difference in the knowledge of antimalarial drugs sold as complete course as the best medicine for malaria treatment (*F*=2.32, *p* =0.003, partial eta squared=0.09).

This analysis of the relationship between participants' socioeconomic status and level of knowledge on the best type of medication to treat malaria went further to explore the effect using other measures of socioeconomic status like the type of settlement and employment status. There was a statistically significant difference among the types of settlement on the combined dependent variables on best medicine for malaria treatment (Wilks' Lambda value=0.965, *F*=2.46, *p*=0.023, partial eta squared=0.02). Breaking the analysis down to the

relationship of type of settlement to the individual dependent variables under the best treatment for malaria indicated that no statistically significant difference exist among the types of settlement on the knowledge of mixed antimalarial drugs as the best medicine for malaria treatment (F=0.02, p=0.981) and on the knowledge of herbal medicine for malaria as the best medicine for malaria treatment (F=0.79, p=0.455). There was, however, a statistically significant difference between the types of settlement on the knowledge of antimalarial drugs sold as complete course as the best medicine for malaria treatment (F=6.57, p=0.002, partial eta squared=0.03). Consideration of the mean scores for this significant result showed that suburban dwellers had the lowest mean (Mean=4.1); this was followed by the rural dwellers (Mean=4.3) while the urban dwellers had the highest mean (Mean=4.6). The mean score differences between the groups were, however, small.

In addition, the results also indicated that a statistically significant difference existed among the employment status groups (employed and unemployed) on the combined dependent variables on best medicine for malaria treatment (Wilks' Lambda value=0.959, F=5.84, p=0.001, partial eta squared=0.04). Consideration of differences among employment status groups on each of the dependent variables separately, showed no statistically significant difference on the knowledge of mixed antimalarial drugs as the best medicine for malaria treatment (F=0.08, p=0.775) and on the knowledge of antimalarial drugs sold as complete course as the best medicine for malaria treatment (F=3.55, p=0.060). Nevertheless, the difference in the employment status groups on knowledge of herbal medicine as the best medicine for malaria treatment was statistically significant (F=12.30, p =0.001, partial eta squared=0.03). Further consideration of the mean scores for this significant result indicated that the unemployed group had a lower mean score (Mean=2.48) compared to the employed (Mean=2.54). Again, the difference in the mean scores between the groups is small.

The combined effect of type of settlement and employment status on best medicine for malaria treatment showed a statistically significant relationship (Wilks' Lambda value=0.957, F=3.04, p=0.006, partial eta squared=0.02). When the results for each dependent variable was considered separately for type of settlement and employment status (combined independent variables), there was a statistically significant difference among the groups on the knowledge of mixed antimalarial drugs as the best medicine for malaria treatment (F=3.70, p =0.026, partial eta squared=0.02) and knowledge of antimalarial drugs sold as a complete course as the best medicine for malaria treatment (F=4.62, p=0.010). However, there was no statistically

significant difference on the knowledge of herbal medicine for malaria as the best medicine for malaria treatment.

Summary of Results for Hypothesis Eight

These analyses tested the differences in the level of knowledge about malaria infection among participants of different socioeconomic positions. Educational level and type of settlement together had a statistically significant interaction effect on the knowledge of mosquito bite as a cause of malaria, fatty food consumption as a cause of malaria, spiritual attack as a cause of malaria, and fever as a malaria symptom. Given these significant relationships, the null hypothesis was rejected. However, the interaction effect of educational level and type of settlement was not statistically significant on the knowledge of dirty environment as a cause of malaria, vomiting as a malaria symptom, and bitterness of mouth as malaria symptom.

On the knowledge of the best medication for malaria treatment all the measures of socioeconomic factors in this analysis -educational level, type of settlement, household income, and employment status- showed a statistically significant relationship.

7.21 Hypothesis Nine

H0: Socioeconomic status does not affect perceptions about malaria infection.

H1: Socioeconomic status affects perceptions about malaria infection.

The variables used in testing this hypothesis were:

- Independent variables: variables on socioeconomic factor (educational level, household income, type of settlement and employment status). The independent variables were all used as categorical.
- Dependent variables: variables on the perception of malaria as a treatable condition, the perception of malaria as a life-threatening condition, and perception on sickle cell gene as protective against malaria. The dependent variables were scale variables

Multiple analysis of variance (MANOVA) was used in testing this hypothesis. The first MANOVA included educational level and household income while the second MANOVA included the type of settlement and employment status.

There was a statistically significant difference among the educational levels/groups on the combined dependent variables on perception about malaria (Wilks' Lambda value=0.927, F=2.47, p=0.003, partial eta squared=0.03). Evaluating the results for each dependent variable separately indicated a statistically significant difference existed among educational levels/groups on the perception of malaria as a treatable condition (F=3.83, p =0.005, partial eta squared=0.04) and on the perception of sickle cell gene as protective against malaria (F=2.71, p=0.030, partial eta squared=0.03). However, there was no statistically significant difference among the educational groups on the perception of malaria as a life-threatening condition (F=0.68, p=0.604). An inspection of the mean scores for the significant results on the separate variables indicated that on the perception of malaria as a treatable condition, those with no formal education had the lowest mean (Mean=2.8) while those of tertiary education had the highest mean (Mean=4.3). There was a progressive difference in mean as the educational level increased up till tertiary education. For perception of sickle cell gene as protective against malaria, those with no formal education also had the lowest mean (Mean=1.9), however, the highest mean was for primary education (Mean=2.8).

There was no statistically significant difference among the household income groups on the combined dependent variables on perceptions about malaria (Wilks' Lambda value=0.968, F=0.83, p=0.642).

The combined effect of educational level and household income groups on the combined dependent variables on perception about malaria showed a statistically significant relationship (Wilks' Lambda value=0.760, F=2.32, p<0.001, partial eta squared=0.9). When the results for each dependent variable was considered separately for the combined independent variables (educational groups and household income), there was a statistically significant difference between the groups on the perception of malaria as a life-threatening condition (F=2.40, p =0.002, partial eta squared=0.09) and perception of sickle cell gene as protective against malaria (F=3.04, p<0.001). There was no statistically significant difference in the perception of malaria as a treatable condition (F=1.60, p =0.067).

Further analysis of the perceptions about malaria involved a second MANOVA using type of settlement and employment status as independent variables. There was no statistically significant difference among the employed and unemployed groups on the combined dependent variables on perceptions about malaria (Wilks' Lambda value=0.983, F=2.39, p=0.068).

There was a statistically significant difference among the types of settlement on the combined dependent variables on perceptions about malaria (Wilks' Lambda value=0.966, F=2.39, p=0.027, partial eta squared=0.02). Further evaluation of the difference among types of settlement on each of the dependent variable showed a statistically significant difference in the perception of malaria as a treatable condition (F=3.42, p=0.034, partial eta squared=0.02) and the perception of sickle cell gene as protective against malaria (F=3.96, p=0.20, partial eta squared=0.02). No statistically significant difference observed among the types of settlement on the perception of malaria as a life-threatening condition (F=0.06, p=0.942). Comparing the mean score of the significant results showed that, on the perception of malaria as a treatable condition, the rural dwellers had the lowest mean (3.7) while the urban dwellers had the highest mean (Mean=4.3); while on the perception of sickle cell gene as protective against malaria the rural dwellers had the highest mean score (3.0) followed by the urban dwellers (Mean=2.6) with the suburban dwellers scoring the lowest (Mean=2.4).

The combined effect of type of settlement and employment status on the perceptions about malaria showed a statistically significant relationship (Wilks' Lambda value=0.969, F=2.14, p=0.047, partial eta squared=0.02). The results on each dependent variable indicated that on the perception of malaria as a treatable condition and the perception of sickle cell gene as protective against malaria, there was no statistically significant difference when the two independent variables are entered together in the model. However, a statistically significant difference between the groups was observed on the perception of malaria as a life-threatening condition (F=4.79, p =0.009, partial eta squared=0.02).

Summary of results for Hypothesis Nine

There was a statistically significant difference among the educational levels and also among types of settlement on the perceptions of malaria as a treatable condition, and sickle cell gene as protective against malaria; however, there was no statistically significant difference among the educational levels and among the types of settlement on the perceptions of malaria as life-threatening condition. There was no statistically significant difference among household income groups on the perceptions about malaria. The null hypothesis is therefore rejected as socioeconomic factors were significantly associated with perceptions about malaria.

7.22 Hypothesis Ten

H0: The use of preventive measures is not associated with level of socioeconomic measures

H1: The use of preventive measures is associated with level of socioeconomic measures

In collecting data on the use of malaria preventive measures, participants were provided with a list of different methods used in malaria prevention in the study population, and were instructed to indicate the methods they use for malaria prevention by selecting a point on a feive-point Likert scale (scale running from never use to always use) that represents their frequency of use for each method. The listed preventive methods include the use of insecticides, local insecticides (Otapiapia, Tusatusa etc.), mosquito bednets, door and/or window mosquito nets, and avoidance of stagnant water around the house. Further analyses were conducted using the preventive measures most prominent in the population to explore the predictors of their use.

In testing the association between socioeconomic measures and use of malaria preventive measures, the logistic regression method was used. The choice of this statistical test for this relationship is based on the type of dependent/outcome variables (dichotomous categorical), and the type of independent/predictor variables -continuous (household income level), scale (educational level) and dummy coded categorical variables (type of settlement and employment status). In addition to the logistic regression, a contingency table with a chi-square test was used in exploring the reasons for inconsistency for participants from different levels of the socioeconomic measure who reported inconsistency in use of preventive measures.

The variables used in testing this hypothesis include:

- Predictor/independent variables: educational level, household income, type of settlement, and employment status
- Outcome/Dependent variables: malaria preventive methods used, and reasons for inconsistency in using mosquito bed-nets.

The logistic regression models built in testing this hypothesis all contained six predictor variables on socioeconomic measures–with the original variable on type of settlement with three categories (of rural suburban and urban) dummy coded into dichotomous categories with each category recoded into a new variable of yes and no based on the response.

The first logistic regression was conducted to assess how well the measures of socioeconomic postion predict the use of insecticides for malaria prevention. The full model containing all the predictors was statistically significant, χ^2 (df 5, N=415) =86.087, p<0.001, showing that the model was able to differentiate between respondents who reported they use insecticide and those who reported they do not. Overall, the model explained between 25.5% (Cox & Snell R square) and 45.7% (Nagelkerke R squared) of the variance in use of insecticide and correctly classified 86.7% of cases. As shown in Table 7.22.1, only three of the independent variables made a statistically significant contribution to the model (educational level, urban settlement, and suburban settlement). The strongest predictor of use of insecticide was educational level with an odds ratio (OR) of 1.9 (1.27, 2.79). This indicates that the odd of a person using insecticide for malaria prevention is 1.9 times higher with one unit increase in participant's educational level (according to the scale used in this study). Urban and suburban types of settlement both had negative odds ratio with the use of insecticide suggesting that the odds of a person using insecticide is lower for someone who lives in urban or suburban settlements than for a person who does not.

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	.632	.201	9.892	1	.002	1.881	1.269	2.789
Employment status	.118	.454	.067	1	.796	1.125	.462	2.736
Income group	.049	.178	.076	1	.783	1.050	.741	1.489
Settlement. Urban(1)	-4.321	1.068	16.378	1	.000	.013	.002	.108
Settlement. Suburban(1)	-1.209	.383	9.958	1	.002	.298	.141	.632
Constant	3.650	1.440	6.427	1	.011	38.456		

Table 7.22.1: Logistic Regression predicting the likelihood of using insecticide for malaria prevention

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	.435	.170	6.575	1	.010	1.545	1.108	2.153
Employment status	.730	.447	2.661	1	.103	2.074	.863	4.985
Settlement Urban	-1.402	.430	10.630	1	.001	.246	.106	.572
Settlement Suburban(1)	-1.287	.394	10.696	1	.001	.276	.128	.597
Income group	-.537	.115	21.768	1	.000	.585	.467	.732
Constant	3.047	.962	10.028	1	.002	21.042		

Table 7.22.2: Logistic Regression predicting the likelihood of using mosquito bednets for malaria prevention

The second logistic regression was used to test the relationship between the measures of socioeconomic factors and the use of mosquito bednets for malaria prevention. The full model containing all the predictors was statistically significant, χ^2 (df 5, N=415) =26.565, p<0.001, showing that the model was able to differentiate between respondents who reported they use mosquito bednets and those who reported they do not. As a whole, the model explained between 6.2% (Cox & Snell R square) and 10% (Nagelkerke R squared) of the variance in use of mosquito bednets and correctly classified 80.7% of cases. As shown in Table 7.22.2, only four of the independents made a statistically significant contribution to the model (educational level, urban settlement, suburban settlement, and household income). Of these, educational level was the strongest predictor of use of mosquito bednets with an odds ratio of 1.5 (95% C.I=1.11, 2.15). This indicates that the odd of a person using mosquito bed net is 1.5 times higher with one unit increase in participant's educational level (according to the scale used in this study). Urban and suburban types of settlement and household income all had negative odds ratio with the use of mosquito bed-nets.

Furthermore, the use of door and/or window nets for malaria prevention was assessed. The overall model containing all the predictors was statistically significant, χ^2 (df 5, N=415) =97.960, p<0.001, showing that the model was fit to distinguish between participants who reported they use door and/or window nets and those who reported they do not. Overall, the

model explained between 21% (Cox & Snell R square) and 34.2% (Nagelkerke R squared) of the variance in use of door and window nets, and correctly classified 86.7% of cases. As shown in Table 7.22.3, only three of the independent variables made a statistically significant contribution to the model (educational level, suburban settlement, and household income). Of these, educational level was the strongest predictor of use of door and window nets for malaria prevention with an odds ratio of 1.9 (1.3, 2.7). This was followed by household income with an odds ratio of 1.6 (1.2, 2.1).

The last phase of the analysis for the hypothesis involved crosstabulation or contingency table in assessing the relationship between socioeconomic factors and the reasons given by the respondents for inconsistency in the use of mosquito bednets.

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	.652	.181	12.951	1	.000	1.919	1.345	2.736
Employment status	.273	.409	.447	1	.504	1.314	.590	2.926
Settlement Urban	-.574	.418	1.889	1	.169	.563	.248	1.277
Settlement Suburban(1)	-1.440	.408	12.448	1	.000	.237	.106	.527
Income group	.465	.140	11.030	1	.001	1.592	1.210	2.094
Constant	-.671	.972	.476	1	.490	.511		

Table 7.22.3: Logistic Regression predicting the likelihood of using mosquito bednets for malaria prevention

The variable on not using mosquito bednets consistently because of sweating when sleeping under the net was statistically associated with the type of settlement only, χ^2 (df 1, N=415) =18.285, p<0.001, phi = 0.234 (small effect size). There was no statistical association with other socioeconomic factors -household income (p=0.282); employment status (p=0.058); educational level (p=0.988).

The variable on inconsistency in using mosquito bednets because of discomfort from the embedded insecticide, was statistically significant with employment status alone χ^2 (df 1, N=415) =11.955, p=0.003, phi = 0.189 (small effect size). Other socioeconomic factors showed

no statistical association –household income (p=0.060); educational level (p=0.094); type of settlement (p=0.144).

Finally, the variable on inconsistency in using mosquito bednets because bednet owned is too small for bed, three of the socioeconomic factors were showed a significant association – household income χ^2 (df 5, N=415) =13.760, p=0.017, phi = 0.205 (small effect size); employment status χ^2 (df 1, N=415) =8.158, p=0.004, phi = 0.158 (small effect size); and educational level χ^2 (df 4, N=415) =11.551, p=0.021, phi = 0.188 (small effect size). Only type of settlement had no significant association (p=0.430).

Summary of Results for Hypothesis Ten

These analyses tested the effect of the measures of socioeconomic position in predicting the use of malaria preventive measures. Educational level was a significant predictor of the use of insecticides, mosquito bednets, and door and/or window nets. Urban and suburban settlement significantly predicated the use of insecticides and mosquito bednets. In addition, suburban settlement was a significant predictor of door and/or window net use. Also, household income was a significant predictor of the use of mosquito bednets. The null hypothesis was therefore rejected based on the results of these tests.

7.23 Hypothesis Eleven

H0: There is no difference in malaria treatment seeking behaviours for children across the levels of socioeconomic measures

H1: There is difference in malaria treatment seeking behaviours for children across the levels of socioeconomic measures

This hypothesis focused on exploring malaria treatment seeking behaviours for children from different levels of socioeconomic measures. To effectively test this hypothesis using the available data from this survey, a logistic regression was used.

The variables used in testing this hypothesis include:

- Predictor/independent variables: educational level, household income, type of settlement, and employment status

- Outcome/Dependent variable: use of malaria diagnostic test for children, and the type of health facility normally used for malaria treatment for a child

The logistic regression was conducted using the variables on socioeconomic factors as the predictor variables; and the variables on use of malaria diagnostic test for children as the dependent variables. The result of the model with all the predictor variables was statistically significant, indicating the model is adequate in distinguishing between those who used malaria diagnostic test prior to the last malaria treatment for a child and those who did not χ^2 (df 5, N=415) = 52.311, p<0.001. Generally, between 11.8% (Cox & Snell R square) and 16% (Nagelkerke R squared) of the variance in the use of malaria diagnostic test prior to the last malaria treatment for a child was explained by the model. Also, the model was able to correctly classify 68.7% of the cases. Results of the predictive effects, represented in Table 7.24.1, shows that only four of the predictor variables (educational level, employment status, urban settlement, and suburban settlement) made a statistically significant contribution to the model. Two of the predictor variables (household income and rural settlement) made no significant contribution to the model. Amongst the significant contributors, the strongest predictor of using malaria diagnostic test prior to last malaria treatment for a child was employment status, with the odds of using malaria diagnostic test prior to last treatment for a child two times for those who are employed compared to those who are not (OR=2.1, 95% C.I=1.1, 3.9) (see Table 7.24.1).

Furthermore, a logistic regression was used to assess the relationship between the reported type of health facility normally used for malaria treatment for a child (dependent/outcome variable) and socioeconomic factors (predictive variables). The result of the model with all the predictor variables was not statistically significant χ^2 (df 5, N=415) = 5.080, p=0.406. Participants' level of socioeconomic measures made no significant impact on the type of health facility they usually used for malaria treatment for a child. Descriptive analysis showed that 90% of the participants usually use formal health facilities for malaria treatment for a child.

	B	S.E.	Wald	df	p	Odds Ratio	95% C.I for Odds Ratio	
							Lower	Upper
Educational level	.269	.135	4.013	1	.045	1.309	1.006	1.704
Income group	-.066	.083	.632	1	.427	.936	.796	1.101
Employment status	.734	.316	5.384	1	.020	2.084	1.121	3.874
Settlement Urban	-1.489	.358	17.345	1	.000	.226	.112	.455
Settlement Suburban	-1.218	.331	13.536	1	.000	.296	.155	.566
Constant	1.060	.779	1.851	1	.174	2.885		

Table 7.23.1: Logistic Regression predicting the likelihood of always using malaria diagnostic test prior to treatment for a child using socioeconomic predictors

Summary of Results for Hypothesis Eleven

Educational level, employment status, urban settlement, and suburban were statistically significant predictors of using malaria diagnostic test prior to malaria treatment in children; while household income and rural settlement were not significant predictors of this practice. The measures of socioeconomic position were statistically independent of the type of health facility usually used for malaria treatment for a child. The null hypothesis was rejected as malaria treatment seeking behaviour of having a parasite-based diagnostic test prior to treatment differed across the levels of some socioeconomic measures.

7.24 Additional analysis

7.24.1 Source of Malaria Treatment

More than half of the participants (62.2%) had taken an antimalarial drug within the month of the survey. The source of the last antimalarial drug was statistically significant with the type of antimalarial drug used the last time (Pearson chi-square = 151.426, $p<0.005$). Those who got the antimalarial drug they used last from the chemists were least likely to have used ACT than those who got their last antimalarial drugs from other sources. Of the 163 participants who reported they used ACT the last time, 33.7% got their antimalarial drug from pharmacies, 28.2% were from the public/government hospitals/clinics, 25.8% from the private hospitals,

6.1% from chemists, while 6.1% were from health centres/community health workers. Within facility analysis for the chemists showed that of the 88 participants who got their last antimalarial drug from chemists, only 6.1% used an ACT; 75% used mixed drugs for malaria treatment.

Furthermore, half (50%) of the 33 participants who used artemisinin monotherapies the last time they treated malaria got the drug from a pharmacy; 18.2% got from the chemist while 24.2% got from public hospitals. These three facilities were also the source for 87% of those who used non-artemisinin antimalarial drugs. Unlike the chemists, most of the non-artemisinin antimalarial drugs from government hospitals were received by pregnant women as intermittent preventive therapy.

As shown in the descriptive statistics table 7.2.4 in the appendix, the pharmacy was the most reported usual source of antimalarial drugs; however, when asked what facility will be their first point of seeking malaria treatment if the cost was not a problem, the most reported facility was public/government hospitals, followed by private hospitals. This shows that the population still trusts the quality of service from formal health facilities.

Further analysis of the relationship between the usual source of antimalarial drugs for participants and socioeconomic variables using a contingency table with Pearson chi-square test showed a significant relationship with educational level (Pearson chi-square = 153.149, $p<0.001$); household monthly income (Pearson chi-square = 1587.533, $p<0.001$); employment status (Pearson chi-square = 17.065, $p=0.007$), and type of settlement (Pearson chi-square = 36.490, $p<0.001$).

Those with a lower level of education were more likely to use the chemist as their usual source of antimalarial drugs than those of other levels of education (72.7% and 60.7% of those of no formal education and primary education respectively). However, participants who had tertiary education were more likely to use the pharmacies than other groups.

For those in rural areas, the most usual source of antimalarial drugs was the chemist (59% of rural dwellers). This was different for those in the urban areas where the most usual source of antimalarial drugs was pharmacies (55.3%).

There was a statistically significant relationship between the type of facility participants were seeking malaria treatment from at the time of the survey their most usual source of malaria

treatment (Pearson chi-square = 238.550, p<0.001). For most of the participants, where they were seeking malaria treatment at the time of the survey was different from where they would normally seek malaria treatment (see figure 7.24.1). For instance, among those who were seeking treatment from the private hospitals at the time of the survey, 53.1% use the pharmacy as the most usual source for malaria treatment; while only 25.5% will use private hospitals as their most usual source of malaria treatment. For those who were seeking treatment from government/public hospitals/clinics, 34.5% usually seek treatment from the government/public hospitals/clinics while 28.6%, 22.8%, and 2.4% usually seek malaria treatment from the pharmacies, chemists, and private hospitals respectively. For those who were seeking treatment from the chemists, 77.5% use the chemists as their most usual source of malaria treatment while 12.5% and 10% usually use pharmacies and government/public hospitals respectively. None of those recruited from the chemists used private hospitals as their most usual source of malaria treatment. For those currently seeking treatment from the pharmacies, 78.9% normally use pharmacies as their most usual source of antimalarial drugs; 5.6% will use government/public hospital and 9.9% will use private hospitals. None of those recruited from the pharmacies reported the chemist as their most usual source of malaria treatment.

This pattern indicates that most of the patients recruited from formal healthcare facilities are likely to first seek treatment from an informal health facility before using the formal facilities. Among those who have previously sought treatment for the current malaria episode, (280), 52% were currently seeking treatment from public/government hospitals, 21.1% from private hospitals, 12.2% from chemists, while 14.7% were from pharmacies. Together, the formal health facilities (private and public/government hospitals) were used by 73.1% of those who have previously sought treatment for the current episode. Also, based on their reported most usual sources of malaria treatment, most of those recruited from the formal health facilities do not usually use such facilities.

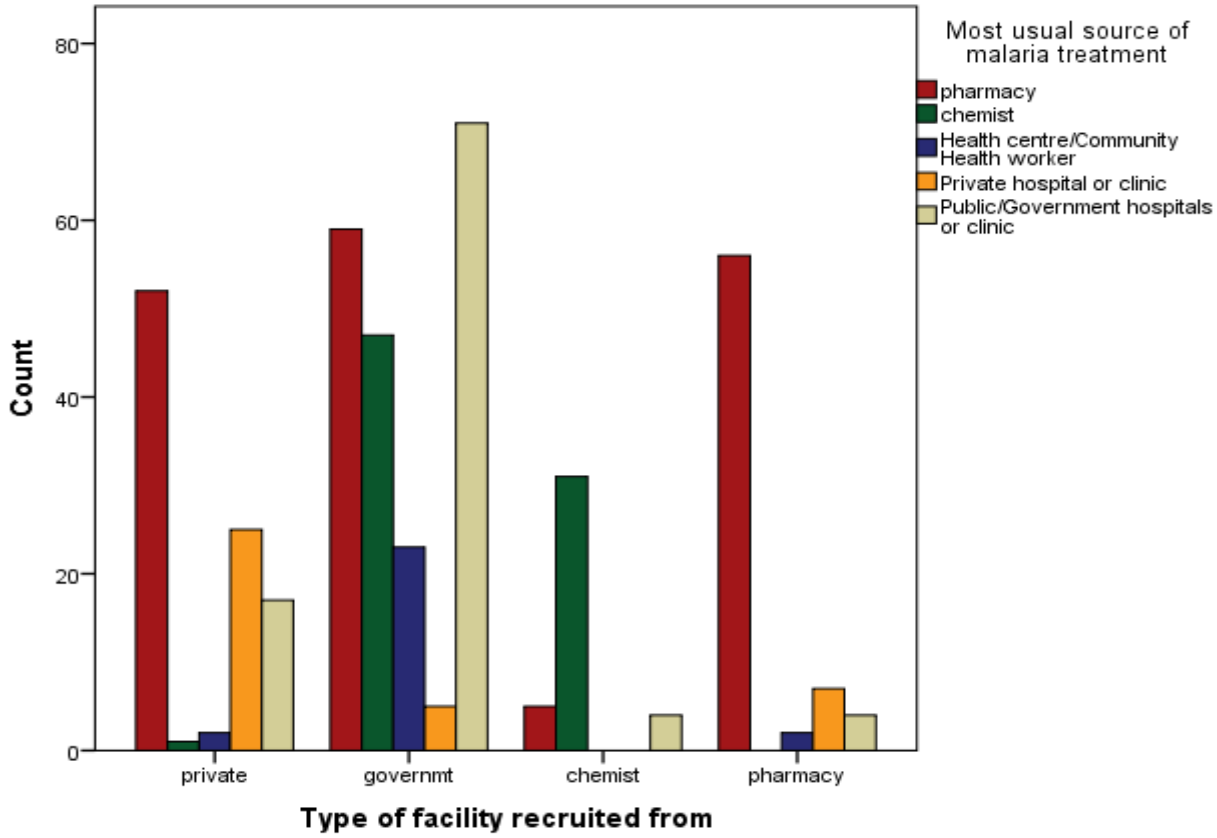

Figure 7.24.1: Chart showing relationship between type of facility used at the time of the survey and most usual facility used for malaria treatment

7.24.2 Decisions on where to seek malaria treatment

This survey went further to investigate factors that influence decisions on where to seek malaria treatment. The most common factors indicated by the participants as important in their decision on where to seek malaria treatment were affordability, good quality of service, waiting time, and availability of antimalarial drugs (see table 7.2.4 in the appendix for descriptive statistics).

The analysis went further to consider the socioeconomic level of participants who said affordability was either important or very important in their decision on where to seek malaria treatment. There was a statistically significant relationship between participants' educational level and how important affordability of the cost of treatment is in their decision on where to seek malaria treatment (Pearson = 61.500, $p<0.001$). Affordability of the cost of treatment was more likely to be important in deciding where to seek malaria treatment for those of lower educational level than those of higher level of education. All participants who had no formal

education reported affordability as an important or very important factor in their decision on where to seek malaria treatment. For participants with tertiary and postgraduate education, about half (53% and 51.1% respectively) reported this as important or very important.

This trend was similar, with a statistically significant relationship between participants' perceived importance of affordability in their decision on where to seek malaria treatment and other measures of socioeconomic status like household income level (Pearson chi-square = 86.990, $p<0.001$); type of settlement (Pearson chi-square = 48.108, $p<0.001$); and employment status (Pearson chi-square = 21.205, $p<0.001$).

7.24.3 Current Malaria Treatment

Although all participants received an antimalarial prescription from the formal or informal health facilities at the time of the survey, 5.1% did not receive an antimalarial drug. Of those who received antimalarial drug on the day of the survey (390 participants), only 71% (277 participants) reported they received the complete course of the antimalarial drug. The most important reason reported for not getting the complete antimalarial course was the price of the complete course (mean score of 3.59, see Table 7.2.4 on descriptive statistics in the appendix).

Participants also reported on the cost of the malaria treatment they have received. This was broken down into two variables: the cost of the malaria treatment, excluding the cost of transportation; and then the cost of transportation. The reported cost of the malaria treatment received ranged from ₦0 to ₦10,000 with a mean cost of ₦1,702 (see table 7.2.4 on descriptive statistics in the appendix). Most of those who reported the cost as ₦0 or no payment were those who had the national or a private health insurance. More than one-third of the participants (38.8%) disagreed or strongly disagreed that this cost malaria treatment is readily affordable to them.

Type of settlement was statistically significant to the participants' opinion about the affordability of the cost of the malaria treatment they received ($p<0.005$). Those from the rural areas were more likely to disagree or strongly disagree that the cost of treatment is readily affordable to them than those from suburban and urban areas. In addition, there was a strong positive correlation between participants' opinion about their affordability of the cost of the malaria treatment they received at the time of the survey and their educational level (Pearson correlation = 0.439, $p<0.001$) as well as with their household income level (Pearson correlation = 0.367, $p<0.001$). Those at the lower levels of the socioeconomic measures were less likely

to identify the cost of their malaria treatment at the time of the survey as affordable than those at higher levels.

Although the most reported method of payment was cash at the point of use (80.2% of participants), other methods of payments like private health insurance (5.1%), national health insurance (5.8%), paying in instalments (1%), credit/post service payment (5.3%) and payment in the form of exchange for services (2.2%) were also reported. While cash payment at the point of use as a payment option was available to patients from all facilities, private health insurance payment option was only reported as a method of payment by participants from private and government hospitals. Also, national health insurance was only reported as a method of payment in private and government facilities. All four participants who reported paying in installments were from government/public hospitals. Payment in exchange for services was reported by participants from private hospitals, government/public hospitals, and pharmacies.

7.24.4 Type of facility participants were recruited from

Further analyses were conducted on the type of facilities participants were seeking treatment from at the time of this survey. There was a statistically significant relationship between the type of facility participants sought treatment from during the study and their type of settlement (Pearson chi-square = 164.704, $p<0.001$). Most of the participants who sought treatment from the chemists (75%) were from rural areas. While most of those who used the private hospitals (85.7%) were from the urban areas. (see figure 7.14.5 in the appendix for crosstabulation on this). Categorizing the types of facilities into formal and informal and running a crosstabulation of this new variable with type of settlement (see figure 7.14.5 in the appendix) shows urban dwellers were the most recruited from formal health facilities, with rural dwellers as the least.

The relationship between the type of facility where participants were recruited from and whether ACT prescription was received was also statistically significant (Pearson chi-square = 104.244, $p<0.001$). Those who were recruited from the chemists were the least likely to have received an ACT (only 2.6% of those who received ACT were from the chemists) than those from other types of facilities. Within the chemists, only 20% received an ACT; this was low compared to the within facility percentages for other facilities –private hospitals (98%), pharmacies (85.9%), government/public hospitals and clinics (67.0%).

Also, there was a statistically significant relationship between the type of facility participants were recruited from, and their getting the complete malaria treatment course on the day of the survey (Pearson chi-square = 71.591, $p<0.005$). Those recruited from the chemists were less likely to had the complete treatment course than those from other facilities.

7.24.5 The Use of Herbal Medicine for Malaria Treatment

As shown in Table 7.2.4 on descriptive statistics in the appendix, the use of herbal treatment was not common (mean score of 1.8 (5 points Likert scale on the frequency of use)). Similarly, the practice of combining herbal malaria treatment with orthodox malaria treatment was not common (mean score of 1.4)

Type of settlement and the use of herbal medicine was also statistically significant (Pearson chi-square, $p<0.001$) with those in the rural areas more likely to use herbal medicine for malaria treatment than participants from other types of settlements. In addition, compared to participants from other types of settlement, rural dwellers were more likely to have combined herbal medicine for malaria treatment with any other antimalarial drug.

CHAPTER EIGHT

DISCUSSION

8.1 Introduction

This chapter offers a discussion of the results of this study. It looks at the implications of the findings of this study while connecting the findings to that of the existing studies in malaria treatment and drug resistance. In addition to these, it considers the importance of the results of this study to malaria control and the overall health of the public.

As earlier stated, this study sets out to explore the contributory role of socioeconomic factors to the development and spread of antimalarial drug resistance; with the aim of creating an understanding of how socioeconomic relations can explain the distribution of the identified antimalarial drug use behaviours and treatment experiences that promote the development and spread of drug resistance. The results of this study suggest that socioeconomic measures (especially educational level, household income, and type of settlement) can influence drug use behaviours (like mixing of drugs, presumptive treatment, stopping treatment to save drugs for future use, sharing of an antimalarial course with others) which can promote the development and spread of antimalarial drug resistance. The results also indicate that the accumulation of socioeconomic disadvantages predisposes some groups of individuals to these health behaviours and affects their malaria treatment experiences and outcomes. See Figure Eight for the identified behaviours and related socioeconomic measures

In further discussing the findings of this study and their implications, this chapter is structured around the identified drug use behaviours and patients' experiences important in antimalarial drug resistance. In discussing each behaviour or treatment experience, the findings of this study are related to the issue under study, and the existing literature. As with other aspects of this work, the social production of disease theory guided the interpretation of the results of this study.

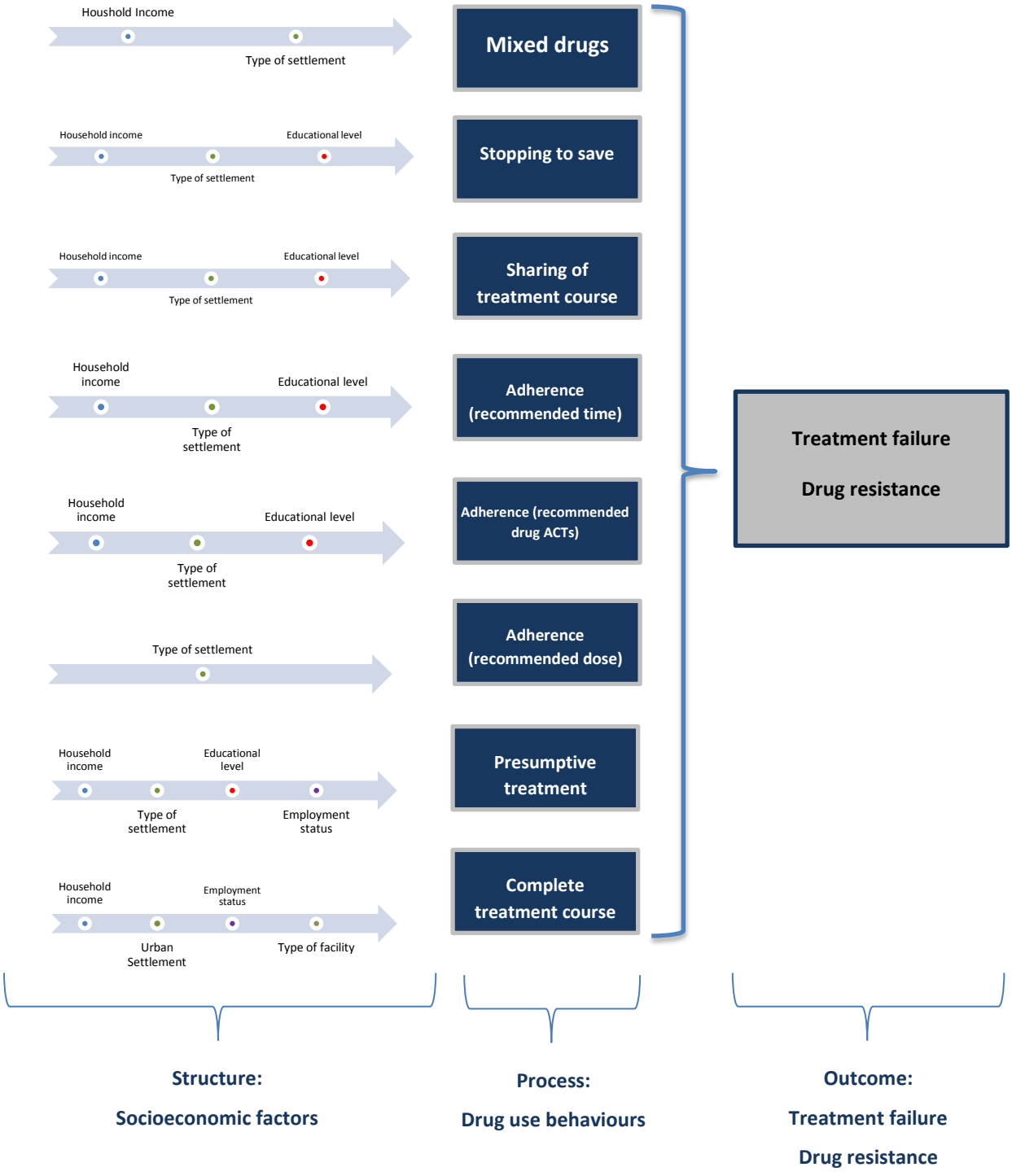

Figure 8.0: Relationships between Socioeconomic Factors and Identified Behaviours

8.2 Adherence to malaria treatment guidelines

Adherence to treatment guideline is an important aspect of malaria treatment as it has the ability to affect treatment experience, the outcome, as well as the efficacy of antimalarial drugs. To

ensure that the efficacy of antimalarial drugs like ACTs is preserved, antimalarial drugs need to be used properly (World Health Organization, 2016d). In assessing adherence rate of participants in this study, questions on adherence to the recommended dosage, getting the complete treatment course, use of recommended antimalarial drugs like ACTs were used.

This study reported a statistically significant difference between some measures of socioeconomic position (educational level, household income, and type of settlement) and the combined indicators of adherence. However, a socioeconomic measure like employment status was not significantly associated with this practice. Nevertheless, living in an urban area was associated with higher level of adherence to treatment guideline compared to living in rural and suburban areas, with the level of adherence poorest among rural dwellers. The individual indicators of adherence were further assessed for a relationship with socioeconomic measures.

8.2.1 Taking the recommended dosage

As an adherence factor, dosing is very important in achieving therapeutic success and in maintaining the efficacy of a drug, especially in cases of antimicrobial drugs used to inhibit the activities of a pathogenic organism (AIDSinfo, 2013; Brown & Bussell, 2011). Therefore, taking the right dose is important as little alterations in the quantity of antimicrobial drugs that pathogenic organisms are exposed to can affect their susceptibility to the drug (Brown & Bussell, 2011).

In relation to malaria infection, adherence to the recommended dosage helps to limit the chances of the parasite surviving treatments and mutating to develop resistance traits. As such, non-adherent behaviours like not taking the recommended dose of an antimalarial drug can have health consequences that transcend the level of the individual adopting the behaviour to affect the wider population.

The findings of this study show that adherence behaviours like taking the recommended dose do not occur randomly, but are rather patterned in association with the type of settlement as a socioeconomic factor. Educational level and employment status were not significantly associated with the practice of administering the recommended dose of antimalarial drugs. The statistical independence of educational level in relation to the practice of administering the recommended dose of antimalarial drug can be an indication that educational level is not an important determinant of whether or not patients administer the recommended dose of their antimalarial drug.

On the type of settlement, urban dwellers in this study reported the highest rate of adherence to the recommended dose than those from other types of settlements. Existing studies have suggested that there is a close relationship between the type of settlements and the type of healthcare facility commonly available and used (Basu, Andrews, Kishore, Panjabi, & Stuckler, 2012; Wagstaff, 2002). Also, the quality of care offered by these different facilities differs (Onwujekwe et al., 2005). As such, the quality of care and the validity of the treatment instructions received from a health facility will affect the way antimalarial drugs are used. Given that most of the urban dwellers (74%) in this study used formal health facilities for their malaria treatment, the high rate of adherence to the recommended dose demonstrated by the urban dwellers in this study might be related to the quality of care and service they received.

8.2.2 Getting the complete treatment

Another practice assessed as an indicator of adherence to treatment guideline in this study was getting the complete treatment course. Although most antimalarial drugs come in blister packs containing the complete treatment course for an individual, however, in some instances, patients using drug vendors can have a complete blister pack shared and sold to them (as seen in mixing). This practice, which leads to under-dosage, and possibly treatment failure, has the potential to prolong the malaria morbidity (in other words, a longer period of transmissibility of the *Plasmodium* parasite) and invariably can lead to the development of resistance. Studies like Watsierah et al., (2011) have also reported the practice of not buying full treatment course among malaria patients in Kenya.

The survey result shows that among the significant predictor of getting the complete malaria treatment course, household income is the strongest. The interpretation of this result can be in line with the fact that household income can determine what resources are available to be spent on health in a household (World Health Organization, 2004). With the cost of antimalarial drugs like ACTs very high (about N1970 ($6.46) for Coartem -Artemether-Lumefantrine) (price from H-medix online Pharmacy as at 24/01/2017) in relation to the earnings of the population (where more than 46% are living below $1.25 per day (World Bank, 2016)); cost/affordability of the recommended antimalarial drugs becomes an important deterrent to getting the complete treatment. Evidently, socioeconomic measures, like household income can affect health behaviours and outcomes by, for example, constituting a barrier to individuals making healthy decisions (Eckenrode, Smith, McCarthy, & Dineen, 2014; López, Loehrer, & Chang, 2016; Pickett & Wilkinson, 2015; Wilkinson & Pickett, 2009). When an individual is

unable to afford the complete course of treatment, they resort to options like buying as many doses as they can afford, especially when this option exists. This is further demonstrated by the survey result which also shows that the higher the household income, the more the likelihood of a participant getting the complete treatment course.

Furthermore, educational level was not a significant predictor of taking the complete treatment course. This might be because, despite their report of this practice, the overall level of participants' knowledge on the complete treatment course as the best way to treat malaria among the participants was high (4.4 out of 5-point scale). So, in other words, despite their understanding of complete treatment course as the best for malaria treatment, socioeconomic factors still constrain their decisions of whether or not to get the complete course.

Apart from the socioeconomic measures that were significant predictors of getting the complete treatment course, type of health facility was another significant predictor of this practice. This highlights the important impact of the health facilities and providers on patients' treatment and illness experience, and the disparity in the quality of care received from different health facilities. Those who used private hospitals (formal health facilities) were the most likely to get complete treatment course; while those from the chemist were the least likely. This trend is related to the result showing that treatment options that promote getting the incomplete course, like mixing, are mostly available in the chemists. Invariably, this links back to the significant association between getting the complete treatment course and household income, given that household income is also associated with the type of health facilities participants used.

8.2.3 Use of the recommended antimalarial drugs for uncomplicated cases -ACTs

The use of combination therapies like ACTs, which is recommended by key policy makers in malaria control in this population, (like the World Health Organization (World Health Organization, 2016d) and the Federal Ministry of Health, Nigeria (Federal Ministry of Health Nigeria, 2011b)) is crucial to the effective treatment and reduction of the morbidity, transmission period, and indeed mortality from malaria infection. As such, compliance, by using the recommended drug, is of importance. Using the recommended drugs helps to reduce wastage and unnecessary costs by ensuring that drugs that the *Plasmodium* parasites in the population are sensitive to are used in malaria treatment (World Health Organization, 2016d). Nevertheless, the decision to use the recommended ACTs or not can be influenced by the interaction of different factors, importantly socioeconomic.

Participants' educational level, household income and type of settlement all had a significant effect on the decision to use ACTs or not. As expected, given its high cost in relation to other antimalarial drugs (Morel, 2004), ACTs were used more by those at higher levels of socioeconomic measures of education and household income, as well as those of urban settlement. The contingency table showing the within group percentages of ACT usage showed that the percentage of those who used ACT within each household income level/group increased as the income level progressed. This result supports the fact that cost and affordability play key roles in ACT usage (Morel, 2004; Yeung, Van Damme, Socheat, White, & Mills, 2008). Important features of ACTs, like their cost, remain key barriers to their use as it places this group of antimalarial drugs outside the reach of the majority poor in malaria endemic countries. Accordingly, the cost of ACT remains a key factor in determining its use and the sustainability of its efficacy in malaria treatment. As long as the level of poverty in Nigeria and other malaria-endemic populations remains high, and the financial cost of first-line treatments for malaria, like ACTs, remains high, the usage of these drugs will be skewed to the disadvantage of those at lower levels of socioeconomic gradient, and their misuse will continue to occur widely in forms like drug mixing, sharing and stopping to save.

8.3 Practice of Mixing Drugs for Malaria Treatment

As stated in chapter six on the qualitative result, the concept and practice of mixing drugs for malaria treatment first came up in the interviews with participants from one of the rural areas and subsequently repeated by other participants from rural and urban areas covered by this study. Further review of malaria literature shows that, despite its popularity in rural areas, the practice of mixing of drugs for malaria treatment has not been reported prior to this study. Although slightly similar, the practice of mixing differs from that of co-prescription in malaria treatment which has been reported long ago in malaria treatment in Nigeria (Gbotosho et al., 2009). Although in both cases one of the rationales for adding other non-malaria therapies is for treatment of the symptoms (like vomiting in the case of co-prescription with anti-histamine (Gbotosho et al.,2009)); nevertheless, unlike in mixing, in cases of co-prescription, the complete course of the drugs, especially the antimalarial drug, is usually given to the patient. But with mixing, the drugs (including antimalarials) are all dispensed as individual single doses that are put together to form a mixed dose; and the users have the option of buying as many doses as they want.

Also, it is important to note that the practice of mixing is different from polypharmacy which appeared in literature more than a century ago (Duerden, Avery, & Payne, 2014). Polypharmacy refers to the concurrent use of multiple medications (usually four or more drugs) by a patient or an individual (Wise, 2013). The difference is that in polypharmacy, the drugs are used as multiple treatments for multiple conditions, whereas in mixing, the drugs are all used for the treatment of one disease condition, malaria. Also, in polypharmacy, unlike in mixing, the complete courses of the drugs are expected to be taken; this is however not the case in mixing, where users only get as much doses as they can afford. As a result of the importance of the practice of using mixed drugs in patient treatment experience and outcome, its use was also assessed in the survey strand of this study; hence the third hypothesis in the survey was the practice of mixing drugs for malaria treatment.

Although generally, the level of agreement among the survey participants on mixed drugs as the best for malaria treatment was low (mean score of 2.4 out of a 5-point scale), more than half (52%) still reported they have used mixed drugs for malaria treatment before. As such, there was need to assess whether the prevalence and distribution of this practice were patterned in line with levels of socioeconomic measures.

8.3.1 Socioeconomic measures associated with the practice of mixing drugs for malaria treatment

One of the key features of the social production of disease theory used in this study is 'contextualization'. Understanding the environment, like the socioeconomic context, in which health and disease outcomes, such as drug resistance, occur is important in epidemiologic studies (Krieger, 2011b). Amongst the socioeconomic factors used in this study, household income and type of settlement were the significant predictors of the practice of mixing.

As earlier stated, the income level of a household can determine the amount of resources available for health and medical care (World Health Organization, 2004). In settings like Nigeria where the cost of healthcare is high -with healthcare expenditure accounting for most of the domestic spending (Onwujekwe et al., 2005), the use of appropriate treatments and therapies becomes challenging for the less well-off. As such, practices like using mixed drugs for malaria treatment was found more among the low-income earners. The odds of using mixed drugs for malaria treatment decreased as income level increased. This finding is a further pointer to the impact of the cost of drugs on the decision of what drug to use. In describing their experience of using mixed drugs for malaria treatment, the interview participants

demonstrated that their use of mixed drugs is driven by the cost of the complete course of malaria treatment. Mixing offers a cheaper route to malaria treatment, even though many of those in the survey who reported that they use mixed drugs did not see it as the best malaria treatment. Given the high cost of antimalarial drugs like ACTs (which is the recommended treatment for malaria); those who cannot afford the cost of the drug devise means of coping with the recurrent malaria episodes. Nevertheless, the interview result shows that some of the participants who have mixed reported the failure of the drug to treat the infection after use. This was further corroborated by the survey result showing a statistically significant relationship between the practice of mixing and suspected treatment failure. More than half of those within the suspected treatment failure group reported they use mixed drugs. Equally important in the practice of mixing and patients' treatment outcome is type of health facility.

Although different types of health facilities exist in Nigeria, the quality of care offered by these facilities differs. The high level of agreement by the participants in this study that the formal health facilities are the best source for malaria treatment might be related to the evidence that they adopt a better standard of practice and offer a better quality of care than the informal health facilities (Basu et al., 2012). In order words, the treatment experience of people using different types of health facilities for malaria treatment will differ. Considering that the distribution of these types of health facilities among the types of settlement in Nigeria is not equal, it is expected that the treatment experience of people from different types of settlements will also be different.

Indeed, the treatment experience with regards to the use of mixed drugs for malaria treatment differed among individuals from different types of settlement. The proportion of those who have used the mixed drug before within each type of settlement was highest among the rural dwellers, with 89.2% reporting they have used mixed drugs for malaria treatment. Apart from the fact that those in rural areas are usually of lower income level and as such, cost is important to their use of appropriate treatment for malaria, living in rural area also limits their choice of health facility for malaria treatment to mostly informal facilities. The dangers of using the informal health facilities in Nigeria is that, with the absence of adequate regulation, the quality of care offered to patients who use these services is usually poor (Basu et al., 2012). This is replicated by the findings from this study which showed that 75% of those who got their last antimalarial drugs from the chemists reported they got a mixed drug for malaria treatment.

Furthermore, with the understanding that mixed drugs are not the best for malaria treatment, some participants use mixed drugs as an initial measure to reduce the symptoms pending when they can afford the complete treatment. However, as antimalarial drugs are added to the mixture, using mixed drugs as palliative measures for suspected malaria cases still amounts to incomplete treatment as the complete course of the antimalarial drug is usually not administered. Also, there is no guarantee that a complete course will follow, or when the patient can afford this.

8.3.2 Public health implications of mixing drugs for malaria treatment

Although adopted as a strategy to cope with the cost of malaria treatment by individuals, the possible health implications of using mixed drugs for malaria treatment goes beyond the individual. The possible public health implications of this practice include its possible impact on drug resistance, distribution of expired as well as fake antimalarial drugs, amongst others.

8.3.2.1 Impact of use of mixed drugs on antimalarial drug resistance

Irrespective of the reason for using mixed drugs, their effect on the individual and public's health remains serious. Mixing paves way for different factors that promote the development and spread of antimalarial drug resistance. It does so by exposing the parasite to insufficient dose, as such encouraging the development of drug resistance (Bloland, 2001; White, 2004).

In addition to this, mixing drugs for malaria treatment also affects patients' access to information relevant to ensure adherence. Mixing of drugs for malaria treatment involves taking a dose from the original pack of each drug to be used, and combining the individual doses to form a mixed dose; as such, the drugs are not dispensed in their original packaging. With this, the users/customers are deprived of access to information which they could get from the drug packaging or leaflet. As an important aspect of pharmaceutical products, packaging provides visual communication for consumers, information about the product, and helps in the marketing of the product (Kauppinen-Räisänen, 2014; Roullet & Droulers, 2005; Thompson & Davidow, 2004). Most pharmaceutical products, especially drugs/medications, contain a patient information leaflet which provides further information about the drug, such as its clinical pharmacology (the drug's breakdown, absorption and elimination from the body); therapeutic indications (how and when the drug should be used); contraindications (how and when not to use the drug); adverse/side effects; expiration date; dosage; strength; amongst others (Medicine and

Healthcare Products Regulatory Agency, 2016; Veronin, 2011). These crucial information contained in the packaging can sometimes be the only information available to the patient on how to administer the drug (Thompson & Davidow, 2004; Wolf & Parker, 2007).

8.3.2.2 Impact of mixing on the distribution of expired and degraded drugs

Furthermore, mixing of drugs can promote the sale of expired drugs to unsuspecting users. With the expiry date being one of the important information contained in the packets or cartons of drugs, dispensing them in envelopes (as reported in the interviews) without the original packet means users have no knowledge of the expiry dates of the drugs contained in the mixture. When asked during the interview and survey if they do know the expiry date of the mixed drugs they used, many of the participants reported they do not know.

The chemical, microbiological and physiological stability of the drugs is another concern with the practice of mixing drugs for malaria treatment. In addition to containing important information on the drug and its use, the packaging of drugs plays a crucial role in protecting and maintaining the quality/integrity of the drug against degradation (Veronin, 2011). Drugs, when removed from their original packaging while being dispensed, should be placed in containers similar to that in which the manufacturers used to package the drug (Veronin, 2011). Failure to do this can expose the drugs to conditions that may lead to their degradation and alteration of their composition. Although not necessarily related to drug resistance, the transfer of the individual drugs from their original packages to an envelope during mixing, thereby exposing them to atmospheric air and other conditions may lead to degradation. Subsequent consumption of these drugs with altered composition may result in treatment failure or other health issues and complications; thereby increasing the malaria morbidity and the illness experience of patients.

8.3.2.3 Impact of mixing on the distribution of fake drugs

A linked problem to the distribution and sale of expired drugs through the practice of mixing is the distribution and dispensation of fake antimalarial drugs. The mixed drugs, which are not sold in their original package, deprive users the ability to assess the drugs they are buying for originality. As in expired drugs, dispensing the mixed drugs without their original packaging offers a safe route to the sale and subsequent use of fake antimalarial drugs. The packaging of products, like drugs, (in relation to the outer covering, which in most drugs is a carton) is an important player in the identification of fake drugs. Characteristics such as the physical

appearance of the packaging can reliably indicate authenticity (P. Newton et al., 2001). The physical appearance of the packing such as unclear barcode printing, unclear blister pack printing, absence or forged holograms are all indicators of counterfeit drugs (P. Newton et al., 2001). Occasional misshapen trademark imprints on drug packaging are also one of the features of the fake drugs that can help in their identification (Masland & Marshall, 1990).

Another important aspect of fake drugs in relation to the subject area of this research is that some fake or counterfeit antimalarial drugs contain the active ingredient but in inadequate quantities (Bloland, 2001; Kaur et al., 2016), usually below the recommended quantity. As such their administration invariably means exposure to the parasites to sub-therapeutic concentrations of antimalarial drugs which can, in turn, contributes to the selection of resistant parasites (Bloland, 2001; Nayyar et al., 2012; White, 2004; World Health Organization, 2015a), thereby evolving mechanisms for the development of resistance to the antimalarial drug.

In addition, when it comes to fake or counterfeit drugs, the poor who are of low socioeconomic position, bear more of the burden. One characteristic of fake or counterfeit antimalarial drugs that makes them attractive to those at lower levels of socioeconomic measures is their lower price in relation to the original drugs (Masland & Marshall, 1990; P. Newton et al., 2001).

8.3.2.4 Mixing and Drug Interaction

Another compelling issue with mixing is the composition of the mixed drugs. The drug vendor interviewed listed drugs like antimalarial, analgesics, and antibiotics as components of the mixed drugs for malaria treatment. One of the explanations for the choice of drugs that constitute the mixture, as depicted from the interviews with the drug vendor and pharmacy attendant interviewed, is the symptoms the patient presents. As such, there are indications that apart from the antimalarial drug, other drugs added to the mixture are targeted at addressing specific symptoms patients complained about, like headache. As the patient is not getting the full course of malaria treatment, these drugs are added with the understanding that they will help relieve the symptoms of malaria. Although, as the practice of mixing has not been reported in malaria literature, hence there is no evidence of the outcome of the invivo interaction of the drugs used in the mixture; nevertheless, there are indications that the interaction of these drugs when administered together might affect their effectiveness. Some studies have reported that concurrent treatment involving the use of antimalarial drugs and other drugs can contribute to drug resistance and treatment failure (Bloland, 2001; van Hensbroek et al., 1995).

8.4 Stopping malaria treatment to save drugs for future use

The practice of stopping malaria treatment to save drugs for future used was first picked up by the systematic review strand of this study. One of the studies used in the review that reported this practice was by Watsierah et al. (2011) which looked at the antimalarial drug use behaviours of participants from Kenya. Although Watsierah et al. (2011) reported this behaviour among peri-urban dwellers, their study did not explore the relationship between socioeconomic factors like type of settlement, and this practice. Hence, in addition to exploring the occurrence and frequency of this practice in the Nigerian population, its distribution among different levels of socioeconomic measures was also assessed in this study.

Evaluation of the evidence from existing studies (Watsierah et al., 2011) and the results of this study on stopping malaria treatment prior to completion of the course showed that, for those who engage in this practice, two factors determines when they stop treatment. These are the achievement of either therapeutic failure or therapeutic success.

Therapeutic failure in terms of persistent or increased morbidity/disease symptoms after the commencement of malaria treatment can lead to participants stopping treatment. It is important to state that this therapeutic failure can be perceived or actual (as side effects from treatment can sometimes be misinterpreted as treatment failure).

On the other hand, among the survey participants in this study who reported they did not complete the course of their last malaria treatment, therapeutic success was the most reported reason. Some participants reported that when they feel better during treatment, they become reluctant to continue taking the drugs (despite the overall satisfactory response rate on the importance of completing malaria treatment demonstrated by the study participant). Amongst those who stop malaria treatment as a result of therapeutic success are those who stop the treatment to save the drugs for future use.

In cases where patients are truly malaria positive, the decision to stop treatment before completing the treatment course can result in the exposure of the parasite to sub-therapeutic doses, which is a driver of antimalarial drug resistance. Overall, the practice of stopping malaria treatment to save drug for future use was reported by 13.3% and 33% of the participants from the qualitative interview and quantitative survey respectively. Probing on this practice during the interviews to know why it was not reported more than this rate showed that some participants, especially those from rural areas, were weary of this practice. Reason being that a

good proportion of the rural population use mixed drugs which have no indication of the expiry dates of the individual drugs in the mixture; therefore, some of them tend to take all the drugs when they buy them, or dispose the leftovers rather than saved. Nevertheless, with one-third of the survey participants reporting they have engaged in this practice before, there was need to assess its relationship with factors like socioeconomic measures.

8.4.1 Socioeconomic measures and stopping malaria treatment to save drugs for future use

Apart from their ability to stratify the population into different socioeconomic levels or positions; political systems and government policies can directly and/or indirectly affect patient treatment behaviours and illness experiences (Nugent & Knaul, 2006). Just as fiscal policies like taxes, subsidies, location and provision of health services can be used to encourage healthy behaviours, when not well targeted and designed, such policies can discourage the adoption of health-promoting behaviours (Nugent & Knaul, 2006). Some of the policies in developing countries that are related to health are product of the influence of higher hands like those of western countries. For instance, the International Monetary Fund (IMF) is one of the proponents of the concept of neoliberalism and privatization of sectors to encourage free market (Rowden, 2013). One of the consequences of policies underpinned by principles of neoliberalism like privatization is the commercialization of health. For instance, the policy on out of pocket payment for health services at the point of use, which is presently adopted in Nigeria (Onwujekwe, Dike, Uzochukwu, & Ezeoke, 2010), works to the disadvantage of the poor in the society. Such policies affect treatment seeking behaviours, and drug use behaviours among the less well-off who end up devising means to cope with the cost –which can be deleterious to health. Socioeconomic factors like type of settlement, educational level, and household income were significantly associated with the practice of stopping malaria treatment to save drugs for future use in this study.

The practice of stopping treatment to save drugs was more among the rural dwellers. The rural areas, in comparison with the suburban and urban, are more disadvantaged in terms of location and access to formal health facilities. As such, type of settlement can affect access to important information on malaria treatment and availability of antimalarial drugs; especially the subsidized ones which are usually distributed through formal health facilities (Harding, 2009).

Also, negative norms and perceptions about malaria (like the perception that malaria is not treatable) were more in the rural areas where African culture, tradition and social constructions

still strongly hold. These factors invariably impact on treatment behaviours and outcomes. Constructs or perceptions like that of malaria treatments as a palliative rather than curative, which was demonstrated in the qualitative interview with a rural participant, can be contributory to using antimalarial drugs only when symptoms are present and stopping the treatment as the symptoms disappear, to save drugs for the future reappearance of symptoms.

The rural dwellers in this study were also the least educated, mostly from the lowest income group (72% of the rural dwellers had attained at most secondary education with household income of N50,000 (£121) and below) As such, it is not surprising that educational level and household income were also significantly associated with stopping treatment to save of drugs for future use.

Higher educational level has repeatedly been identified as associated with higher level of adherence to antimalarial treatments like ACTs (Beer et al., 2009; Cohen et al., 2012; Depoortere et al., 2004; Fogg et al., 2004; Onyango et al., 2012). With higher educational level comes a better understanding of the importance of adherence, especially in terms of treatment completion. The survey results on the relationship between stopping to save and educational level were significant; indicating an inverse relationship -as educational level increases, the practice of stopping treatment to save drugs for future use reduces. The significant association between educational level and this practice can also be interpreted in relation to the former's effect on household income. Those with higher educational level generally have a higher income (as demonstrated in this study and other studies reporting this (Strauss, 2011)); hence can easily afford the complete course of malaria treatment compared to those of lower educational level. As such, this group will be less likely to stop treatment for the reason of saving drugs for future use.

As a strategy to cope with the cost of treatment, the practice of stopping treatment to save drugs for future use was significant among the lower household income groups. Although seen as economical by those who use it as it allows for the use of one course to treat more than one malaria episode, stopping malaria treatment to save drugs for future use can lead to treatment failure and encourage resistance development by the *Plasmodium* parasite.

8.5 Sharing of an antimalarial course with others

A similar factor in incomplete treatment which was reported in this study was sharing of an antimalarial course with others (that is, more than one person taking one malaria treatment

course) which was reported mostly as a measure to deal with the cost of antimalarial drugs. This practice as shown in the systematic review strand has been previously reported by some studies on antimalarial drug use behaviours in other parts of Africa, like Kenya (Ogolla et al., 2013; Watsierah et al., 2011).

In the current study, the participants who adopt this practice can be categorized into those who share with the intention of acquiring additional course to complete the treatment later, and those with no intention of doing so. For some of those who shared with the intention of acquiring an additional dose, the benefit of sharing is that it helps to spread the cost of the treatment.

In addition, although the practice was reported mostly as a recurrent behaviour by the interview participants, one participant reported this as a one-off practice. For those who reported it as a recurrent behaviour during the interviews, sharing of an antimalarial course with others was more of a strategy to cope with the cost of malaria treatment by maximizing the use of a treatment course when they buy one.

8.5.1 Socioeconomic measures and sharing of an antimalarial course with others

Initially reported in the interviews, the survey also validated the fact that the practice of sharing increases as income level increases, with those at lower levels of socioeconomic measures having the highest prevalence of this practice. Also, the interview result showed that for the only participant of higher socioeconomic position (higher educational and income level, and urban dweller) who reported sharing antimalarial drug with another person, the practice was a one-off in a situation where antimalarial drug could not be accessed due to the time.

The results of the survey analysis showed a significant relationship between socioeconomic factors and sharing of an antimalarial course with others. Although this practice was significant with educational level, household income, and type of settlement, amongst all three, educational level was a stronger predictor of this practice as it had the highest effect size. There was an inverse relationship between educational level and sharing of an antimalarial drug with others; with the practice more prevalent among those of lower levels of education.

Furthermore, as earlier stated, sharing of a malaria treatment course is also used in spreading the cost of treatment. For one of the participants, sharing helped him to spread the cost of malaria treatment for two people by enabling him, as the household head, buy one malaria treatment course which is then shared by two members of his family who have suspected

malaria; and when the first course is finished, he can buy the second course at a later date. As economical as this might seem, the impact on the individual and public health far outweighs the perceived economic benefit. Firstly, there is a possibility of time difference between when the first treatment course finishes and when the second one is acquired. This might take hours or days which can mean the persons involved missing one or more doses, as such giving the uncleared parasites time to replicate and possibly mutate. This can also contribute to the development of new traits that may reduce the susceptibility of the parasite to antimalarial drugs. Secondly, it is possible for those who have shared with the intention of buying a second course to complete the treatment, to change their mind about a second course when they feel better.

In sharing an antimalarial course with others (even with the intentions of buying more course to complete the treatment), there is no guarantee that the persons involved will get an equal number of doses. As such, some of the persons involved might end up underdosed or overdosed in relation to the others. Expectedly, the situation will be worse when the antimalarial drug shared is a combination therapy that is not co-formulated -like Camosunate (Artesunate and Amodiaquine) as sold in Nigeria.

The dangers of sharing, especially where no additional course is shared to complete the treatment, is that all the patients involved end up having incomplete treatment. This, as with other aspects of incomplete treatment reported in this study, can further drive the development of resistance to antimalarial drugs by the parasite.

The practices of sharing of an antimalarial course with others and stopping treatment to save drugs for future use are both deleterious drug use behaviours, influenced by measures of socioeconomic position, and reinforced by the same underlying need to cope with the cost of treatment. Both practices also have the similar outcome of under-dosage which promotes the development of drug resistance.

8.6 Presumptive treatment

The need to ensure all suspected malaria cases are confirmed prior to treatment informed the Test, Treat and Track (TTT) strategy rolled out by the WHO in 2012 (World Health Organization, 2012). Malaria treatment in cases where the patient is not malaria positive will lead to overuse of antimalarial drugs as well as higher morbidity as the real cause of the illness is left untreated (World Health Organization, 2016d). Parasite-based confirmatory test for

malaria prior to treatment ensures that only those who need antimalarial drugs get them, thereby controlling the overuse of antimalarial drugs (WHO, 2015). Also, accurate and prompt diagnosis improve the management of malaria symptoms and the overall patient experience of the disease (World Health Organization, 2016d). Despite the availability of malaria diagnostic tools like RDTs, and their benefits over laboratory-based microscopy, the issue of presumptive treatment of malaria is well grounded in most endemic countries like Nigeria.

The findings of this study suggest that presumptive treatment of malaria is fostered by four main factors: availability and access to malaria diagnostic tests; affordability of the cost of malaria tests; confidence in self-diagnosis of malaria; and acceptance of existing tests as effective in detecting malaria infection and availability of antimalarial drugs as over the counter drugs. Apart from confidence in self-diagnosis of malaria and acceptance of existing malaria tests as effective in malaria detection, the other two factors have socioeconomic connotations.

Presumptive treatment of malaria was the only treatment seeking behaviour whose prevalence was well spread across different levels of socioeconomic measures -this trend is observed in the qualitative as well as the quantitative studies in this inquiry. The difference in the adoption of this practice by participants from different socioeconomic positions, however, lies in the factors that foster such behaviours. The qualitative interviews show that, for those at the higher levels of socioeconomic measures, presumptive treatment is fostered by factors like confidence in self-diagnosis of malaria; hence some people at these levels who treat malaria presumptively see this practice as a time-saving route to malaria treatment. Nevertheless, for those at lower levels of socioeconomic measures, this practice is fostered by factors like availability and access to malaria diagnostic test and the cost of the tests; hence, those at this socioeconomic level who treat malaria presumptively see this practice as a cost-saving route to treatment. This is because presumptive treatment is believed to eliminate both the direct cost of the laboratory test as well as the indirect cost in form of opportunity cost as a result of forgone productive time which is spent in waiting for the test results to be ready before the commencement of treatment. In line with this, presumptive treatment was also seen as a better treatment route for reducing the period of malaria morbidity.

Another way in which affordability promotes presumptive treatment is through the behaviour of using previous results of malaria diagnostic tests, and the prescription received, to treat subsequent episodes with similar symptoms. According to one of the qualitative interviewees, this practice was a strategy that helps to save the cost of treatment. This replicates the findings

from previous studies like Watsierah et al. (2011) which reported that 23% of those who were seeking malaria treatment presumptively and without prescriptions gave their use of the same drug for similar symptoms as the reason for the practice. One important similarity between the study by Watsierah et al., (2011) and the current study, is that the participants who reported this practice in both studies were of lower socioeconomic position.

Indeed, the similarity between affordability, availability, and access lies in the fact that their role in presumptive treatment is linked to the socioeconomic position of participants. For instance, availability of diagnostic test differs with different types of health facilities in Nigeria. And, as shown in the results and other existing studies (Basu et al., 2012; Uzochukwu & Onwujekwe, 2004), socioeconomic factors are important in the decision on the type of health facility treatment will be sought. They found a significant relationship between the type of health facility and the use of malaria diagnostic testing prior to the current malaria treatment. Those who were recruited from chemists were 5.6 times less likely to have used diagnostic testing prior to the treatment received than those who did not. This result is similar to that of existing studies that have identified the chemist/drug vendor as a key contributor to presumptive treatment (Isiguzo et al., 2014). This association between the chemist/drug vendor and presumptive treatment becomes more pronounced when one considers the fact that the informal health facilities (like the chemists) cater for 60% of the malaria cases in Nigeria (National Population Commission, 2012). Further evaluation of the reason for the significant practice of presumptive treatment in the chemists points to the health policy adopted in Nigeria which stipulates that informal health facilities are not authorized to provide diagnostic testing for conditions like malaria (Onwujekwe et al., 2010; Onwujekwe et al., 2010b; Uzochukwu et al., 2014). Therefore, with the large proportion of the population that use the chemists/drug vendors, there is a possibility that the issue of presumptive treatment from the informal health facilities can be more intense than reported.

Furthermore, although more of a driver of presumptive treatment among those at the high socioeconomic level, the confidence in diagnosing malaria is a common feature of malaria endemic settings (Chandler et al., 2011; Comoé et al., 2012). This confidence is as a result of the high rate of malaria infection in the Nigerian population (World Health Organization, 2016d) (also demonstrated in the survey result with more than half of the study population reporting they have used an antimalarial drug within the month of the survey). Hence, people have frequent malaria experiences; and with these experiences, some people develop the

confidence that once some specific symptoms present, malaria is ruled in. Although the issue of confidence in diagnosing malaria was not further followed up in the survey after its report in the interview, however, the results from the qualitative interviews as well as the findings from other studies (Cohen et al., 2015) indicate that it is common in malaria endemic settings.

Another factor in presumptive treatment was acceptability. Acceptance of the results of malaria diagnostic tests is an issue that applies to the patients as well as the providers (Altaras et al., 2016; Diggle et al., 2014). Evidence of the role of providers in this regard is in the prescription of antimalarial drugs even when diagnostic tests, especially RDTs, shows a negative result (Altaras et al., 2016; Manyando, Njunju, Chileshe, Siziya, & Shiff, 2014). Failure to accept conventional methods of malaria diagnosis, like RDTs and microscopy, as efficient in malaria detection can encourage the adoption of presumptive treatment option. Tradition and cultural factors can also influence the acceptance and subsequent use of diagnostic tests. This was identified in the interview with one of the participants who stated that he never goes for malaria diagnostic test. The reason for this being that his parents and ancestors never believed in the orthodox diagnosis of malaria.

8.6.1 Socioeconomic measures and presumptive treatment

Despite its widespread across different levels of socioeconomic position, there was a significant association between presumptive treatment of malaria and some measures of socioeconomic position. On the use of malaria diagnostic test for their malaria treatment at the time of the survey, employment status was the only socioeconomic measure that significantly predicted this behaviour; educational level, household income, and type of settlement made no significant contribution to this practice. The higher odds of using diagnostic test among the employed might be related to the affordability of diagnostic test. It is expected that, generally, the cost will be more of a factor in treatment for those unemployed than for those in employment.

Apart from the socioeconomic measure of employment status, type of health facility used was also a significant predictor of the use of the diagnostic test. Among the types of health facilities, the use of chemists was the strongest in predicting diagnostic test use for current malaria treatment. As expected, the odd of not using diagnostic test prior to treatment (that is presumptive treatment) was higher when a chemist is used, as against not using a chemist. Nevertheless, those using private hospitals had the highest odds of having a diagnostic test prior to treatment. Although, as private organizations with the aim of profit maximization, the high level of diagnostic test in the private hospitals might be interpreted as incentivized (as a

way of making more profit by insisting patients get tested), notwithstanding this possibility of a financial motive, if test results are followed in prescribing treatments, the higher rate of testing prior to malaria treatment in private hospitals will help in ensuring antimalarial drugs are not overused.

Another issue in relation to presumptive treatment, which was tested in the survey, was consistency in the use of diagnostic testing for malaria treatment. The analysis of the relationship between socioeconomic factors and consistency in the use of malaria diagnostic test prior to treatment showed that educational level and household income were the only socioeconomic factors that significantly predict this practice. The odds of consistently using diagnostic test prior to malaria treatment is more as educational level increases. Same applies to household income. The relationship between educational level and use of malaria diagnostic test malaria prior to treatment has been reported in other studies (UNESCO, 2012; Uzochukwu, Onwujekwe, Uguru, Ughasoro, & Ezeoke, 2010). With higher education, it is expected that people will have a better understanding of the essence of aspects of treatment like diagnostic test before treatment.

Indeed the role of cost in malaria treatment is well established (Uzochukwu & Onwujekwe, 2004). Given the demographic and socioeconomic profile of malaria-endemic populations, the role of cost in treatment cannot be overemphasized. As a socioeconomic measure directly linked with financial resources, household income can affect the affordability of treatment, especially in aspects like diagnostic testing. From the findings of this study, the situation with diagnostic testing for malaria prior to treatment for those at the lower socioeconomic position, is more of prioritizing between a proper route to treatment with a more definite outcome, but more expensive; and a 'gamble' with an unpredictable outcome, which is cheaper. Nevertheless, the constraint posed by socioeconomic structures limits their option to the latter.

Evidently, the perception of an individual or a group about a specific issue affects their relationship and behaviours towards that issue (Ferguson & Bargh, 2004). The perception of the participants on the importance of malaria diagnostic test was another significant contributor to the use of malaria diagnostic test.

8.6.2 Presumptive treatment for malaria and its implication on drug resistance

Presumptive treatment of malaria remains an important driver of antimalarial drug resistance. With two common causes of hospital visit in Nigeria, Typhoid and malaria (World Health

Organization, 2013a), having similar symptoms, especially fever (World Health Organization, 2015c, 2016d) the practice of presumptive treatment can encourage high drug pressure through the overuse of antimalarial drugs, especially in cases of non-malaria febrile cases (World Health Organization, 2016d). Overuse of antimalarial drugs through presumptive treatment has been reported to exert selective pressure on the *Plasmodium* parasite population (Bloland, 2001).

In addition to this, presumptive treatment might explain the addition of antibiotics like amoxicillin to the mixed drugs for malaria treatment. With typhoid and malaria among the leading causes of hospital visits in Nigeria, the presence of drugs for these two conditions in some mixed dose (Amoxicillin used in typhoid treatment, and antimalarial drugs for malaria) can be an indication of the trial and error that underpins presumptive treatment of malaria. With the uncertainty that the presenting symptoms in a patient are malaria and their inability to rule out other common conditions like typhoid, the chemists in mixing add drugs for both conditions. The practice of co-prescription of antimalarials and antibiotics from formal and informal health facilities in Nigeria is also well reported in literature (Ezenduka, Ogbonna, et al., 2014; Ezenduka, Okonta, & Esimone, 2014; Gbotosho et al., 2009).

8.7 Herbal medicine for malaria treatment

The use of herbal medicine for malaria treatment was reported during the interviews with rural dwellers. Living in a rural settlement was the strongest predictor of the use of herbal medicine. The interview accounts show that these herbal medicines are usually home-made with respondents reporting different formulations, herbal ingredients, and routes of administration. Also, the herbs are usually readily available and locally sourced at no direct financial cost.

Apart from their being cheaper in comparison to orthodox antimalarial drugs, other factors like the availability of the raw material (which are freely sourced from the bushes), encourage the use of herbal medicine for malaria treatment. Some of the herbs reportedly used by the interviewees have been used in malaria treatment in Africa for centuries (Biswas, Chattopadhyay, Banerjee, & Bandyopadhyay, 2002; Duddeck, 2016; Odetola & Basir, 1980; Odugbemi, Akinsulire, Aibinu, & Fabeku, 2007).

Indeed, there is evidence that some of the herbs reportedly used by the participants for preparing malaria drugs, like *dogwonyaro* –botanical name *Azadirachta indica*- have some antimalarial properties (Duddeck, 2016; Khalid, Farouk, Geary, & Jensen, 1986). The dangers

associated with using herbal medicine for malaria treatment is that; firstly, there is no standard regarding the components of the formulation. Secondly, users have no knowledge of the concentration of the active ingredients (as the medicines are mostly self-prepared, usually by boiling of the herbs in water), hence no standard in terms of the dosage. As such the possibility of under or overdosing is very likely. These issues become more pronounced when one considers the fact that some important antimalarial drugs like artemisinin and quinine come from plant sources (*Artemisia annua* and *Cinchona* plants respectively) (Flanagan et al., 1995; World Health Organization, 2016b). It remains to be seen the impact of the dosage of herbal malaria medicines on the development and spread of antimalarial drug resistance.

8.8 Malaria treatment-seeking behaviours in children

Evidence from existing studies demonstrates that a significant disparity exists in the malaria treatment seeking behaviours when a child is involved as against when an adult is, usually to the advantage of the former (Liu et al., 2015). This is further reiterated by the disparity in the usual choice of facility for malaria treatment for a child and that for an adult. Unlike the adults, the formal health facility was the most common choice of the facility to seek malaria treatment for a child. Similar to this finding, is that of a survey in sub-Saharan Africa by the WHO between 2013 to 2015 which reported that a higher proportion of febrile children (used as an indicator for malaria) sought treatment from the formal public (mostly formal) sector than in the private sector (mostly informal) (World Health Organization, 2016d).

The reason for this disparity in treatment seeking behaviour for children and adults was explained by some of the interviewees in the qualitative study. They expressed their views that, because of the high risk of malaria faced by children in Nigeria, coupled with the inability of a child to vividly explain their symptoms (which is very important when seeking treatment from informal health facilities like chemists where treatment is based on the presenting symptoms), treating children in informal health facilities is risky, hence their use of formal health facilities when a child is involved.

Nevertheless, there is insufficient evidence in literature to demonstrate whether there is a disparity in malaria treatment seeking behaviour among children from different levels of socioeconomic measure. The analysis of the survey data show that participants' level of socioeconomic measures made no significant impact on the type of health facility normally used for malaria treatment for a child, as notwithstanding their socioeconomic position, most participants reported they use formal health facilities for malaria treatment in children.

Also, the disparity in malaria treatment seeking behaviour among children from different levels of the socioeconomic measures was assessed using the variable on the use of diagnostic test prior to treatment in children. The survey results showed that socioeconomic measures like educational level, type of settlement (urban and suburban) and employment status were significantly associated with the use of parasite-based diagnostic test prior to malaria treatment in children.

8.9 Type of health facility and malaria treatment

The disparity in access and use of different health facilities is a good reflection of inequality in health in a society (Basu et al., 2012). As the quality of care and treatment offered by different types of health facilities differs so does their cost of treatment and the characteristics of their users. Indeed, differences in quality of care exist between the two broad health sectors -public and private- as well as within each sector. The description of the difference between two popular informal health facilities under the private health sector (the chemists and pharmacies) by participants in the qualitative interview demonstrates the disparity in the quality of care both facilities offer, and the demography of those they service.

The chemists are drug shops run and managed by persons informally trained (Isiguzo et al., 2014). The chemists, which are found in the rural areas, are poorly regulated (Isiguzo et al., 2014; Oladepo et al., 2008; Salako et al., 2001). They were described by some participants in this study as health facilities that are fit for the poor. One interviewee reported that the activities of the chemists permit different practices, and so one can get, in the words of the interviewee, "all manner of drugs" here. Those of lower educational level, rural settlement, of lower household income, are the most likely user of chemists for malaria treatment.

The pharmacies, on the other hand, constitute a minority of the informal health facilities in the private health sector in Nigeria (Isiguzo et al., 2014). They were described as more regulated informal health facilities found mostly in the urban areas. Overall, the pharmacy was the most usual source for malaria treatment by the participants in this study. It is also the most usual source of antimalarial drugs for those in the urban areas.

Evidence from studies on malaria treatment seeking behaviour in Nigeria shows that a higher proportion of the population (60%) will first use drug shops in the private health sector (National Population Commission, 2012). This pattern of treatment found in the Nigerian population also exists in other low and middle income countries like Uganda, Kenya, Ghana,

Sri Lanka where higher proportions use private facilities (Agampodi & Amarasinghe, 2007; Bustreo, Harding, & Axelsson, 2003; Hamel, Odhacha, Roberts, & Deming, 2001; Mbonye, Hansen, Wamono, & Magnussen, 2009). Many of the private facilities used by those in low and middle-income countries like Nigeria are informal and poorly regulated (Marriott, 2009). The study by Hamel of home treatment of malaria in children in Kenya documented that in malaria-endemic areas like Kenya, about 50-80% of the population will first presumptively seek malaria treatment from a private drug shop (Hamel et al., 2001). The results of the survey conducted in this study corroborate this as it reported that the pharmacy was the most usual source of malaria treatment by the majority of the participants. An important reason why majority of the participants used the pharmacy as their most usual source of malaria treatment is that most of the participants were recruited from the urban areas, which is where the pharmacies are mostly found.

Studies like Basu et al., (2012) documented that formal health facilities are mostly used when treatment from the informal health facilities fails or when malaria case is perceived as severe or complicated. The result of the survey in this study shows that more than half of those who have previously sought treatment for the current episode were using formal health facilities at the time of the survey.

8.9.2 Quality of care/service from different health facilities

Many studies have documented disparity in the quality of care and treatment offered by the private and public sectors. The quality of care and treatment (in relation to diagnostic accuracy, dispensation of necessary medications, standard of medical practice) offered by the private health sector, in comparison with the public sector, has repeatedly been reported as poor (Auer, Lagahid, Tanner, & Weiss, 2006; Dato & Imaz, 2009; Greaves, Ouyang, Pefole, MacCarthy, & Cash, 2007; Udwadia, Pinto, & Uplekar, 2010). For instance, there was a significant relationship in this study between different types of health facilities used for malaria treatment and the type of antimalarial drugs received from the facilities.

This disparity in the quality of care offered by different facilities is, however, recognized by the population. Some of the interviewees in the qualitative strand of the current study who used the chemists reported they are aware of the less quality of care offered by the chemists, which they can tell from their treatment experiences and outcomes. Nevertheless, the poor still depend on these informal health facilities for treatment (Harding, 2009) for reasons like affordability, access, social structure, and cohesion, amongst others.

As earlier stated, one of the areas the quality of care offered by different health facilities differs is in the type of drug patients receive. Patients who used the chemists for their last malaria treatment were the least likely to have used ACT than those who used the other sources. This poor quality of care in relation to not receiving the first line treatment for malaria from the informal health facilities is attributed to behaviours of both the users and the providers.

Furthermore, the results of this study show that informal health facilities contribute more to the use of monotherapies against treatment guideline. Despite the WHO report (2015) that identified Nigeria as one of the countries that have stopped the use of artemisinin monotherapies, the use of Artesunate was well reported, with the pharmacy as the most reported source of these drugs. As stated in chapter two, artemisinin drugs have a short half-life. This means that, in using Artesunate monotherapy (an artemisinin derivative) for malaria treatment, a multiple-dose regimen is required, usually about seven days (Saunders et al., 2012). With the multiple-dose regimen, the likelihood of non-adherence in terms of administration time, dosage and completion of the treatment course are higher (Bloland, 2001). Nevertheless, the availability of monotherapies, like Artesunate, in the informal health facilities is related to their demand by customers.

Indeed, as with other business ventures, the behaviours of the patients and providers are connected, with the former usually informing the later, especially in private health sector. For instance, private health facilities like the chemists/drug sellers are business ventures with the main purpose of profit maximization, as such, they conduct their business in line with the characteristics of their target market -the rural dwellers- and the demand for their services. A mixed method study by Cohen et al., (2010) reported that for drug vendors, stocking of drugs is based on the demand by customers. As these drug vendors mostly serve the poor, ACTs, which are more expensive, were seen as "slow moving drugs" hence are not well-stock as other antimalarial drugs (Cohen et al., 2010).

With the high drug use and the high rate of poverty in malaria endemic areas like Nigeria (World Health Organization, 2016d), the use of cheaper antimalarial drugs (like monotherapies and mixed drugs) which can promote the development of drug resistance, will be favoured over more expensive effective therapies like ACTs. The description of the levels of socioeconomic measure of those using different facilities shows that the chemists were mostly used by rural dwellers who also had a low level of education and low household income. The relationship

between socioeconomic measures like household income and the choice of health facilities for malaria treatment points to the issue of cost and affordability.

8.9.3 Cost as a factor in choice of health facility

Although not a direct measure of socioeconomic position, the choice of the health facility to seek malaria treatment is directly influenced by the level of the socioeconomic position. Affordability was identified as the most important factor in decisions on where to seek malaria treatment. This was favoured over factors like good quality of service, waiting time, and availability of drugs. The importance of cost to malaria treatment cannot be over-emphasized given its relevance in the study setting. Resistance-promoting cheaper options like monotherapies and mixed drugs still flourish amidst better treatment options like ACTs. The findings of this study show that, as expected, affordability was more of a concern when deciding where to seek treatment for those at lower levels of socioeconomic measure than those at higher levels. The role of cost in choosing health facility for treatment was further demonstrated in this study using the hypothetical question on where participants will seek malaria treatment if the cost was not a factor.

Overall, the actual choice of health facility by the participants was different from their choice in the hypothetical scenario where cost is not a factor. Although the pharmacy (informal health facility) was the most reported usual source of malaria treatment by the participants, this choice will be different if the cost of treatment was not a factor; the hospitals (formal health facility) would be the usual choice facility. Most of the participants indicated they would use formal health facilities (that is, public/government hospitals and clinics, private hospitals and clinics, Health centres) for malaria treatment if cost was not a problem. This shows the extent of trust for the quality of care offered in the formal health facilities; while also highlighting the barrier posed by the cost of treatment from formal health facilities to their use.

8.9.4 Social and political structures and their impact on choice of health facilities

In line with existing evidence (Berkman et al., 2014; Krieger, 2011b), this study found that the social systems and structures existing in a given population can affect how individuals seek malaria treatment as well as their illness experiences. As such, the qualitative interview demonstrated the impact of social cohesion in the trust and acceptability of health providers, which subsequently affected treatment seeking behaviour of participants regarding where they usually seek treatment. The trust demonstrated by some rural interviewees for the chemists and drug vendors was earned through the vendor/chemist's membership of the community they do

business in. As such, the interviewee's acceptance can also be a reflection of the sense of ownership of these drug shops/chemists facilities despite the user's awareness of the quality of treatment they offer, in relation to formal health facilities. The absence of this social factor (which is important in treatment decision) in formal health facilities, is a barrier to their use, especially in rural setting where communal lifestyle still strives. A participant, in describing their perception of the health workers in the formal health facilities, referred to them as "coming from different areas", indicating their perception of the formal facilities and providers as distal and not seen as part of the community.

Evidently, other societal processes, like political structures drive the social patterning and disparity in health and disease in a population (Krieger, 2011b). One of the ways political systems and policies impact on the inequalities in health is in the location of public health facilities. Existing studies, like that of Solar & Irwin (2007), have substantiated the crucial role of the state in shaping the distribution of resources, and indeed determining the social and economic structures in a society. As such the state, through its policies and decisions, can determine the level of socioeconomic inequality in a society, which can subsequently influence the health of the public through disparities in access and availability of treatment.

In the case of rural settings, the decisions of the state with regards to location of health facilities and allocation of resources can lead to restriction of the rural dwellers' choice of health facilities for malaria treatment to mainly the informal health facilities (like the chemist where getting a complete antimalarial course is less likely, and the practice of mixing drugs for malaria treatment prominent). On the long run, these decisions and policies of the state can affect the efficacy of treatments and the development and spread of antimalarial drug resistance.

8.10 Suspected Treatment Failure

As demonstrated in the earlier discussions, the interplay between socioeconomic factors in a population influences related behaviours and disease outcomes and their unequal distribution in a population (Solar & Irwin, 2007). The result on the relationship between socioeconomic and suspected treatment failure identifies with the evidence that population health outcomes are patterned along important social and economic factors (Krieger, 2011b; Solar & Irwin, 2007) especially in line with the distribution of the means of production. To explain this pattern, a description of what 'suspected' treatment failure, as used in this study, means is first covered.

According to the WHO, antimalarial drug resistance can be confirmed using a laboratory test for parasitemia (World Health Organization, 2016b). This study conducted an exploratory cross-sectional study of the contributions of socioeconomic factors to the development and spread of resistance to antimalarial drugs by *Plasmodium* parasites, by looking at participants' present and past treatment seeking and drug use behaviours, and their treatment outcomes. As a cross-sectional survey, participants were only studies at one point in time, hence there was no follow. Therefore, participant's current drug use behaviours and the outcome of the treatment they were receiving at the time of the survey were not covered by this study. Furthermore, since participants were not followed up, resistance was not confirmed as this will require following participants for some days after treatment to conduct a laboratory test to determine the level of parasitemia. Nevertheless, the design of this study enabled the collection of data on the outcome of the last malaria treatment. Although a retrospective data, given the high frequency of malaria infection in Nigeria, it is expected that recollection bias will be minimal with the high frequency.

Overall, the key outcomes assessed in this study were recovery and treatment failure (given that drug resistance can cause treatment failure). Treatment failure can be as a result of inappropriate treatment (in terms of noncompliance to the drug administration procedure) or a manifestation of drug resistance. As such, the patients' last malaria treatment experience and outcomes were used to create a dichotomous variable on 'suspected' treatment failure and used to explore whether the experience differed according to socioeconomic position. Educational level, household income, and type of settlement were significant predictors of this outcome.

It is expected that as household income increases, cost-related factors that constitute barriers to proper malaria treatment will decrease; hence cost-coping strategies like mixing of drugs for malaria treatment, sharing of an antimalarial course, and stopping treatment to save drugs reduces. The significant association between the rural settlement and outcome of 'suspected' treatment failure is not distal from the poor quality of care, the type of drugs, and potentials for the distribution of counterfeit drugs, which are more prominent in this type of settlement. Antimalarial drug use practices like mixing of drugs for malaria treatment, sharing of an antimalarial course with others, and stopping treatment to save drugs which are significantly associated with household income and type of settlement, were also significantly associated with the outcome of 'suspected' treatment failure.

In line with the earlier discussions of disparity in quality of care offered/received from different types of health facility, the results also confirm that the type of health facility participants used is associated with the outcome of 'suspected' treatment failure. The persistent poor quality of care in malaria treatment offered to millions of treatment seekers who use the informal health facilities in Nigeria is evident in the high proportion of the 'suspected' treatment failure cases (75%) significantly associated with the informal health facilities (chemists/drug vendors, and pharmacies). The prescription behaviours of the healthcare providers in the informal health facilities like chemists will foster issues like drug resistance.

8.11 Knowledge and perception about malaria cause

The overall knowledge of the cause of malaria, in relation to mosquito bites, was satisfactory. The knowledge about mosquito bite as a cause of malaria was statistically independent of participants' types of settlements. However, other measures of socioeconomic position, like educational level was significantly related to the knowledge of mosquito bite as a cause of malaria.

The results from both strands of this study show that the reported wrong perceptions about malaria -like consumption of fatty food as a cause of malaria- which is more of a social constructions, are more grounded among those at lower levels of socioeconomic measures. These constructions exist mainly among those in rural areas, and those of lower educational level as both levels of socioeconomic measures are characterized by reduced access to adequate and correct health information. In addition to this, as earlier stated, life in rural areas in Nigeria is characterized by communal living and strong social and cultural influence. As such, it is expected that social constructions will have a stronger impact on the life of rural dwellers in Nigeria than those in urban and suburban settings.

Another important perception about malaria expressed by participants was that of spiritual forces as a cause of malaria. The concept of spiritual forces as causal to disease and illness is commonly obtainable in many settings in African (Omonzejele, 2008). Disease causality, from an African perspective, goes beyond biological mechanisms like organs and tissues malfunctions (Omonzejele, 2008). In the traditional African setting, diseases and ill health are intricately linked with spirituality (Omonzejele, 2008); hence spiritual forces can cause diseases that are manifested as biological impairments. This perception, which was also present in this study (reported in the qualitative and quantitative studies), can be related to the lack of

adequate knowledge and understanding of the cause of illnesses, hence the resort to spirituality as an explanation for things not understood.

The perception of spiritual attack as a cause of malaria was significantly associated with educational level and type of settlement; with the perception more grounded among those with the lowest level of education. As with those at a higher level of education, urban dwellers had the lowest level of the perception of spiritual attack as a cause of malaria. As an important factor in access to information, educational level and type of settlement can impact on beliefs, attitudes, perceptions, and indeed access to information about health and well-being.

Indeed, perceptions and experiences of individuals in an unequal society will affect their health (Fiorati, Arcêncio, & Souza, 2016). One of the effects of the wrong perceptions about the cause of malaria is that it has the ability to affect malaria prevention. For instance, perceiving spiritual forces as a sole or contributory cause of malaria can affect the use of preventive measures against mosquito bite.

8.12 Malaria preventive measures

Participants' knowledge and understanding of the cause of a disease condition plays a major role in shaping their perception which can subsequently reflect in their behaviours in relation to the disease with regards to preventive and treatment seeking behaviours. An equally important factor that can affect the level of knowledge and access to proper information is education.

An individual's level in the socioeconomic gradient determines the level of power they have over important determinants of their health (Solar & Irwin, 2007). Educational level and type of settlement were significant predictors of the adoption of malaria preventive measures, especially those that involve acquiring tools like insecticide sprays and bed nets, which most times need constant renewal. Educational level, which is significantly associated with the knowledge of mosquito bite as a cause of malaria, is also the strongest predictor of the use of insecticides, and mosquito bednets.

Type of settlement was another predictive factor of the use of mosquito bednets, with the rate of consistency low among rural dwellers. The main reason given by the rural dwellers for the inconsistency in the use of bednets is sweating when sleeping under the bednets. To understand this reason, there is need to highlight important contextual factors at play here.

Rural areas in Nigeria are characterized by limited infrastructure like electricity and poor drainage system (Anele, 2012). With the high temperature in Nigeria all year round, sweating at night is a common challenge faced by residents. This issue is further compounded in settings like the rural areas with epileptic power supply (Anele, 2012) as such unsteady electricity to power fans through the nights. Consequently, some of the measures used in coping with the heat at night times, as reported by an interviewee, include opening doors and windows at night time for ventilation; or sleeping out in the open. Although this helps to reduce the issue of sweating at night, those who engage in these behaviours are further exposed to mosquito bites, thereby increasing their risk of malaria infection. Malaria preventive measures are as well important in the spread of drug resistance since both resistant and non-resistant strains are transmitted the same way.

CHAPTER NINE

CONCLUSIONS AND RECOMMENDATIONS

9.1 Conclusions

The conduct of this study and its findings add a new perspective of social epidemiology to the study of antimalarial drug resistance; offering evidence of the interaction between the measures of socioeconomic position and treatment seeking and drug use behaviours that can promote resistance development and spread.

This study set out to answer two key research questions, which are: 'What are the resistance-promoting drug use behaviours adopted in malaria treatment in Nigeria?' and 'How do socioeconomic factors contribute to the adoption of identified malaria treatment seeking and drug use behaviours that can promote the development and spread of antimalarial drug resistance?'. The findings show some already reported antimalarial drug use behaviours as well as those not reported in literature, like mixing. These behaviours were significantly associated with socioeconomic measures.

Overall, the findings of this study emphasize the connection between socioeconomic measures and drug use behaviours; indicating the ability of socioeconomic deprivation to farther the course of development of antimalarial drug resistance. Consequently, for people to use antimalarial drugs better, the socioeconomic context that fosters the misuse of antimalarial drugs needs to be addressed.

The result showed that the practices of stopping treatment to save drugs for future use and sharing of an antimalarial course with others were significant with socioeconomic measures of educational level, household income and type of settlement. Although some participants recognize the disadvantage of adopting these practices especially with regards to treatment failure, this recognition did not hinder the adoption of such practices. Behaviors like stopping treatment to save drugs for future use and sharing antimalarial course with others becomes rational options for managing recurring malaria infections in the face of poverty. Also, for an individual of low educational level and household income who is trying to survive in the mist of recurring malaria infections, the long-term effect of these practices in relation to promoting the development of drug resistance becomes less of a concern.

Furthermore, the use of ACTs, and getting the complete treatment course were also predicted by household income, employment status, and type of settlement. The overarching impact of socioeconomic measures, like education, on health seeking behaviours cannot be overemphasized. Improving the level of education empowers members of a population to be more involved in their treatment by having a better understanding of options available to them, as such making informed decisions with regards to where to seek treatment, what drug to use, among others.

The practice of mixing, as shown, is significantly associated to not just specific health facility -chemists- but also socieoconomic measures. Although educational level was significantly associated to participants' perception of mixing as best for malaria treatment, when it comes to the adoption of this practice, financial ability (household income) and access to facilities offering this option (type of settlement) were the significant predictors. Efforts to stop the adoption of this practice in the society will have to consider these two significant drivers: access to this option which is made possible by living in rural area, and financial constrain which makes such practice a better alternative to complete treatment course.

The fact that behaviours like non-adherence to treatment guideline, mixing, sharing of a malaria course, and stopping to save drugs for future use are socially patterned is the corollary of the determinant effect of socioeconomic factors in the development and spread of drug resistance. The adoption of these drug use behaviours will persist in malaria endemic populations in the presence of poverty. Indeed, the persistence of these behaviours can render artemisinin, and any subsequent antimalarial drug, ineffective in malaria treatment; thereby increasing the morbidity and mortality attributed to malaria infection.

Presumptive treatment of malaria was widely reported across the interview and survey datasets, irrespective of participants' levels of key socioeconomic measures (excluding employment status which showed a significant relationship). In other words, the key socioeconomic measures were not significant predictors of the adoption of this practice, but were significant predictors of how often people use diagnostic test. This issue of presumptive treatment has been persistent in malaria endemic settings, hence its recognition in studies as the most common method of diagnosis and treatment. Socioeconomic position is not as much an issue in this practice as is the social constructions about malaria. There is need to change the existing idea in this population that one can presumptively diagnose malaria. Reducing the waiting time for malaria treatment in formal health settings will also encourage the use of diagnostic testing

prior to treatment. Also, designing and implementing new health policies that empower informal health facilities to offer malaria diagnostic tests like RDTs while ensuring compliance through adequate training and monitoring will contribute in reducing presumptive treatment of malaria.

Treatment failure as an outcome was also reported in this study. Using the concept of the Donabedian model, the statistical analysis assessed the relationship between this outcome variable, and variables on process as well as structure. Structural factors like Educational level, household income, type of settlement, and type of facility used for last treatment were all statistically associated with treatment failure. The outcome of treatment failure was also significantly associated with processes like the behaviours of using mixed drugs for malaria treatment, stopping malaria treatment to save drugs for future use, and sharing an antimalarial course with others. This study anticipates that improvement in structural factors (especially socioeconomic measures) will reduce the rate of processes like mixing of drugs, stopping treatment to save, sharing of an antimalarial course with others, and presumptive treatment; and subsequently reduce the rate of treatment failure and the development of drug resistance in this population.

The conceptual conclusion of this study (shown in Figure 9.0) is that social, economic and political structures affect an individual's socioeconomic level like educational attainment, household income, type of settlement and employment status; which in turn influences malarial treatment and drug use behaviours. The inequalities in the adoption of treatment seeking and drug use behaviours that can promote drug resistance are significant with levels of socioeconomic factor. In other words, these socioeconomic factors can affect malaria illness experiences and the distribution of outcomes such as treatment failure, drug resistance and effective treatment.

Furthermore, the socioeconomic and health inequalities existing in this population are reflected in the skewed distribution of resistance-promoting and deleterious health behaviours like non-adherence to treatment guideline, mixing of drugs, stopping of treatment to save drugs for future use, and sharing of antimalarial drugs, to the disadvantage of the less well-off in the society. As such, interventions that will effectively bring about changes in these behaviours will need to address these underlying socioeconomic predictors.

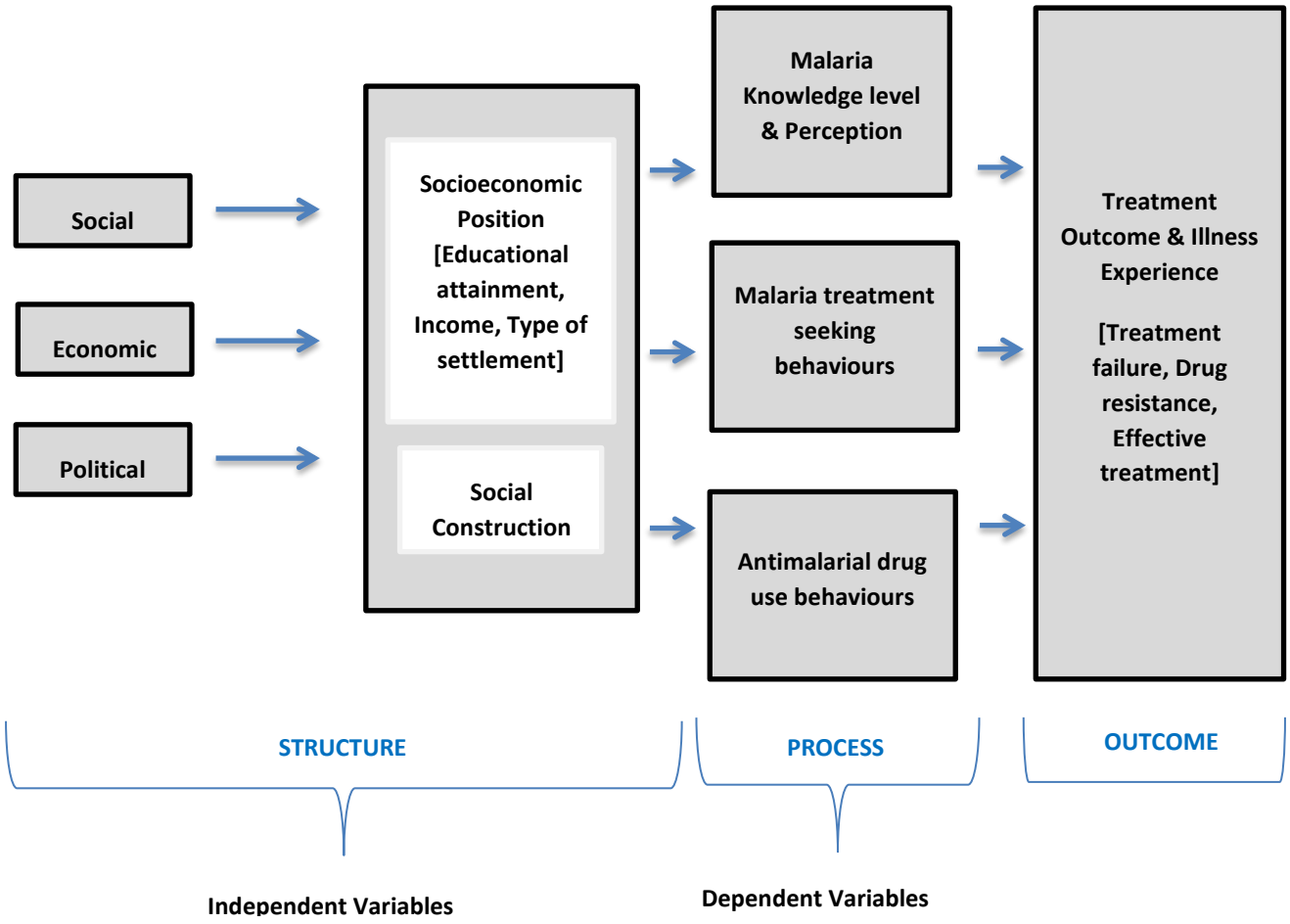

Figure 9.0 Conceptual conclusion based on the findings

Although there is currently no documentation of artemisinin resistance in Nigeria, this does not eliminate the existence of artemisinin-resistant strains of *Plasmodium falciparum* in this population. The absence of this documentation is related to the lack of adequate surveillance program on the use and efficacy of ACTs in Nigeria, hence, artemisinin drug resistant malaria cases are likely to go unnoticed. With the risk Nigeria stands if artemisinin resistance spreads widely in the population, the government and malaria organizations need to deploy effective strategies to prevent this; one of which will be improved surveillance. The demographic feature of Nigeria, its large population, and the high mobility of its citizens across the globe will make the spread of artemisinin resistance in this population a global health issue. It is worth noting that in countries like Cape Verde which is currently at malaria pre-elimination stage, most of the current malaria cases are imported. For Cape Verde, one of the main contributors of the imported cases of malaria each year is people from Nigeria.

Considering the trend in the development and spread of resistance to previous antimalarial drugs like chloroquine, it is clear that the spread of artemisinin resistance in sub-Saharan Africa

will have devastating impact on the overall malaria control, given the high malaria burden in this region.

To sustain the present achievements in malaria control -which is partly attributed to increase in access and availability of ACTs-, there is need to preserve the efficacy of ACT by ensuring these important drugs are used properly.

9.2 Study limitations

As with every research study, this study has some limitations. One of the limitations is that resistance was not confirmed through laboratory test for level of parasitemia. One of the reasons for this is the absence of a follow-up visit in this study. In addition, laboratory confirmation of resistance will require clinical enquiry and more resources.

As stated in the methodology chapter, the survey data were collected from patients seeking malaria treatment from outpatient clinics, pharmacies and chemists (drug vendors). Although the survey questions on their treatment seeking behaviour were mostly on the current malaria episode, data on their drug use behaviours were retrospective (based on previous malaria experiences) as there was no follow-up to determine their drug use behaviour for the current malaria treatment. Given the number of participants in the survey, a follow-up will require more resources and more field workers. Nevertheless, with the high rate of malaria episodes an individual experiences each year in Nigeria (which is also evident in the results of the survey showing 62% of the participants have treated malaria within the last month to the survey), recall bias is reduced. In addition to this, the use of retrospective data helped to ensure the study did not affect or alter the reports on how antimalarial drugs are used as will be the case when participants are expecting a follow-up visit.

Another limitation of this study is that, by adopting a social production of disease theoretical framework, it focused mainly on the contributions of socioeconomic factors. Other factors like cultural and psychosocial factors were not extensively explored in this study. Nevertheless, the focus on socioeconomic factor is justified by the fact that they remain the key players in determining health behaviours and outcomes. And the intrinsic relationship between poverty and malaria makes socioeconomic status an important issue in malaria.

Also, caution should be exercised in the generalizability of the findings to the entire Nigerian population given that data was collected from two sites (one from the northern and one from the southern regions) of Nigeria. Although the northern and southern regions in Nigeria differ

in relation to important factors to malaria treatment (like educational level), slight differences also exist between the different states and ethnic groups within each of the regions in terms of socioeconomic and cultural profile. Nevertheless, this does not disprove the external validity of this study. With a rigorous and appropriate sampling method and adequate sample size, the findings of this study are generalizable to the study population (Abuja and Imo State).

9.3 Recommendations

The results of this study show that socioeconomic factors make significant contributions to the adoption of behaviours that can promote the development and spread of antimalarial drug resistance. Overall, the findings of this study are important to malaria campaign generally, and antimalarial drug resistance control specifically. As such, the findings are important to the Nigerian government and Health Ministry, other malaria endemic populations, governmental and non-governmental organizations with interest in malaria control, malaria researchers amongst others.

As this study was underpinned by the social production of disease theory, the recommendations, which are based on the finding of the study and this theory, are targeted at improving the wider economic and social systems and context that impel or constrain individual actions and decisions in seeking malaria treatment and in using antimalarial drugs.

According to Berkman et al., (2014), to achieve a sustainable improvement in health, campaigns should be targeted at social structures in the society that produce diseases. In malaria campaigns, there is need to broaden the scope of antimalarial drug resistance control strategies to include strategies targeted at improving the socioeconomic condition of people in malaria endemic areas. Population-wide improvements in income, education, environmental and structural conditions of rural areas in malaria endemic settings will encourage behavioural change on how antimalarial drugs are used.

Furthermore, the results of this study shows a significant relationship between types of health facility participants used for malaria treatment and the adoption of drug use behaviours that can promote drug resistance. Practices like mixing and presumptive treatment were reported more by those using the informal health facilities. As stated earlier, the informal health facilities (like the chemists) cater for 60% of the malaria cases in Nigeria (National Population Commission, 2012); nevertheless, malaria interventions in Nigeria as with other endemic countries are mostly implemented through formal health facilities who are not the major

provider of malaria treatment to the population. There is need for malaria endemic countries and organizations involved in malaria programs to involve the informal health sector given their important role in malaria treatment and the quality of care patients receive.

There is also need to improve reporting in Nigeria, especially in the informal health facilities. One of the reasons for the boycott of informal health facilities in malaria interventions is lack of data from these facilities. Without data from the major providers of malaria treatment, the magnitude of the problem will not be well understood, as such it becomes difficult to have effective interventions that will reduce the malaria burden. In addition to improving the rate of reporting is also the need for the government to revise what needs to be reported. Issues arising from malaria case management, like treatment failures need to be reported from both formal and informal sectors. This will be important in early detection of the spread of resistance within the population.

Equally important to address is the issue of regulations. The Nigerian Government, through the Ministry of Health, needs to ensure the existence and enforcement of policies and regulations on antimalarial drug distribution and dispensing. However, this can only successfully reduce the rate of antimalarial drug abuse if the existing underlying factors that promote these behaviours, like poverty, poor access to healthcare services, poor level of education, social constructions, are first addressed. There is need for the Nigerian government to review its policy on out of pocket payment at the point of use for primary healthcare services at public health facilities, especially in rural areas, as this constitutes a barrier to the use of formal health facilities that provides better quality malaria treatment.

In addition, further studies should be carried out on some factors reported in this study, like the practice of mixing drugs for malaria treatment. With this practice not previously reported, there is no evidence of the extent to which it can affect the efficacy of antimalarial drugs and the treatment experiences of people in this population. More studies with wider coverage (in terms of the number of Nigerian states studied, or other malaria endemic countries), need to be conducted to assess the presence and extent of the practice of mixing in malaria treatment.

Finally, as this study is underpinned by a theory that champions equity rather than equality, controlling the rate of drug resistance-promoting behaviours in this population will require ensuring those who are at most risk of this behaviours receive more of the interventions that can change their drug use behaviours. Given the results of this study indicating those at lower levels of socioeconomic factors are more likely to adopt drug use behaviours that promote drug

resistance, and the fact that most of the behaviours were centered around coping with the cost of treatment, malaria control strategies like subsidized antimalarial drugs from Affordable Medicine Facility-malaria (AMFm) should be available more in areas with high proportion of those of low socioeconomic position.

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APPENDIX

Questionnaire

Code: A/U/a

QUESTIONNAIRE ON ANTIMALARIAL DRUG USE

1. Before we get started, do you mind showing me the prescription or drug you got today, if you did?

We would like to start by asking a few questions about you and your household

2. What is your age?

3. What is your sex?

- Male
- Female
- Prefer not to say

4. What is your level of education?

- No formal education
- Primary education
- Secondary education
- Tertiary education
- Post graduate education

5. What is your current relationship status?

- Single
- Married
- Widowed
- Divorced/separated
- Other (*please specify*):

6. What is your household's monthly income from all sources?

7. What is your current employment status?

- Employed
- Self-employed
- Unemployed
- Retired
- In education

8. What occupation is your major source of getting money?

9. Where do you live?

- City
- Small towns
- Village

10. How many people including yourself, live in your household?

11. How many children live in your household?

12. How many of the children in your household are:

Younger than 5 years

Older than 5 but under 11 years

Older than 11 but under 18 years

The following questions are concerned with what you think about malaria.

13. What are the causes of malaria? *(Use the rating scale below and circle the number that best represents what you think)*

	Not sure at all = 1		**–**		***5 = Absolutely sure***
Mosquito bites	**1**	**2**	**3**	**4**	**5**
Dirty environment	**1**	**2**	**3**	**4**	**5**
Eating fatty/oily foods	**1**	**2**	**3**	**4**	**5**
Spiritual attacks	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

14. What are the symptoms of malaria? *(Use the rating scale below and circle the number that best represents what you think)* ***Not sure at all = 1 – 5 = Absolutely sure***

Fever	**1**	**2**	**3**	**4**	**5**
Nausea or vomiting	**1**	**2**	**3**	**4**	**5**
Bitterness of the mouth	**1**	**2**	**3**	**4**	**5**
Loss of appetite	**1**	**2**	**3**	**4**	**5**
Excessive sleep	**1**	**2**	**3**	**4**	**5**
Pain in the joints	**1**	**2**	**3**	**4**	**5**
Catarrh and cold	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

15. Malaria **is a treatable disease**

- Strongly disagree
- Disagree
- Neither agree nor disagree
- Agree
- Strongly agree

16. Malaria is a life threatening condition

- Strongly disagree
- Disagree
- Neither agree nor disagree
- Agree
- Strongly agree

17. Sickle cell gene can protect against malaria

- Strongly disagree
- Disagree
- Neither agree nor disagree
- Agree
- Strongly agree

(The following questions are about what you do to prevent malaria infection)

18. Which of these methods do you use to prevent malaria infection?

Insecticides	Never	Sometimes	Always
Local insecticides (Otapiapia, Tusatusa etc)	Never	Sometimes	Always
Mosquito bed nets	Never	Sometimes	Always
Door and window mosquito nets	Never	Sometimes	Always

Avoiding standing water around the house	☐ Never	☐ Sometimes	☐ Always
Other (please specify):	☐ Never	☐ Sometimes	☐ Always

19. If you have a mosquito treated bed net, how frequent do you use it?

○ Every night ○ Most nights ○ Few nights ○ Never use it

20. If you do not use the bed net every night, what are your reasons? *(Tick all boxes that apply)*

☐ Sweating when sleeping under the bednet

☐ Discomfort because of the embedded insecticide

☐ Net too small for bed

☐ No bed-pole to fix/tie the net on

☐ Others (please specify)

The following questions are about the current episode of malaria

21. Did you visit this facility today to seek treatment for yourself or for someone else? *(Tick the box that applies)*

○ For myself

○ For a member of my household

○ For myself and a member of my household

○ Others (please specify)

22. I chose this facility today because: *(Use the rating scale below and circle the number that best represents how important the option is to you)*

	Not at all important = 1		**–**		***5 = Very Important***
It is affordable	**1**	**2**	**3**	**4**	**5**
It offers good quality of service	**1**	**2**	**3**	**4**	**5**
The drugs are usually readily available here	**1**	**2**	**3**	**4**	**5**
It is close to my home or work place	**1**	**2**	**3**	**4**	**5**
The facility offers credit payment option	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

23. Did you or the patient get an antimalarial prescription today?

○ Yes I did

○ Yes the patient did

○ No antimalarial prescription was given today

24. Did you or the patient receive **antimalarial drugs today?**

- Yes I did
- Yes the patient did
- No antimalarial drug was received today

25. Did you or the patient have a malaria diagnostic test?

- Yes I did
- Yes the patient did
- No diagnostic test was conducted

26. Is the prescription or drug you received today ACT (Artemisinin based combination therapy)?

- Yes
- No
- Don't know

27. Did you or the patient get the complete malaria treatment dose today?

- Yes
- No
- Don't know

28. Which of the following influenced your decision to get the complete treatment dose? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

	Not at all important = 1				***5 = Very important***
Price of the complete dose	**1**	**2**	**3**	**4**	**5**
Availability of the complete dose in the service	**1**	**2**	**3**	**4**	**5**
The side effects	**1**	**2**	**3**	**4**	**5**
If I have already started taking some doses	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

29. How much did it cost you to receive this malaria treatment, excluding the cost of transportation?

Naira (₦)

30. How much did you spend on transportation today?

Naira (₦)

31. How did you pay for the treatment cost today? (Tick all boxes that apply)

- ☐ Cash and carry
- ☐ Private health insurance
- ☐ National health insurance
- ☐ Instalment
- ☐ On credit
- ☐ In exchange for services
- ☐ Other (please specify): _____

32. The cost of this treatment is readily affordable to me

- ☐ Strongly disagree
- ☐ Disagree
- ☐ Neither agree nor disagree
- ☐ Agree
- ☐ Strongly agree

The following questions will be about the current malaria episode and the time you/the patient used an antimalarial drug

33. Is today the first time that you are seeking treatment for the current malaria episode?

- ○ Yes
- ○ No
- ○ Don't know

34. Have you/**the patient** taken an antimalarial drug for the current episode before?

- ○ Yes
- ○ No
- ○ Don't know

35. If yes, what is your reason(s) for seeking treatment again?

- ☐ I felt better but the symptoms returned
- ☐ I never felt any better
- ☐ I never felt better, symptoms got worse
- ☐ Other (please specify): _____

36. When was the last time that you/the patient used an antimalarial drug?

- ☐ This current week
- ☐ Last week
- ☐ Last month
- ☐ Within the last three months
- ☐ More than three months ago

37. What is the name of the antimalarial drug you/the patient used the last time?

38. Where did you seek malaria treatment the last time? *(Tick all boxes that apply)*

- ○ Pharmacy
- ○ Chemist
- ○ Health centre/Community Health worker
- ○ Private hospital or clinic
- ○ Public/Government hospitals or clinic
- ○ Native healer
- ○ Other *(please specify)*:

39. The last time you used antimalarial drugs, w**here did you get them from?** *(Tick all boxes that apply)*

- ○ Pharmacy
- ○ Chemist
- ○ Health centre/Community Health worker
- ○ Private hospital or clinic
- ○ Public/Government hospitals or clinic
- ○ Native healer
- ○ Other *(please specify)*:

40. Did you/the patient complete the last malaria treatment

○ Yes ○ No ○ Don't know

41. What were the reasons for not completing the last treatment? *(Tick all boxes that apply)*

- ☐ Felt better
- ☐ Did not feel
- ☐ Symptoms got worse
- ☐ Did not buy the complete dose
- ☐ Saved drugs for future use
- ☐ Shared drugs with someone else
- ☐ No food for taking the drugs
- ☐ Other (please specify): _____

42. Last time, did you/the patient take the antimalarial drugs at the recommended time of the day?

○ Never ○ Rarely ○ Sometimes ○ most times ○ Always

43. Last time, did you/the patient take the number of tablets as recommended?

○ Never ○ Rarely ○ Sometimes ○ most times ○ Always

The following questions will be about your overall malaria treatment behaviours.

44. Which of the following is your <u>most usual</u> source of antimalarial drugs? *(Tick the box that is most applicable)*

- ○ Pharmacy
- ○ Chemist
- ○ Health center/Community Health Worker
- ○ Private hospital or clinic
- ○ Government hospitals
- ○ Native healer
- ○ Other (*please specify*): _____

45. How important are the following factors in your decision on where to seek malaria treatment? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

Not at all important = 1 – 5 = Very Important

Affordable	**1**	**2**	**3**	**4**	**5**
Good quality of service	**1**	**2**	**3**	**4**	**5**
Availability of antimalarial drugs	**1**	**2**	**3**	**4**	**5**
Closeness to my home or work place	**1**	**2**	**3**	**4**	**5**
The facility offers credit payment option	**1**	**2**	**3**	**4**	**5**
The waiting time at the he facility	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

_____

46. How important are the following factors in your decision about where to seek malaria treatment? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

	Not at all important = 1		**–**		***5 = Very Important***
My income level	**1**	**2**	**3**	**4**	**5**
Where I live	**1**	**2**	**3**	**4**	**5**
My type of job	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

47. Do you think it is important to go for a laboratory test for malaria prior to treatment?

- ☐ Not at all important
- ☐ Somewhat important
- ☐ Neither important nor unimportant
- ☐ Important
- ☐ Very important

48. How often do you/the patient go for a laboratory test before you treat malaria?

○ Never ○ Rarely ○ Sometimes ○ most times ○ Always

If you ticked 'always', please move on to question 51

49. Which of the following factors discourages you from going for a malaria laboratory test? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

	Not at all important = 1		**–**		***5 = Very Important***
Can't afford the test	**1**	**2**	**3**	**4**	**5**
Laboratory services not available	**1**	**2**	**3**	**4**	**5**
Long waiting time	**1**	**2**	**3**	**4**	**5**
Confidence in diagnosing malaria	**1**	**2**	**3**	**4**	**5**
I do not like to give blood samples	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

50. How often do you use herbal medicine to treat malaria?

○ Never ○ Rarely ○ Sometimes ○ most times ○ Always

51. Have you ever combined herbal treatment for malaria with any other antimalarial drug at the same time?

○ Never ○ Rarely ○ Sometimes ○ most times ○ Always

52. If cost were not a problem, where would be your first point of seeking malaria treatment? *(Tick the box that is most applicable)*

- Pharmacy
- Chemist
- Health center/Community Health Worker
- Private hospital/clinic
- Government hospitals/clinics
- Native healer
- Other (please specify):

53. The very first time you had malaria, where did you seek treatment?

- Pharmacy
- Chemist
- Health center/Community Health Worker
- Private hospital/clinic
- Government hospitals/clinics
- Native healer
- Other (please specify):

54. Did you go for a malaria diagnostic test when you had malaria for the first time in your life?

- Yes
- No
- Cant remember

Can we ask you some questions on how you seek for malaria treatment for your child(ren). If you have never sought malaria treatment for children, please move to Q59

55. Where would you <u>normally</u> seek malaria treatment for a child?

- Pharmacy
- Chemist
- Health center/Community Health Worker
- Private hospital/clinic
- Government hospitals/clinics
- Native healer
- Other (please specify):

56. Why did you choose this facility for a child? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

	Not at all important = 1		–		*5 = Very Important*
It is affordable	1	2	3	4	5
It offers good quality of service	1	2	3	4	5
The drugs are usually readily available here	1	2	3	4	5
It is close to my home or work place	1	2	3	4	5
The facility offers credit payment option	1	2	3	4	5
Other (please specify):	1	2	3	4	5

57. The last time you sought malaria treatment for a child, did he/she have a malaria diagnostic test before treatment?

- ○ Yes
- ○ No
- ○ Don't know

58. Who normally decides what type of antimalarial drugs you should use?

- ○ Healthcare practitioner
- ○ Pharmacist
- ○ Chemist
- ○ Myself
- ○ A member of my family
- ○ Other (please specify):

59. What factors determine the antimalarial drug you buy? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

	Not at all important = 1		–		*5 = Very Important*
Effectiveness of the drug	1	2	3	4	5
The price of the drug	1	2	3	4	5
Side effects from the drug	1	2	3	4	5
Number of tablets I will have to take	1	2	3	4	5
Number of doses I will have to take	1	2	3	4	5
Other (please specify):	1	2	3	4	5

60. When using antimalarial drugs, how do you know the number of doses and time to administer?

- ☐ Oral instructions from healthcare provider
- ☐ Drug leaflets
- ☐ Knowledge from previous treatments
- ☐ Other (please specify):

61. Which of these would you do if you forget the number of doses or time to take your antimalarial drugs? *(Tick all boxes that apply)*

- ☐ Take it as I deem fit
- ☐ Read the drug leaflet
- ☐ Read my prescription sheet
- ☐ Call my healthcare provider
- ☐ Miss or stop the treatment
- ☐ Other (please specify): _____

62. Do you find the instructions on how to administer malaria drugs easy to remember?

- ○ Not easy at all
- ○ Somewhat easy
- ○ Neither easy nor uneasy
- ○ Easy
- ○ Very easy

63. How often have you stopped your malaria treatment to save the drugs for future use?

○ Always ○ Most times ○ Few time ○ Never

64. How often have you shared your antimalarial drugs with someone else?

○ Always ○ Most times ○ Few time ○ Never

65. Have you ever used the mixed antimalarial drugs before?

○ Never ○ Rarely ○ Sometimes ○ most times ○ Always

66. If you have mixed antimalarial drugs before, w**hat factors encouraged your practice of mixing?**

- ○ It is cheaper
- ○ It is more effective
- ○ It is the only option offered

67. What facility is most likely to mix drugs for malaria treatment? *(Use the rating scale below and circle the number that best represents the likelihood)*

	Not likely at all = 1		**–**		***5=Very likely***
○ Pharmacy	**1**	**2**	**3**	**4**	**5**
○ Chemist	**1**	**2**	**3**	**4**	**5**
○ Health center/Community Health worker	**1**	**2**	**3**	**4**	**5**
○ Private hospital or clinic	**1**	**2**	**3**	**4**	**5**
○ Government hospitals or clinic	**1**	**2**	**3**	**4**	**5**

68. Malaria is best treated by taking? *(Use the rating scale below and circle the number that best represents your level of agreement)* ***Strongly agree = 1 - 5 = Strongly disagree***

Mixed drugs	**1**	**2**	**3**	**4**	**5**
Antimalarial drugs sold as complete course	**1**	**2**	**3**	**4**	**5**
Herbal medicine	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

69. Do you usually know the expiry date of the mixed antimalarial drugs?

- Yes
- No

70. What determines the number of doses you get when mixing drugs for malaria treatment? *(Use the rating scale below and circle the number that best represents how important the option is to you)*

Not at all important = 1 – 5 = Very Important

The number of doses I can afford	**1**	**2**	**3**	**4**	**5**
The chemist's expertise	**1**	**2**	**3**	**4**	**5**
The number of dose I want	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

71. How often do you buy antimalarial drugs sold as a complete treatment course?

Always Most times Few times Never

72. For good quality antimalarial drugs, which of the following facilities would you recommend? ***Not recommend at all = 1 – 5 = Strongly recommend***

Pharmacy	**1**	**2**	**3**	**4**	**5**
Chemist	**1**	**2**	**3**	**4**	**5**
Health center/Community Health worker	**1**	**2**	**3**	**4**	**5**
Private hospital or clinic	**1**	**2**	**3**	**4**	**5**
Government hospitals or clinic	**1**	**2**	**3**	**4**	**5**
Other (please specify):	**1**	**2**	**3**	**4**	**5**

73. Is there anything else you want to add?

Additional Comments:

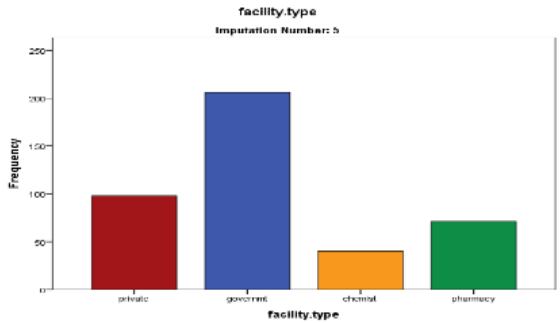
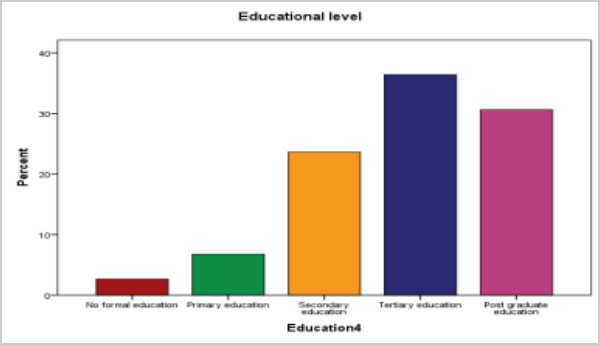
Citations for included studies in systematic review

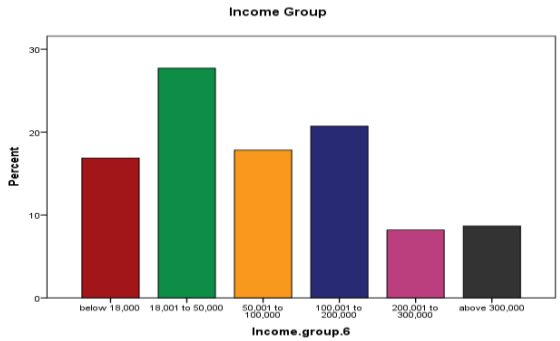
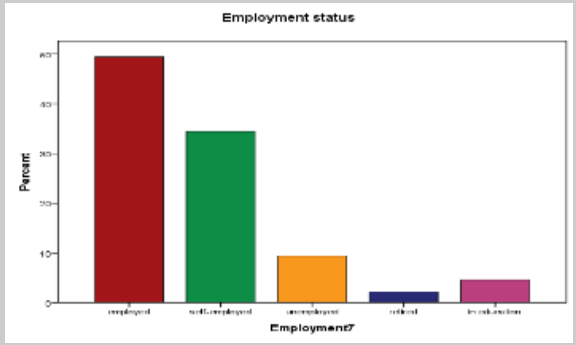
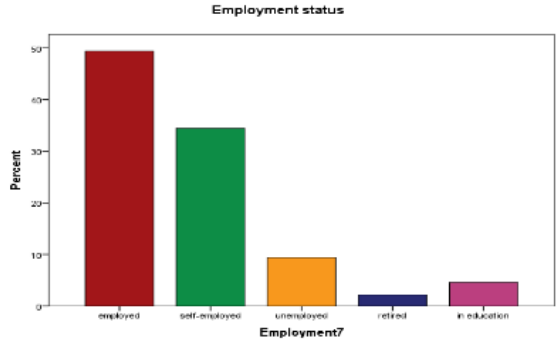
Figure 5.2: List of Included Studies for the Systematic Review	
S/N	**Citation**
1	Deressa, W., Ali, A., & Berhane, Y. (2007). Household and socioeconomic factors associated with childhood febrile illnesses and treatment seeking behaviour in an area of epidemic malaria in rural Ethiopia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *101*(9), 939-947.
2	Watsierah, C. A., Jura, W. G., Raballah, E., Kaseje, D., Abong'o, B., & Ouma, C. (2011). Knowledge and behaviour as determinants of anti-malarial drug use in a peri-urban population from malaria holoendemic region of western Kenya. *Malaria journal*, *10*(1), 99.
3	Onwujekwe, O., Hanson, K., Uzochukwu, B., Ezeoke, O., Eze, S., & Dike, N. (2010). Geographic inequities in provision and utilization of malaria treatment services in southeast Nigeria: diagnosis, providers and drugs. *Health Policy*, *94*(2), 144-149.
4	Oguonu, T., Okafor, H. U., & Obu, H. A. (2005). Caregivers's knowledge, attitude and practice on childhood malaria and treatment in urban and rural communities in Enugu, south-east Nigeria. *Public health*, *119*(5), 409-414.
5	Beer, N., Ali, A. S., Rotllant, G., Abass, A. K., Omari, R. S., Al-mafazy, A. W. H., ... & Källander, K. (2009). Adherence to Artesunate–amodiaquine combination therapy for uncomplicated malaria in children in Zanzibar, Tanzania. *Tropical Medicine & International Health*, *14*(7), 766-774.
6	Gerstl, S., Dunkley, S., Mukhtar, A., Baker, S., & Maikere, J. (2010). Successful introduction of Artesunate combination therapy is not enough to fight malaria: results from an adherence study in Sierra Leone. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *104*(5), 328-335.
7	Onyango, E. O., Ayodo, G., Watsierah, C. A., Were, T., Okumu, W., Anyona, S. B., ... & Ouma, C. (2012). Factors associated with non-adherence to Artemisinin-

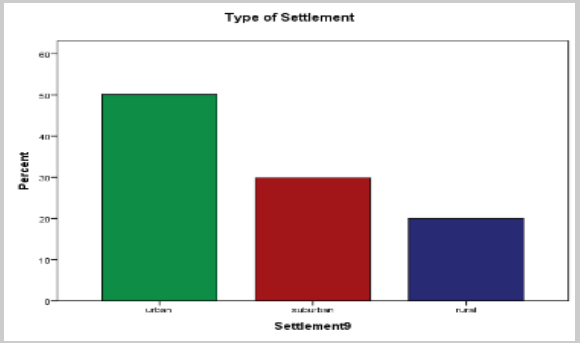
	based combination therapy (ACT) to malaria in a rural population from holoendemic region of western Kenya. *BMC infectious diseases*, *12*(1), 143.
8	Cohen, J. L., Yavuz, E., Morris, A., Arkedis, J., & Sabot, O. (2012). Do patients adhere to over-the-counter artemisinin combination therapy for malaria? Evidence from an intervention study in Uganda. *Malaria Journal*, *11*(1), 83.
9	Wongsrichanalai, C., & Meshnick, S. (2008). Declining Artesunate-Mefloquine Efficacy against Falciparum Malaria on the Cambodia–Thailand Border-Volume 14, Number 5—May 2008-Emerging Infectious Disease journal-CDC.
10	Cohen, J. M., Sabot, O., Sabot, K., Gordon, M., Gross, I., Bishop, D., ... & Goodman, C. (2010). A pharmacy too far? Equity and spatial distribution of outcomes in the delivery of subsidized artemisinin-based combination therapies through private drug shops. *BMC Health Services Research*, *10*(1), S6.
11	Ogolla, J. O., Ayaya, S. O., & Otieno, C. A. (2013). Levels of adherence to coartem© in the routine treatment of uncomplicated malaria in children aged below five years, in kenya. *Iranian journal of public health*, *42*(2), 129.
12	Akoria, O. A., & Arhuidese, I. J. (2014). Progress toward elimination of malaria in Nigeria: Uptake of artemisinin. based combination therapies for the treatment of malaria in households in Benin City. *Annals of African medicine*, *13*(3), 104-113.
13	Exavery, A., Mbaruku, G., Mbuyita, S., Makemba, A., Kinyonge, I. P., & Kweka, H. (2014). Factors affecting uptake of optimal doses of sulphadoxine-pyrimethamine for intermittent preventive treatment of malaria in pregnancy in six districts of Tanzania. *Malaria journal*, *13*(1), 22.
14	Simba, D. O., Kakoko, D., Tomson, G., Premji, Z., Petzold, M., Mahindi, M., & Gustafsson, L. L. (2012). Adherence to artemether/lumefantrine treatment in children under real-life situations in rural Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *106*(1), 3-9.
15	Bruxvoort, K., Kalolella, A., Cairns, M., Festo, C., Kenani, M., Lyaruu, P., ... & Goodman, C. (2015). Are Tanzanian patients attending public facilities or private retailers more likely to adhere to artemisinin-based combination therapy?. *Malaria journal*, *14*(1), 87.

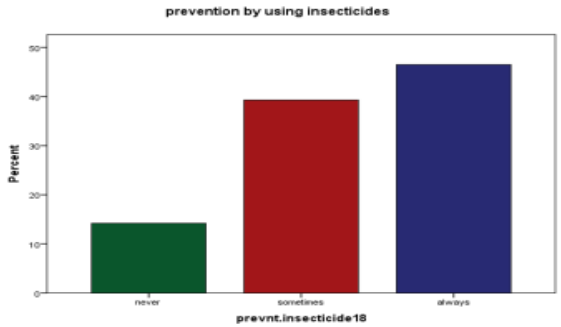
16	Win, T. Z., Zaw, L., Khin, W., Khin, L., Tin, O. M., Tun, K. T., & Zin, T. K. (2012). Adherence to the recommended regimen of artemether-lumefantrine for treatment of uncomplicated falciparum malaria in Myanmar. *Myanmar Health Sci Res J*, *24*(1), 51-5.
17	Watsierah, C. A., Jura, W. G., Oyugi, H., Abong'o, B., & Ouma, C. (2010). Factors determining anti-malarial drug use in a peri-urban population from malaria holoendemic region of western Kenya. *Malaria journal*, *9*(1), 295.

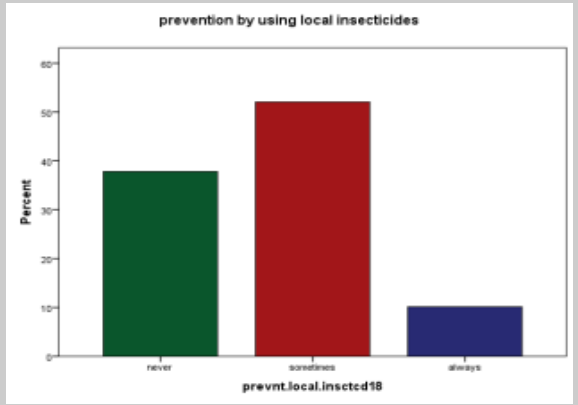
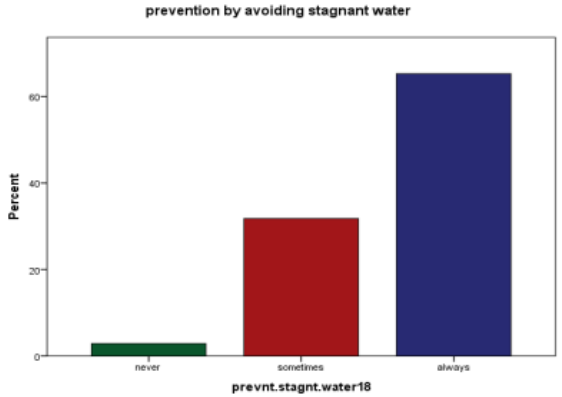
Table on results of descriptive statistics

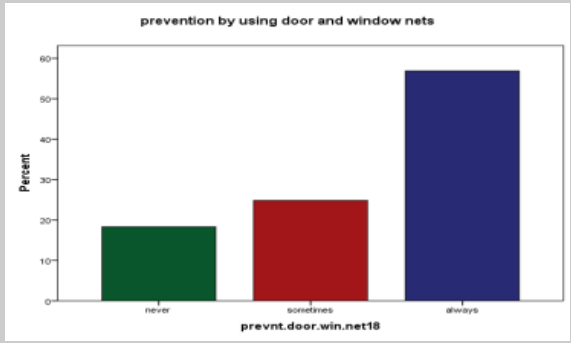
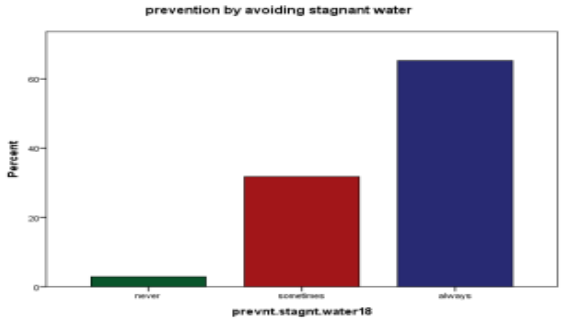
TABLE 7.2.4: RESULTS OF DESCRIPTIVE STATISTICS				
VARIABLE	MEAN	MEDIAN	MODE	PERCENTAGE AND CHART
Type of facility recruited from				
Age (in years)	**34**	**33**	**29**	
Gender				**Male = 36%; Female = 64%**
Educational level				

Income	**₦121,217**	**₦72,182**	**₦40,000**	
Employment status				
Occupation				

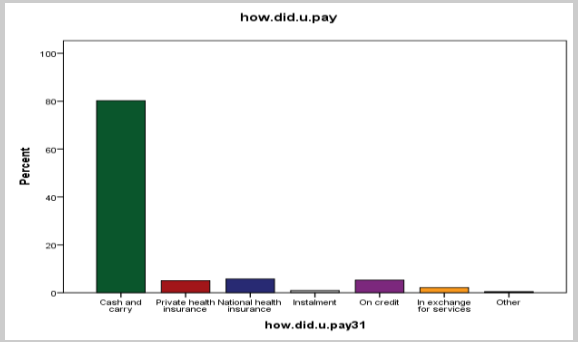
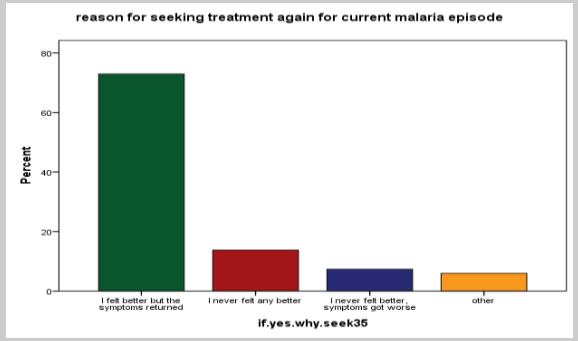
Type of Settlement				
Household size	**4**	**4**	**4.6**	
Number of children in household	**2**	**2**	**2.4**	
Knowledge of malaria causes (5-point scale):				
Mosquito	**4.4**	**5**	**5**	
Dirty environment	**3.6**	**4**	**5**	
Fatty food	**2.5**	**2**	**1**	
Spiritual attack	**2.2**	**1**	**1**	
Malaria symptoms (5-point scale):				
Fever	**4.6**	**5**	**5**	
Nausea	**4**	**4**	**5**	
Bitter mouth	**4.2**	**4**	**5**	

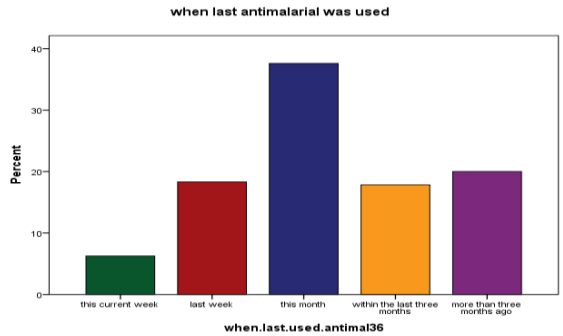
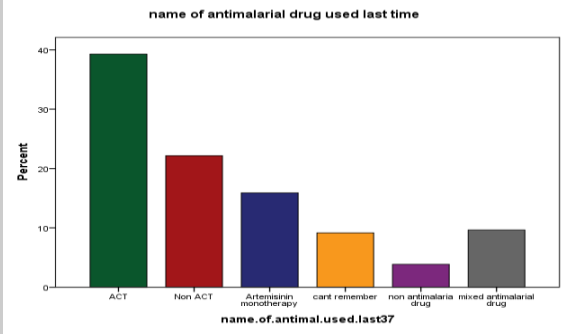
Loss of appetite	**3.9**	**4**	**5**	
Excessive sleep	**2.8**	**3**	**1**	
Body pains	**3.3**	**3**	**1**	
Catarrh	**3.1**	**3**	**5**	
Perception of malaria as treatable (5-point scale):	**4**	**4**	**5**	
Perception of malaria as life threatening (5-point scale):	**4**	**4**	**4**	
Perception of sickle cell gene as protective against malaria (5-point scale):	**2.6**	**3**	**3**	
Malaria prevention practices: **Use of insecticides**				

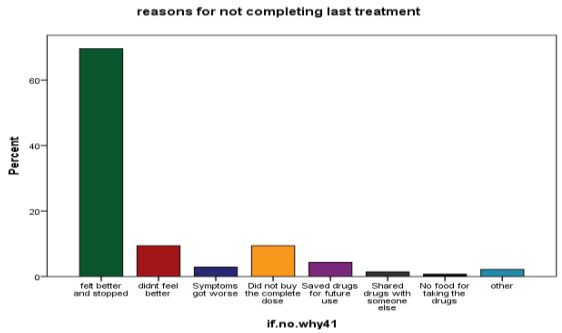
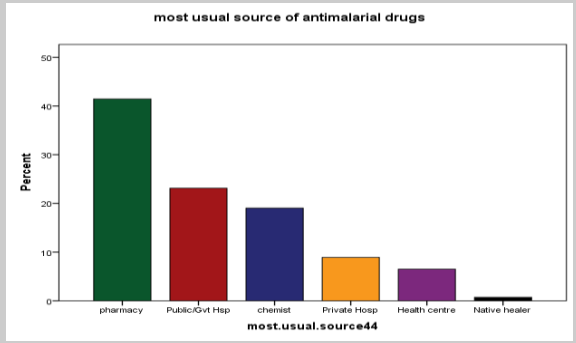
Use of local insecticides				
Use of mosquito bednets				
Use of door and window nets				

Avoiding stagnant water				
				
Frequency of use of mosquito bednet (5-point scale):	**2.3**	**2**	**1**	
Reasons for inconsistence in use of malaria bednet:				
Sweating when using				**Yes = 46.5%; No = 34%; N/A = 19.5%**
Discomfort because of embedded insecticide:				**Yes = 25%; No = 55%; N/A 20= %**
Net too small for bed				**Yes = 10%; No = 68%; N/A = 22%**
No hook/pole to fix/tie the net on				**Yes = 14%; No = 65%; N/A = 21%**

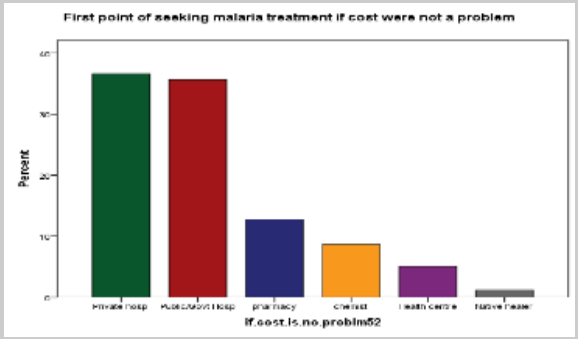
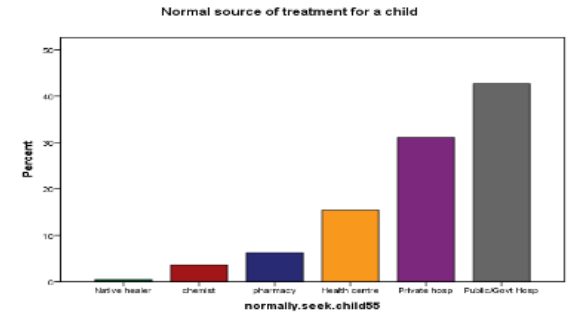
Reason for choice of facility (5-point scale):				
Affordability	**3.8**	**4**	**5**	
Good quality of care	**4.1**	**4**	**5**	
Drugs readily available	**3.9**	**4**	**5**	
Closely located	**3.9**	**4**	**5**	
Offers credit payment option	**2.7**	**2**	**1**	
Received antimalarial drug today				**Yes = 96%; No = 4%**
Had diagnostic test today				**Yes = 56%; No = 44%**
Received an ACT drug or prescription				**Yes = 73%; No = 23%; Don't know = 4%**
Received the complete treatment course today				**Yes = 68%; No = 28%; Don't know = 4%**
Reasons for not getting complete course (5-point scale):				
Price of the complete dose	**3.59**	**4**	**5**	
Availability of the complete course in the service	**3.28**	**4**	**5**	
Side effects of the drugs	**2.48**	**2**	**1**	
Already started taking some doses	**2.16**	**2**	**1**	
Cost of treatment excluding transport	**₦1701.7**	**₦1200**	**₦1000**	
Cost of transportation to receive treatment	**₦429.6**	**₦300**	**₦200**	

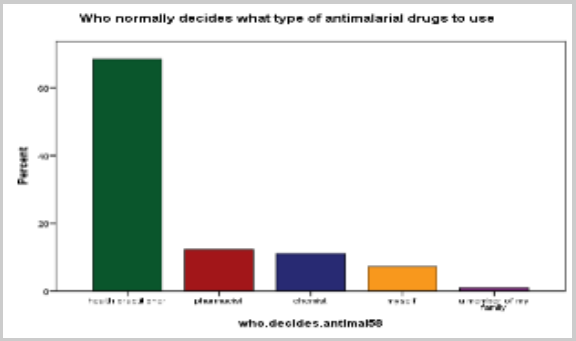
Medium of payment for treatment				
Affordability of treatment cost (5-point scale):	**3.1**	**4**	**4**	
Seeking treatment for the first time for the current malaria episode				**Yes = 33%; No = 65%; Don't know = 2%**
Had previously taken antimalarial drugs for current episode.				**Yes = 53%; No = 45%; Don't know = 4%**
Reason for seeking treatment again				

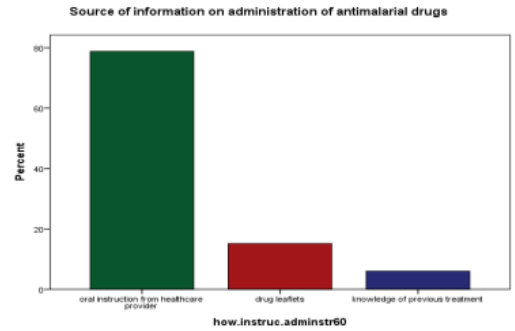
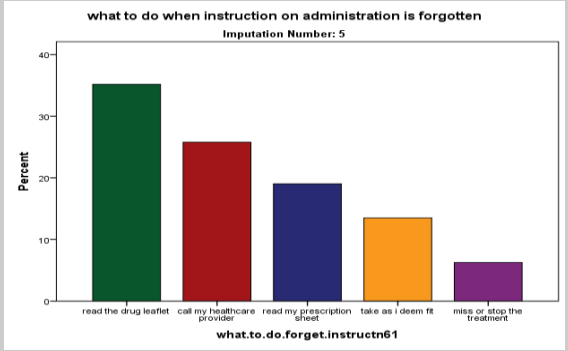
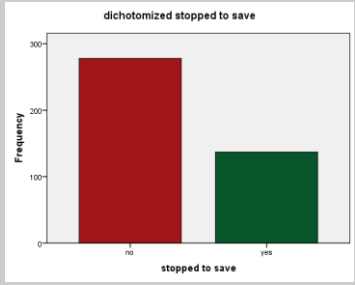
Last time antimalarial drug was taken				
Name of antimalarial drug used last time				
Source of last malaria treatment				**Informal health facility = 41%;** **Formal health facility = 59%**
Completed last malaria treatment course				**Yes = 73%; No = 27%**

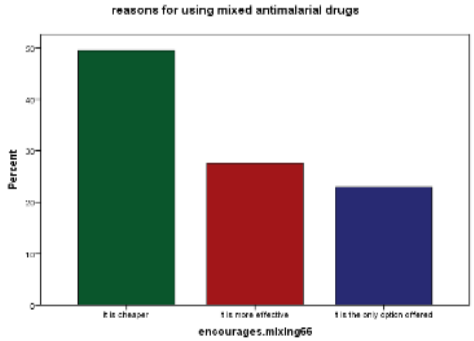
Reasons for not completing last treatment course				
Administered the last course at the recommended time (5-point scale):	**4.2**	**5**	**5**	
Administered the recommended number of doses for last course (5-point scale):	**4.5**	**5**	**5**	
Most usual source of treatment				
Factors important in decisions on where to seek malaria treatment (5-point scale): **Affordability of service**	**3.7**	**4**	**5**	

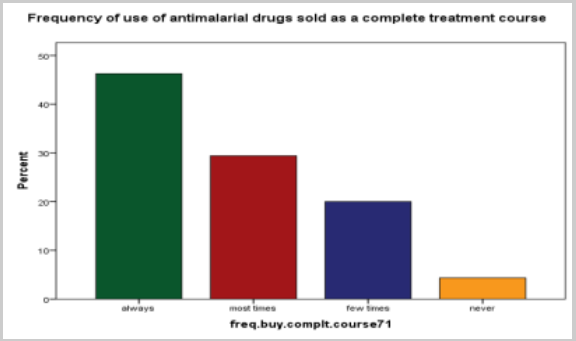
Good quality of service	**4.20**	**5**	**5**	
Availability of antimalarial drugs	**4.3**	**5**	**5**	
Closeness to my location	**3.9**	**4**	**5**	
Offers credit payment option	**2.46**	**2**	**1**	
Waiting time	**3**	**3**	**3**	
Importance of SEFs in treatment-seeking decisions (5-point scale):				
Income level	**3.7**	**3**	**3**	
Type of settlement	**3.7**	**4**	**5**	
Occupation	**2.8**	**3**	**1**	
Perception about importance of malaria diagnostic test (5-point scale):	**4**	**4**	**5**	
Frequency of use of malaria diagnostic test prior to treatment (5-point scale):	**3**	**3**	**3**	
Reasons for inconsistency in using malaria diagnostic test prior to treatment (5-point scale):				
Cannot afford the test	**3**	**3**	**1**	
Diagnostic test not available	**3**	**3**	**1**	
Long waiting time	**3.5**	**4**	**5**	
Confidence in diagnosing malaria	**3**	**3**	**5**	
Do not like to give blood sample	**2.5**	**3**	**1**	

Frequency of use of herbal medicine for malaria treatment (5-point scale):	**1.8**	**1**	**1**	
Combining herbal malaria drugs with other antimalarial drugs (5-point scale):	**1.4**	**1**	**1**	
First Point of seeking malaria treatment if cost was not a problem				
Normal source of treatment for a child				
Reasons for choice of facility for child (5-point scale):				
Affordability of service	**3.5**	**4**	**5**	
Good quality of service	**4.6**	**5**	**5**	

Availability of antimalarial drugs	**4**	**4**	**5**	
Closeness to my location	**3.6**	**4**	**5**	
Offers credit payment option	**1.6**	**1**	**1**	
Use of malaria diagnostic test prior to last malaria treatment for a child				**Yes = 59%; No = 36%; Don't know = 5%**
Who normally decides what type of antimalarial drugs to use				
Determinants of choice of anti-malarial drugs (5-point scale):				
Effectiveness of the drug	**4.5**	**5**	**5**	
Price of the drug	**3.2**	**3**	**5**	
Side effects	**3.5**	**4**	**5**	
Number of tablets to take	**3**	**3**	**1**	
Number of doses	**3.2**	**3**	**5**	

Source of information on administration of antimalarial drugs				
What to do if you forget the number of doses or time to take your antimalarial drug				
Easy of remembering malaria treatment instructions (5-point scale)	**3.7**	**4**	**4**	
Frequency of stopping treatment to save drugs for future use (5-point scale)	**3.5**	**4**	**4**	**Dichotomized into those who have and those who have never** 

Frequency of sharing antimalarial course with others (5-point scale)	**3.5**	**4**	**4**	
Have used mixed drugs before				**Yes = 52%; No = 48%**
Reasons for mixing				
Facility most likely to mix drugs for malaria treatment (5-point scale):				
Pharmacies	**3**	**3**	**5**	
Chemists	**4.5**	**5**	**5**	
Health centres	**2.3**	**2**	**1**	
Private hospitals	**1.8**	**1**	**1**	
Government hospitals	**2.2**	**2**	**1**	
Malaria is best treated by taking (5-point scale):				
Mixed antimalarial drugs	**2.4**	**2**	**1**	
Antimalarial drugs sold as complete course	**4.4**	**5**	**5**	
Herbal medicines for malaria	**2.8**	**3**	**4**	
Knowledge of expiry date of the mixed antimalarial drugs				**Yes = 23%; No = 39%; N/A = 38%**

Determinants of number of doses when mixing (5-point scale):				
The number of doses I can afford	**3.6**	**4**	**5**	
The chemist's expertise	**3.8**	**4**	**5**	
The number of doses I want	**3.6**	**4**	**5**	
Frequency of use of antimalarial drugs sold as a complete treatment course				
Recommendation on facility for good quality antimalarial drugs (5-point scale):				
Pharmacy	**3.7**	**4**	**5**	
Chemist	**2.2**	**2**	**1**	
Health centre	**3.3**	**3**	**3**	
Private hospital	**4.4**	**5**	**5**	
Government hospital	**4.5**	**5**	**5**	

Publications from the thesis