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Felix Boakye-Agyeman

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Walden University
2017

Abstract

Quantifying the Quality of Antimalarial Drugs in Ghana

by

Felix Boakye-Agyeman, MD MPH

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

December 2017

Abstract

Malaria is still an epidemic in many parts of the world—about 220 million people are still infected with malaria worldwide and about 700 thousand people die from this disease per year. Most of the drugs used to treat malaria work well if they are used as required and they contain the right amounts of the active ingredient; however, it is estimated that more than 10% of drugs traded worldwide are counterfeits including 38% to 53% of antimalarial tablets produced in China and India. Due to the lack of data covering the extent of counterfeit antimalarial drugs in Ghana, the purpose of this quantitative study was to determine the percentage of counterfeit antimalarial drugs sold in Ghana by assessing the amounts of the 2 most common antimalarial drugs, artemether (ATMT) and lumefantrine (LMFT) sold in Ghana retail outlets. These drugs were purchased from retail outlets in Ghana and analyses at the Mayo Clinic Pharmacology core lab (Rochester, MN). The quality of the drugs were characterized by comparing the actual amount of ATMT & LMFT in each tablet to the expected amount. Using explanatory theory along with dose response-response occupancy theory, the researcher addressed quantitative solutions to questions related to the percentage and distribution of counterfeit ATMT and LMFT tablets. The results revealed that overall 20% of the drugs are counterfeit; this is not dependent on the location or kind of outlet but rather depends on whether the tablets were imported or locally manufactured and whether the tablets had a pedigree scratch panel. This study provides a better understanding of how much antimalarial medication is counterfeit in Ghana, which will aid interventions to minimize the adverse effects of counterfeit antimalarial medication in Ghana.

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Dedication

I dedicate my dissertation work to my family. A special feeling of gratitude to my loving parents, wife, children, and siblings. My wife Linda has always been supportive all the way, been the rock, and I pushed on because she never gave up on me. Special thanks to my children Felix, Jr., Anthony, Audrey, and Isabelle for always understanding, even when I spent less time with them because of my dissertation. My special gratitude to my parents Anthony and Vida Boakye who made sure I had the foundation, encouraged me to persevere, instilled in me the tenacity work hard, discipline, and dedication. To my siblings Rosemary, Kennedy, Bright, and Daniel, who have always been cheerleaders and never left my side, I want to say thank you.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

About 220 million people are infected with malaria worldwide and thousands of people die from it yearly (Nadjm & Behrens, 2012; World Health Organization [WHO], 2013). The prevalence and mortality rate in sub-Saharan countries related to malaria is very high, and the rate of deaths for children from these countries is worse. Malaria is caused by parasites called plasmodium sp. (Zhou et al., 2014), which use mosquitos as vectors for transmission to humans. Malaria eradication and treatment has been based on the different stages of the life cycle of the plasmodium parasite. Malaria can be treated with several drugs, and a majority of these drugs work well if used appropriately and they contain the right amounts of the active ingredient. It is believed that a high percentage of these drugs may be counterfeit in Ghana, especially those imported from Southeast Asia (Amin, Snow, & Kokwaro, 2006). At this time, little is known about how much of these medications are fake. I addressed the counterfeit problem by empirically finding out how much antimalarial medication is counterfeit.

Background of the Study

Malaria has been in existence and has been well known for over 2,000 years, but a majority of discoveries regarding malaria happened in late 19th century. Several Nobel Laureates made discoveries, including Laveran, who discovered the parasite in 1880, and Ross, who discovered that malaria is transmitted by mosquitos in 1897 (Rajakumar & Weisse, 1999). At the turn of the 20th century, several public health departments including the United States Public Health Service (USPHS) began trying to find ways to treat and eradicate malaria (Centers for Disease Control and Prevention [CDC], 2009).

This resulted in the discovery of Chloroquine as an effective drug for treating malaria, while Dichloro-diphenyl-trichloroethane (DDT), an insecticide, was used to control and eradicate malaria in the US and most western countries (Roberts, Laughlin, Hsheih, & Legters, 1997). Eradication efforts were very successful in many countries due to the efforts of the CDC, which started as the Communicable Disease Center as a part of malarial control and eradication centers in the US (CDC, 2009); however, sub-Saharan countries were not part of efforts for malaria eradication. Malaria is still an epidemic in sub-Saharan countries and a majority of the region's population die yearly from this disease (Nadjm & Behrens, 2012; WHO, 2013). About one-third of 100 countries worldwide suffer from a high mortality rate due to malaria, and more than 95% of these countries are in sub-Saharan Africa. Ghana, like most of developing sub-Saharan countries, is still struggling with challenges with basic health care. The lack of effective health care makes the system very vulnerable and easy for counterfeit medication to infiltrate the market; over 100,000 deaths per year in Africa are due to counterfeit medication (WHO, 2014). In recent years, there has been some coverage about counterfeit antimalarial drugs in Ghana because it directly affected s politician (Daily Guide, 2013). It is believed that majority of the counterfeit medication comes from South East Asia (Bate & Hess, 2010), but the extent of counterfeit medication in Ghana is not known except as described in a few publications and pilot studies (Asuamah, Owusu-Prempeh, & Antwi-Boateng, 2013; Bate & Hess, 2010). This study will make up for this lack of research by describing quantitatively the extent of antimalarial medication in Ghana.

Statement of the Problem

Most information on the percentage of counterfeit drugs in the sub-Saharan African region is speculative or based on anecdotal evidence; there has not been an extensive study on the whole country that has empirically determined the percentage of counterfeit antimalarial medication in the Ghana (Asuamah et al., 2013). This study will fill this gap in literature to address potential for intervention. The two most commonly used antimalarial medication in this region are artemether (ATMT) and lumefantrine (LMFT) (Lozano et al., 2012). This study empirically determined the percent of antimalarial medication using ATMT and LMFT that is counterfeit in pharmaceutical retail outlets in Ghana.

Purpose of the Study

The purpose of this quantitative study was to explore the extent of antimalarial counterfeiting by looking at the percentage of ATMT and LMFT in drugs sold in retail outlets in Ghana that is counterfeit. Fake drugs pose three direct threats to patients: failure to provide effective treatments, which is estimated to cause thousands of deaths per year; adulteration with toxic chemicals that leads to fatalities; and substandard drugs that expose the parasites to sublethal doses, which can cause them to develop a resistance to the medications (Attaran et al., 2012). To reverse the trend of fake and substandard drugs, we need an understanding of the extent of counterfeit medication in Ghana. With this understanding, we can develop proper interventions to potentially minimize the adverse effects of counterfeit antimalarial medication in Ghana. One covariate I assessed was the cost of the antimalarial medications. Other variables that I assessed will include

the differences between pharmacies and licensed chemical stores and geographical implications on the percent of counterfeit medication in Ghana.

Filling Gaps in the Literature

Professional Applications

This study provides the information and data needed to understand the geographical spread of the counterfeit problem in Ghana, which is relevant for intervention. Adequate mechanisms for treating malaria ailments must be in place to have proper interventions to prevent and fight this disease. Since this study was performed at different geographical regions in Ghana, it gave us the opportunity to look at the trend of counterfeit medication within different regions of the country. It can also help us to measure the impact of an intervention.

Social Change Implications

The implications for positive social change include a better understanding of how much the anti-malaria medication is counterfeit and the extent of counterfeit medication in Ghana, which is needed for interventions that will potentially help minimize the adverse effects of counterfeit antimalarial medication in Ghana.

Framework

For this study, I combined explanatory theory, which is a public health theory, with the dose response-receptor occupancy theory in pharmacology. Glanz and National Cancer Institute (2005) write that explanatory theory illustrates the nature of the problem such as the factors that cause the problem and the changes required to rectify the issues against malaria. In this case, the research investigated the malaria epidemic and its

treatment and other related factors affecting the treatment. One of the factors affecting malaria treatment is the distribution of counterfeit drugs, which works with the dose response-receptor occupancy theory used in pharmacology, as it was even used to explain the effect of the amount of dose in a malaria drug, the efficacy of the drug, or toxicity of the drug (Rang, 2006). Researchers use this theory to examine how the effect or response to a drug is directly proportional to the number of receptors occupied by that drug. A drug will only produce a maximum effect if all the receptors needed to elicit the effect or responses are occupied (Brunton et al., 2011). This means that for antimalarial medications, the total efficacy can only be achieved if all the receptors needed to destroy the plasmodium parasite are occupied. A counterfeit drug is defined by WHO (2013) as a drug whose identity and source has been deliberately mislabeled. Counterfeit products have a wide spectrum; this includes those with wrong active ingredients, expired drugs, and those with subtherapeutic amounts of the active ingredient. For a counterfeit drug, whether substandard or fake, either the receptors are not fully occupied, or they are not occupied at all. This means that substandard and fake drugs will not produce the required effect, thereby affecting the treatment and the malaria epidemic.

The burden of malaria is still high in Ghana, with almost 350 cases reported per 1,000 of cases of malaria among young children below the age of 5 years (Asante et al., 2011). The prompt treatment or management of malaria is necessary for the control and elimination of the disease (Band et al., 2013). Effective treatment can also reduce drug resistance since it reduces the frequency of mutation of the parasite. Ineffective treatment can make matters even worse as it increases the population of resistive strains, which

makes the disease difficult to treat as it renders current medications ineffective (Tordrup, Virenfeldt, Andersen, & Petersen, 2011). The WHO highly recommends artemisinin-based combination therapies (ACTs); two of the most commonly used are generic ATMT and LMFT (Lozano et al., 2012). Unfortunately, according to the CDC (2013), it is estimated that 10% to 30% of all medicines sold in the developing world are counterfeit. A report from the Institute of Medicine (2013) says that counterfeit drugs were sold in more than 124 countries in 2011 alone. Most of these counterfeit medications are in sub-Saharan Africa ranging from about 12% to 50%. Some studies in parts of Africa has shown that about 45% of sulphadoxine-pyrimethamine (SP) and 33.0% of LMFT were counterfeit (Amin, Snow, & Kokwaro, 2005). Most of these counterfeit drugs are shipped from Asia (Newton et al., 2011) and are a result of the lack of effective health care and regulations. Few studies have been conducted on the quality of the medication in Ghana, and researchers have worked with limited samples and insufficient theories. The results of a small pilot study in 2013 on the quality of artemether and lumefantrine found that 17% of the drugs they tested had quality issues (Affum et al., 2013). Bate et al. (2008) found that about 35% of the drugs were counterfeit in Ghana and other African countries; however, they did not look at the efficacy of the drugs (Bate et al., 2008). Others saw the percentage of counterfeit drugs in Ghana ranging from 54% to 94% depending on the method used to check the quality of the drug. Using a receptor theory is more effective in examining counterfeit malaria drugs, because researchers can see the actual concentration of the drug, which affects efficacy.

Research Questions

While it may not be possible at this time to ensure all drugs in Ghana are not counterfeit, it is a goal to strive for. For now, researchers can investigate if a minimum percentage of the drug in the country is counterfeit and as a result assess a low threshold for counterfeit product.

RQ1: Is there a difference between the percentage of counterfeit medication in pharmacies found in the cities and those found in the rural areas?

Ho1: There is no difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

Ha1: There is a difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

RQ2: Is there a difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers?

Ho2: There is no difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers.

Ha2: There is a difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers.

RQ3: Is there a difference in the percentage of counterfeit drugs between imported artemether and lumefantrine and locally manufactured ones?

Ho3: There is no difference in the percentage of counterfeit drugs between imported Artemether and Lumefantrine versus locally manufactured ones.

Ha3: There is a difference in the percentage of counterfeit drugs between

artemether and lumefantrine that is imported versus locally manufactured ones.

RQ4: Is there a difference in the percentage of counterfeit drugs between government hospitals and those from nongovernmental hospitals?

Ho4: There is no difference in the percentage of counterfeit between government hospitals and those from nongovernment sources.

Ha4: There is a difference in the percentage of counterfeit drugs between government hospitals and those from nongovernment sources.

Nature of the Study

This study was a cross sectional correlational study and the samples was chosen using a statistically suggested sample size to ensure that there is enough power for the population to reduce any biases. The quantitative method was used because it is the best way to assess a situation or a problem analytically (Fowler, 2009). This study required systematic measurement of study samples in the lab using validated analytical techniques. The study variables were the concentration of artemether and lumefantrine (dependent) which is measured in milligram per milliliter of solution. The independent variables were the pharmacies and licensed chemical sellers (LCS) where the samples were acquired, which included different locations for private and government owned pharmacies, wholesale stores, and licensed chemical sellers. I acquired the samples from the retailers and sent them to the lab to determine the concentration of artemether and lumefantrine using High Pressure Liquid Chromatography (HPLC). The covariate of the study was the cost of the drugs. A more detailed description of the variables is located in Chapter 3.

Definition of Terms

Antimalarial medication: Drugs used to prevent or cure malaria. This includes the treatment individuals with both confirmed and suspected infection. These drugs may sometimes be used for prevention.

Concentration of drug: The amount of drug per volume of solution. This can either be milligrams per milliliters or grams of drug per liter of water.

Quality of drug/medication: In this project, the term quality is based strictly on the amount of drug as compared to the expected amount as written on the label. This was measured in percentage of the drug that is fake or counterfeit.

Counterfeit/fake drug: For this study counterfeit drugs shall refer to drugs without the active ingredients and subtherapeutic amounts of active ingredient.

Subtherapeutic drug: Has the correct ingredient, but the amount of drug is less than the labeled amount.

Active ingredients: The substance/s in the drug that are supposed to provide the therapeutic effect. In this study, the active ingredients are artemether and lumefantrine.

Dose: The quantity of drugs taken or prescribed.

Drug efficacy: A drug's capacity to produce a desired effect or endpoint. For an antimalarial drug, the efficacy is its capacity to kill malaria parasites.

High Pressure Liquid Chromatography (HPLC): An analytical technique used mostly in chemistry used to separate mixture of substances in liquid at high pressures. This is used to identify each substance in the mixture for quantification.

Pharmacies: Stores with registered pharmacists preparing, dispensing, and selling drugs.

Licensed chemical sellers (LCS): Stores mostly run by pharmacy technicians approved by the government of Ghana selling and dispensing some drugs without the supervision of a pharmacist.

Private Pharmacies: Pharmacies run and owned by the private sector and not government.

Government pharmacies: Pharmacies run and owned by the government.

Wholesale: Outlets distributing drugs to the retail outlets including pharmacies and LCS.

Cities: Urban communities that have utilities, public transportation, modern sanitation, large population density, and businesses.

Small towns and villages: Communities lacking some or all utilities like pipe-born water, public transportation, modern sanitation, and businesses.

Assumptions

This quantitative study investigated the extent of counterfeit drug using the two most prescribed antimalarial medication (artemether and lumefantrine) in Ghana. This research included the following assumptions in the study:

1. The data collected from each pharmacy or LCS in a population represents the information for the whole population. This assumption was necessary for the data collected to represent the population.

2. That ATMT and LMFT purchased from a store represent the quality of all ATMT and LMFT from that store. This assumption allowed the use a few drugs to represent all the drugs in a particular store
3. Data from ATMT and LMFT was a good representation most popular anti-malarial medication in Ghana.
4. The drugs are only acquired via the above mentioned outlets. This means that the number of all other possible outlets is so small that their contribution to this data with be insignificant. This validated the fact that the samples used for this study represented all the drugs in the population.

Scope and Delimitations

Artemether-lumefantrine combination tablets from public and private (local retail pharmacies) in Ghana can be obtained in two formalized ways: traditional pharmacies with a trained pharmacist and LCS. LCS sell drugs mostly in suburbs, small towns, and villages, without any supervision of a pharmacist, but they are licensed by the government to sell over-the-counter medication and common medications authorized by the government. Because these are not well controlled or monitored, the LCS sells almost the same medications sold by the pharmacies.

Geographically, Ghana is divided into ten regions; the capital of Ghana is Accra and the second largest city is Kumasi. Most of the pharmacies are in the major cities within the ten regions. The Greater Accra Region has two main sub cities within it: the city of Accra and the industrial city of Tema. Kumasi and its surrounding suburbs are the

main city for the Ashanti Region. According to the Ghana Pharmacy Council, there are 429 Pharmacies and 9,210 licensed chemical sellers throughout the country. Most of the pharmacies are in the four major cities. The city of Accra has about half (233), Kumasi has (79) pharmacies, and the other two major cities have 40, and the rest are spread throughout the country mostly in the bigger towns. The LCS are more spread out as they serve more remote and rural communities. I assessed these areas, with inclusion criteria involving all registered pharmacies (private and government) and all licensed chemical shops in the selected towns; exclusion criteria included unregistered stores that sells drugs or any person selling drugs on the streets illegally.

A generalization for this study was the assumption that a few drugs from one store represent the quality (counterfeit or not) of all drugs in that store. Another generalization was assuming a few randomly picked stores represent the entire pharmaceutical retail outlets in the country.

Limitations

The choice to study Ghana presents a bias because of my connection to that country (place of birth), which may have excluded other sub-Saharan African countries that would present different data. Another limitation of this study was that the study may not capture all possible outlets, which includes possible illegal outlets that may exist in the system. If these numbers are significant, this will affect the internal validity of the study since the outcome of the study may not be a true representation on the population. Other confounding variables like price of the drug and lack prescription that is acceptable in Ghana may also have affected the validity of the study. Some of these were solved by

making sure the data collection process is done correctly, based on statistics and sampling is random.

Significance of the Study

Malaria is still endemic in sub-Saharan countries like Ghana. It is treatable and there are several medications in the market; however, some studies have shown that many of these drugs are counterfeit, with a small pilot study revealing that 30% to 40% of antimalarial medication counterfeit. If this is true, then any eradication program will have to include reducing or eliminating counterfeit medication in these countries. Since there is no data quantifying the percentage of antimalarial drugs that are counterfeit this study was to solve that problem. This study will give information needed to decide if the reduction or eradication of counterfeit medication in Ghana and other sub-Saharan countries should be part of malaria eradications strategies. Since this study was performed at different geographical regions in Ghana, it will also provide the opportunity to look at the trend of counterfeit medication within different regions of the country, which will increase efficiency in intervention and measuring of the impact of such intervention.

Summary

Over 200 million people worldwide are infected with malaria and more than half a million people are dying from it per year. Malaria is a treatable disease with several medications in the market, but several pilot studies have revealed the possibility of counterfeit antimalarial medication as one of the factors affecting the treatment of malaria. However, there has not been a comprehensive study looking empirically at the

extent of counterfeit antimalarial medication in the system (Asuamah, Owusu-Prempeh, & Antwi-Boateng, 2013). Using Ghana as an example and two of the most common antimalarial drugs in Ghana—ATMT and LMFT—this study explored the extent of antimalarial counterfeiting, if any, from pharmaceutical retail outlets in Ghana. This study aimed to address the lack of data on the extent of counterfeit antimalarial drugs in Ghana and sub-Saharan Africa in general. Chapter 2 will include an overall review of the limited literature on the extent of counterfeit antimalarial medication.

Chapter 2: Literature Review

Introduction

Even though there have been speculations about the extent of the counterfeit problem in some of the countries that suffer from malaria epidemics, there has not been an extensive study on the whole country (Ghana) that has empirically determined the extent of counterfeit antimalarial medication in the system (Asuamah, Owusu-Prempeh, & Antwi-Boateng, 2013), and there is little to no empirical evidence of the percentage of drugs in the sub-Saharan region that are counterfeit. Due to this gap in the literature on counterfeit medication, I empirically determined the percent of antimalarial medication that is counterfeit in pharmaceutical retail outlets in Ghana.

In this chapter, I will discuss the strategies used to conduct the literature review as well as the epidemiology, which will include the incidence and prevalence and the mode of infection of malaria. There will also so be emphasis on past research about malaria, the problems with counterfeit drugs, and how counterfeit medication affects the malaria. This chapter will also provide analysis on how drugs are distributed in Ghana, the sources, and where they are manufactured. In addition, I will discuss the explanatory theory which is a public health theory combined with the receptor occupancy theory in pharmacology and how these two theories were applied to the characterization of the quality of antimalarial drugs in Ghana by looking at the percentage of the drugs that are counterfeit.

Literature Search Strategy

Several types and sources of information or data revealing research studies were used for this literature review. The research included a review of other peer reviewed manuscripts and studies on malaria and counterfeit drugs. Most of the research was from primary articles, which means I excluded review articles and reports or studies without original research. Literature search was done using keywords like *malaria*, *counterfeit drugs*, *counterfeit medication*, and *antimalarial medication*, *malaria treatment, malaria in Ghana*, and *receptor occupancy and explanatory theory* in different combinations. Most of the search criteria was based on literature published from 2008–2014. The following databases were used: PUBMED, Library of Congress, EMBASE, MEDLINE, ScienceDirect, Pre-CINAHL, CINAHL, ProQuest and Dissertations & Theses, Web of Science, and the Walden University database of dissertations. Other search engines included Google Scholar, and I examined the WHO and the Centers for Disease Control and Prevention (CDC) websites for relevant information.

Using *malaria* as a keyword alone gave me 69,103 articles. This was obviously difficult to use and unfocused, so I combined some of the keywords for better results. For instance, search results of *malaria* and *Ghana* and *drugs* showed 149 citations; out of these articles, eight articles were found to be acceptable. *Explanatory theory* came up with 27 citations searched as a title, and six citations were acceptable. *Ghana* and *fake medicine* provided five citations, and four were used. The total number of articles used for this literature review was 117.

Theoretical Framework

For this study, I combined two theoretical concepts from two disciplines: explanatory theory, which is a public health theory, with the receptor occupancy theory in pharmacology.

Explanatory Theory

There is a great amount of evidence that suggested public health intervention and promotions based on theories are more effective than those without theories (Glanz & National Cancer Institute [NCI], 2005). Explanatory theory, also known as the theory of the problem, was first used by Shapiro in psychiatry. The theory is used to illustrate the nature of a problem by examining the factors that cause the problem that can be changed (Shapiro, 1953). Researchers have used it in several ways to empirically determine or test several public health issues (Song et al., 2010), such as testing for postpartum fatigue in Korea, explaining metabolic depression in hibernation and major depression (Tsiouris, 2005), and it was recently used to build another social epidemiology theory for depression in mothers (Eastwood, Jalaludin, & Kemp, 2014). It has also been used in other disciplines such as economics with asset evaluation and human capital and in education for studies in learning curves and team learning (Vlismas & Venieris, 2009; Westwood, 1997). The theory helps define the elements that influence particular behaviors, trends, or situations before moving on to find cause and solutions to the problem. There are several concepts considered in this theory in relation to an ecological perspective; this includes intrapersonal, interpersonal, institutional, community factors and public policy (McLeroy, Bibeau, Steckler, & Glanz, 1988; Stokols, 1996).

Intrapersonal factors look at individual characteristics that affect behavior; examples are beliefs, attitudes and personality traits. Interpersonal looks at interpersonal processes and groups that provide support like families and friends. Institutional factors mostly involve rules and regulations and informal structures that could help or make a problem worse (McLeroy et al., 1988). One of the goals of this study was to provide an improved approach in order to enhance the empirical understanding of the problem before developing intervention programs for counterfeit antimalarial medication and the malaria epidemic in general. In this case, the problem is the malaria epidemic and its treatment, and among the many factors affecting the treatment is counterfeit antimalarial medication and its distribution. In addition, receptor occupancy theory, which relates more to drugs and pharmacology, will address the amount of active drugs required for malaria intervention.

Receptor Occupancy Theory

Receptor occupancy theory is used in pharmacology to explain the effect of the dose of a drug and the efficacy or toxicity of the drug (Rang, 2006). The receptor occupancy theory was first postulated by Langley in 1901 after his work on nicotine and curare, even though this idea of receptors controlling the effect of a drug was furthered by Ehrlich around the same period. Langley's model explains how a drugs activity affects receptors and then quantifies the drug concentration and effect elucidated by the drug, which links drug action to the number of receptors occupied by that drug (Christopoulos & El-Fakahany, 1999). Drug effects on biological systems are quantified by assigning mathematical rules to biological systems (Kenakin, 2008). This is done independent of

the biological system, since it is essential for the study of drugs mostly done in test systems. This current study helps to isolate the effect of the drug in different systems and under different conditions. A very important part of the theory is the assertion that the amount of drug bound to the cell is directly proportional to the response. Figure 1 describes the proportionality equation between the amount of drug bound to the receptors and the response.

$$\frac{E}{E_{max}} \alpha \frac{[DR]}{[RT]}$$

Figure 1. Relation between drug bound and physiological effect.
E is some physiological effect that happens as a result of the drug. An example is killing of plasmodium parasite**.** *Emax* is the maximum amount of this effect, *DR* is the amount of drug bound to the receptor and *RT* is the total amount of receptors. Retrieved from http://www.uky.edu/~mtp/pha522drug/OBI836mp06.html

Figure 1 shows that the maximum effect is only realized if all the receptors are occupied by the drug. Addressing the relationship between effect and receptor occupancy is shown in Figure 2. In Figure 2, no matter what the relationship, the maximum effect only happens when all receptors are occupied.

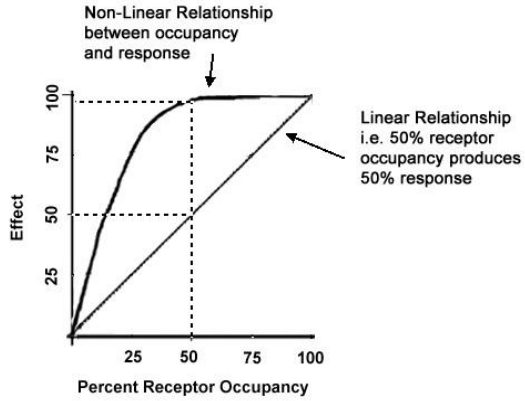

Figure 2. Relationship between effect and percent receptor occupancy. Source: Brunton et al, 2011.

Receptor occupancy theory provides the basic framework of drug interactions and the way the drug behaves on the body, which is known as pharmacodynamics. The theory states that the effect/response of a drug is directly proportional to the number of receptors occupied by that drug. It also states that this drug will only produce a maximum effect if all the receptors needed to elicit the effect or responses are occupied. The approach could be applied to antimalarial medication, because for antimalarial medications, the total efficacy can only be achieved if all the receptors needed to destroy the plasmodium parasite are occupied. Counterfeit drugs have a wide spectrum, which includes those with wrong active ingredients, those that have expired and relabeled, and those with subtherapeutic amounts of the active ingredient. For a counterfeit drug, whether substandard or fake, either the receptors are not fully occupied, or they are not occupied at all. This means that substandard drugs will not produce the required effect since they will not occupy all the receptors, or the fake drug will not occupy the receptors at all, thereby negatively affecting the treatment and the malaria epidemic.

Combination of Explanatory and the Receptor Occupancy Theory

A combination of the two theories starts with the explanatory theory to ask questions and examine the problem (Figure 3). The problem is the distribution of counterfeit antimalarial medication. This theory will ask what the problem is, accessing the extent of the problem. The next step of the process is the evaluation stage, which identifies when the receptor occupancy theory comes to play. The evaluation stage will also look at the concentration on the drugs since this is related to the amount of drug needed to occupy the receptor.

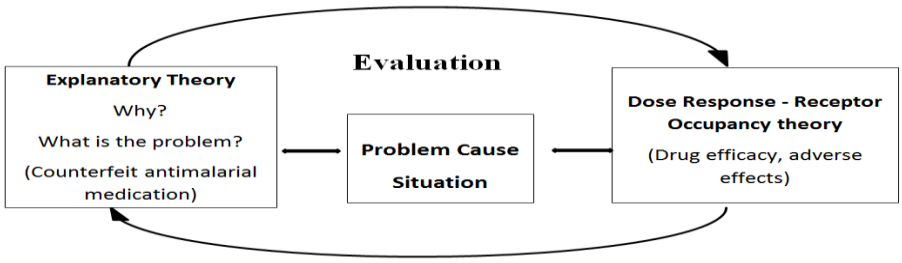

Figure 3. Theoretical framework.

Transmission and Life Cycle of the Parasite

The plasmodium sp. is the parasite that causes malaria (Zhou et al., 2014). The parasite uses two hosts—the mosquito (intermediate host) and the human (primary host)—in its life cycle as shown in Figure 4 (CDC, 2012). There are three sub cycles: the exo-erythrocytic cycle (liver) and the erythrocytic (blood) cycle in the human host and the sporogonic cycle in the Anopheles mosquito (Florens et al., 2002). An infected female Anopheles mosquito transmits the parasite (sporozoites) to the human host during feeding through the saliva, which it uses to prevent the coagulation of the blood; this is the exo-erythrocytic cycle (Beck, Logie, & McGregor, 1970). The sporozoites then move

into the human liver cells where they become schizonts (Mahajan et al., 2008). This stage can be dormant for even years in some species until they rupture to release merozoites (Riley et al., 2000). Merozoites then infect red blood cells, initiating the erythrocytic cycle (Vaughan, Aly, & Kappe, 2008). Merozoites mature into a ring stage called trophozoites which are responsible for the clinical manifestations of the disease and also produces the gametocytes which can be ingested by the Anopheles mosquito after which they enter into the sporogonic cycle (Aguilar et al., 2014). The zygotes are formed in the stomach of the mosquito, which becomes ookinetes; these are mobile and elongated which allows them to invade the wall of the mosquito's stomach where they develop into oocysts. These then rupture to release sporozoites, which move into the salivary glands of the mosquito. Sporozoites can then be transmitted into the human host (Arakawa et al., 2005). As we shall see later, the medication used for the treatment of malaria disrupts the different parts of the life cycle of the plasmodium parasite.

It is important to know that there are several species of the plasmodium parasite (*P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale*), which adds to the variability of the signs, symptoms, and treatment of malaria (Kiwuwa et al., 2013). Breeding of Anopheles mosquitos takes place in water, mostly in stagnant water (Tchouassi et al., 2012). The longer the life spans of the mosquito, the more severe the epidemic, which is present mostly in the tropics (Kiwuwa et al., 2013).

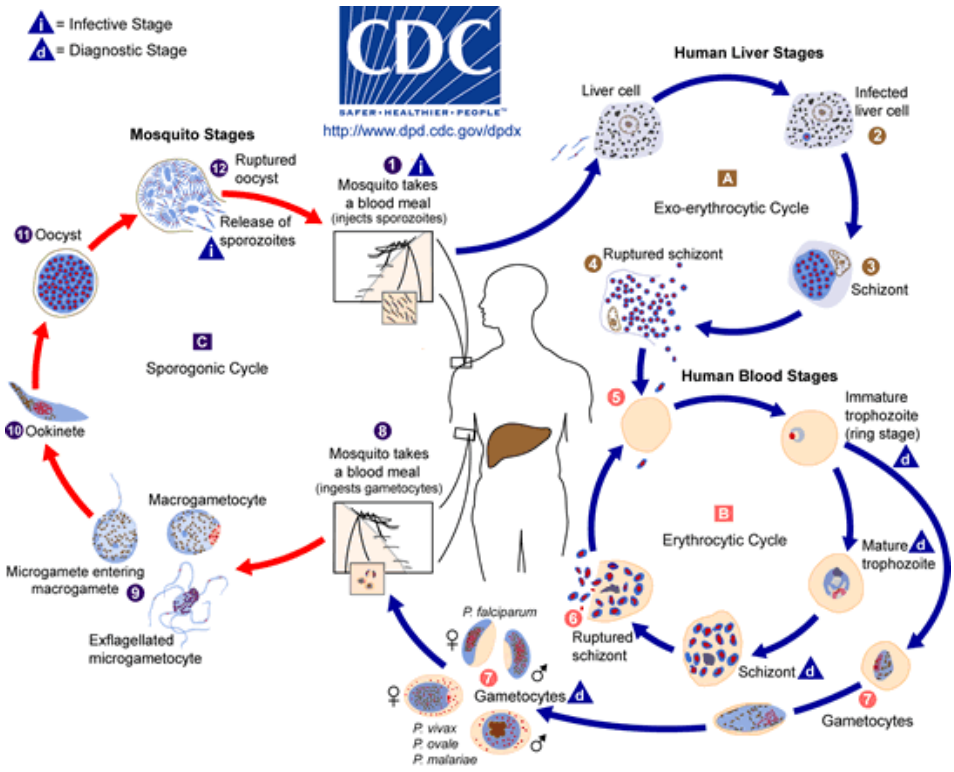

Figure 4. Life Cycle of the plasmodium parasite. Adapted from CDC (2012).

Signs and Symptoms

Malaria symptoms are flu-like on the onset; it is a disease that manifests with acute fevers, headaches, malaise, and chills (Sarkar, Shah, & Murhekar, 2012). Generally the symptoms of malaria appear within 1 week to 2 weeks after infection from the anopheles mosquito (Ohnishi et al., 2007). According to the American Public Health Association (APHA), his disease could also take up to 1 year to appear, especially *with P. vivax* and *P. ovale* infections. These febrile symptoms are cyclical, and cycle is dependent on the kind of parasite. An infection by *P. vivax* or *P. ovale* has a 48 hour cycle, *P. malariae* has 72 hours, but *P. falciparum* does not cause any cyclic fever which happens to be one of the major signs of malaria infection (APHA, 2008). Progression to

severe illness can result within 24 hours of no treatment, and this can be fatal (Anstey, Douglas, Poespoprodjo, & Price, 2012). Adults in malaria endemic areas can develop partial immunity (Snow & Marsh, 1998), which is why children and older populations develop severe malaria frequently after infection (Griffin, Ferguson, & Ghani, 2014; Pistone, Diallo, Mechain, Receveur, & Malvy, 2014; Rizvi et al., 2013). Some of the severe symptoms include anemia, which can be fatal; metabolic acidosis, which results in respiratory distress; and cerebral malaria. Several organs can be affected, which results in the fatalities during malaria infection (Lomar et al., 2005).

Diagnosis

Prompt diagnosis is necessary for effective management, treatment, and control of the transmission of malaria (Tangpukdee, Duangdee, Wilairatana, & Krudsood, 2009). Lack of and delay in the diagnosis of malaria affects the treatment, which happens to be one of the leading causes of complications and death from malaria infection (WHO, 2012). The diagnosis involves the identification of the parasites at the part of the life cycle they are in and antigens in the blood of the patient. Diagnosis can be difficult, especially in endemic areas, since there are five different species of the parasite and each have a unique product, endemicity, and organism within the life cycle. Other differences include different levels of transmission, signs and symptoms, immunity, and parasitemia (Iborra, Garcia, Carrilero, & Segovia, 2013). The diagnosis can also be difficult in areas like the US or other western nations where the disease is not endemic and health care personal have little to no experience with the disease (Magill, 2006). The diagnosis of malaria can be broken down into clinical, laboratory, and molecular diagnosis (Harvey et

al., Polage et al., 2006, 2013; Reynolds et al., 2013; Stephens, Phanart, Rooney, & Barnish, 1999), but clinical diagnosis is the most widely used and the most inexpensive form of diagnosis. This is based on the symptoms and signs of the disease (Maltha & Jacobs, 2011), but because the symptoms at the early stage include fever, headache, weakness, muscle and abdominal pain, malaise, and vomiting, it is hard to identify a specific disease among the many other febrile diseases like bacterial and viral infections that also include these symptoms. There are several algorithms for diagnosis based on these symptoms, but these have been shown to be nonspecific (<10%) even though they are about 100% sensitive especially in Africa (Perkins et al., 1997). This could also result in over diagnosis of malaria and studies have shown that some of these algorithms leads to >30% over diagnosis (Bhandari, Raghuveer, Rajeev, & Bhandari, 2008; Tarimo, Minjas, & Bygbjerg, 2001).

Due to the issue of over diagnosis that occurs in clinical diagnosis, other forms of diagnosis like laboratory diagnosis are used, which will complement or confirm the clinical diagnosis. Laboratory diagnosis is based on conventional microscopy and technicians will look for the parasites in blood smear which is sensitive and specific but requires equipment, good training and time, serological test, which are based on antibodies against parts of the reproductive cycle of the parasite and several rapid diagnostic tests in the market (Fancony, Sebastiao, Pires, Gamboa, & Nery, 2013; Gomes, Espino, Abaquin, Realon, & Salazar, 1994; Maina et al., 2010; Masanja et al 2010). Molecular diagnosis of malaria is based on modern molecular biological techniques like polymerase chain reaction (PCR) which is the gold standard for the

diagnosis of malaria. It has both high sensitivity and specificity (Demiraslan et al., 2013; Khan et al., 2013; Morassin, Fabre, Berry, & Magnaval, 2002). It also requires well trained personnel to test. Moreover, WHO (2012) recommends that suspected malaria should be confirmed using laboratory/molecular techniques or rapid diagnostic test before initiating treatment.

Prevention

The way to prevent malaria infection is to control the life cycle of the plasmodium parasite. Since the life cycle is affected by the anopheles mosquito vector, the control of the anopheles mosquito is the main way to reduce the transmission of malaria within a population. The most popular forms of vector control are through the use of insecticide-treated mosquito nets (ITNs), indoor spraying with residual insecticides and antimalarial medicines. Chemoprophylaxis can also be used especially for travelers and for personnel in the military drugs such as mefloquine, doxycycline or atovaquone-proguanil are used to suppress the malaria infections (Grobusch, 2014; Kersgard & Hickey, 2013). Pregnant women living in areas endemic to malaria are recommended by WHO to use preventive treatment with sulfadoxine-pyrimethamine intermittently after the first trimester during their prenatal visits. The same applies to infants living in endemic areas, preventive treatment with sulfadoxine-pyrimethamine is recommended with routine vaccinations (WHO, 2012). Another important mechanism of controlling mosquitos is the use of insecticides. An example was the use of dichlorodiphenyltrichloroethane (DDT) which was used to eradicate malaria in the US and parts of Europe but was ban by the WHO due to alleged adverse effects on the environment (Wang et al., 2013). The spraying of other

insecticides both indoor and outdoor used to kill the adult mosquitos has been shown to be effective especially if it is combined with other preventative measures like mosquito nets and chemoprophylaxis (Kigozi et al., 2012). Mosquitos are growing resistance to some of the common insecticides like the pyrethroids, which are the class of insecticides mostly used for ITNs (Gatton et al., 2013; Hewitt, Delacollette, & Poirot, 2013).

Treatment/Management

It is important to note that malaria is fully preventable and treatable, and treatment or management of malaria is necessary for the control and elimination of the disease. The prompt treatment of malaria is part of the secondary prevention, which reduces the transmission and spread of the disease (Band et al., 2013). Effective treatment can also reduce drug resistance since it reduces the frequency of mutation of the parasite. As mentioned before, lack of treatment can cause very serious complications. Additionally, ineffective treatment can make matters even worse as it increases the population of resistive strains, which makes the disease difficult to treat as it renders current medications ineffective (Tordrup, Virenfeldt, Andersen, & Petersen, 2011). One such drug is chloroquine which was very effective as mono-therapeutic drug for both complicated and uncomplicated malaria (Tonnesmann, Kandolf, & Lewalter, 2013). Until recently, chloroquine was the prototypic drug due to its effectiveness; it is very cheap, has the best safety profile compared to other antimalarial drugs and one of the most studied (Pfeiffer et al., 2008). Unfortunately, it is not effective in many endemic areas and may not be recommended for treatment in most of these areas even though it is still the first line in some sub-Saharan countries (Takahashi et al., 2012). The focus of

malaria treatment and management addresses the treatment of the disease, monitoring of parasitic drug resistance, chemoprophylaxis and reduction of the spread of the parasite. There are several antimalarial medications, and most of these have been in existence for many years. The WHO (2012) advises against the use of any form of mono-therapy for the treatment of malaria. It recommends combination of at least two active ingredients with different mechanisms of actions. This could be one drug with these ingredients or combinations of drugs. The WHO highly recommends artemisinin-based combination therapies (ACTs). There are five ACTs currently recommend by WHO, and the choices of which combination is normally based on therapeutic efficacy studies (WHO, 2012).

Antimalarial Medications

Most of the antimalarial drugs are active against different parts of the life cycle of the parasite. The most common medications include quinine and it agents, chloroquine, amodiaquine, pyrimethamine, proguanil, sulfonamides, mefloquine, atovaquone, primaquine, artemisinin and its derivatives, halofantrine, doxycycline and clindamycin. The most common non-artemisinin based combination therapies are sulfadoxine-pyrimethamine, pyrimethamine and chloroquine, pyrimethamine and lumefantrine, pyrimethamine and mefloquine. The most common artemisinin-based combination therapies (ACTs) are artemether and lumefantrine, artesunate and amodiaquine, artemether and mefloquine, artemether and sulfadoxine/pyrimethamine, artesinin/piperaguine/primaquine and dihydroartemisinin-piperaquine (Deye et al., 2012; Fryauff et al., 2007; Leggat, 2012; Newton et al., 2011; Njau et al., 2013; Osei-Akoto, Orton, & Owusu-Ofori, 2005; Phanouvong, Dijiba, et al., 2013; Phanouvong, Raymond,

et al., 2013; Tsiamis, Piperaki, & Tsakris, 2013; Wasnik, Manohar, Humaney, & Salkar, 2012).

Antimalarial Drug Policy in Ghana

According to the Ministry of Health of Ghana (2009), there have been several initiatives to roll back malaria for many years mostly with the help of the WHO. Unfortunately, malaria is still endemic in Ghana, and it is still the number one cause of death and mortality in Ghana. Like other countries, the control of malaria in Ghana also suffers from the development of drug resistance by the plasmodium parasites especially from monotherapy. Because of this, Ghana went in line with WHO's antimalarial use of ACT based recommendations for all countries. Based on this, artemether-lumefantrine is used in Ghana for uncomplicated malaria. Other alternative artemisinin combinations recommended for uncomplicated malaria are artemether/ lumefantrine and dihydroartemisinin/piperaquine combinations. Quinine is used for treatment failure and complicated malaria. Intramuscular artemether can also be used for complicated malaria. Similar to most countries, monotherapy is not recommended in Ghana (Ministry of Health, 2009).

General Epidemiology of Malaria

The intensity of malaria transmission depends on factors related to the parasite, the mosquitos, the human host, and the environment. There are several ways malaria is transferred to humans. The most common way of malaria transmission especially in areas endemic to the infections is through the bite of the anopheles mosquito also known as the Mosquito-Borne Malaria. According to the CDC (2013), malaria is transmitted

exclusively through the bites of Anopheles mosquitoes. A small subset of these is the imported malaria, which is a factor in countries that have already eradicated malaria. These can also cause “Airport" Malaria. This is when mosquitoes are transported by plane from one country to the other (from an endemic to a non-endemic country). The other kind of malaria is the Congenital Malaria. In congenital malaria, infected mothers transmit parasites to their child during pregnancy before or during delivery. This is very common in immigrants and refugees (CDC, 1981; Tittle et al., 1982).

Transfusion-Transmitted Malaria is generally very rare, but since malaria is a blood borne disease there is always a potential of it getting transmitted during blood transfusion, organ transplantation and even shared needles (Ozkurt, Erol, Kadanali, Altoparlak, & Tasyaran, 2005; Rojo Medina, 2014). There is still no approved way to screen for malaria parasites in donated tissues; this is partly because most tests are not that sensitive. Even though this is rare, Transfusion-Transmitted Malaria can be common in places endemic with malaria because malaria screening is still not performed in many of these countries even though it is recommended by international policies (Owusu-Ofori, Parry, & Bates, 2010)

According to the WHO (2013), in 2010 there was an average of about 220 million cases globally with over 650,000 estimated deaths. Most of these deaths (91%) came from Africa, and a majority of the deaths globally (86%) came from children under 5 years of age. This shows that malaria is still a big health problem. Majority (91%) of the malaria cases were due to P. falciparum infection (WHO, 2013). Death caused by malaria in Africa is very high compared to that of the rest of the world. It is more so in sub-

Saharan Africa. Even though majority of the prevalence rate of malaria is in Africa, the disease burden and trends vary widely across the continent. The disease burden in the southern African countries is much better than the rest of the continent (Cibulskis et al., 2007; Griffin et al., 2014).

Populations at Risk

As mentioned earlier, malaria is endemic in sub-Saharan Africa, but it is also prevalent Latin America, Asia, Middle East and some parts of Europe but in relative terms, it is not as much as the sub-Saharan regions of Africa (Haq, Mahjour, & Khan, 2013; Makdoembaks & Kager, 2000; Vanderelst & Speybroeck, 2013; Yasuoka & Levins, 2007). According to the WHO (2013), almost 100 countries and territories had populations with ongoing malaria transmission. Out of all the populations, young children, older populations, immune-incompetent patients and pregnant women have the highest risk of complications from the infections.

Malaria Epidemiology in Ghana

Even though there are differences between the regions in Ghana with the northern part being mostly savanna and middle/southern part being the rain forest, the malaria endemic is still very high in all regions. The disease burden of malaria is still very high in Ghana with almost 350 cases reported per 1000 of cases among young children below the age of 5 (Asante et al., 2011). With all the effort to eradicate or decrease the incidence and prevalence rate of malaria, there is little to no evidence that there has been a decrease in the percentage of hospital admission and death from malaria in recent years (WHO, 2011). The transmission rate in Ghana is among the highest in Africa and in the world

with almost 100% of the population being at risk for infection (WHO, 2011). This is not different from most of the other West-African countries. The transmission is mostly due to P. falciparum. It is also worth noting that most of the data collected is based on hospital admissions and deaths, there are a lot of people who go under the radar especially through self-medication (WHO, 2011). In one study carried out in the rain forest area of the country, there were approximately 270 infective mosquito bites per person per annum. In another study, it was found that prevalence rate of the malaria infection was > 50% especially among children < 5 years. Children < 5 years of age had at least 7 episodes of malaria infection per year (Owusu-Agyei et al., 2009).

Counterfeit Drugs

The WHO (2011) cited the Black's law dictionary, when it tried to define counterfeit drug. A counterfeit drug was defined as an imitation of drug prepared without the rights or permission from the original manufacturer with the intention of deceiving and scamming consumers (WHO, 2011). The problem is that there is not a universally accepted definition and theses definitions vary from country to country. Each country or organization has its own definition. For instance, the US Food and Drug Administration (USFDA) define a Counterfeit medicine as a fake medicine, which could contain the wrong active ingredient or the right ingredient contaminated or right active ingredient, but the WHO defines a counterfeit as a drug whose identity and source has been deliberately mislabeled. Counterfeit drugs have a wide spectrum which includes drugs without the active ingredients, those that have fake active ingredients, expired drugs and

sub-therapeutic amounts of active ingredient (Attaran et al., 2012). A sub-therapeutic drug has the correct ingredient, but the amount of drug is less than the labelled amount.

Factors That Fuel Counterfeit Drugs

Generally, this has to do with economics. As mentioned earlier, there are millions of dollars of profit being made from these drugs. Producing good quality drugs come with a price. It cost billions of dollars to come out with one drug; therefore, falsifying drugs has been dubbed a "the perfect crime" because it is very profitable, and it costs much less to make (Dondorp et al., 2004). Another problem is from tiered productions where companies make inferior drugs to inferior markets due to lack of enforcement and less stringent regulations, and it is mostly described as legal. This is basically exploitation by some companies; they produce lower quality drugs, which fit in the definition of counterfeit drugs (Caudron et al., 2008). These systems tie into the weak regulatory systems; countries with high levels of counterfeit drugs have very weak regulatory authorities (Dondorp et al., 2004). The WHO found that in sub-Saharan African countries most of these organizations have no legal authority to perform inspections. As a result, it made it easier for counterfeit medicines to infiltrate the market (Zumoff, 2007). For instance in 2007,a Chinese regulator through corruption and bribery issued several fake/forged in one of the provinces (Liu, 2010). Another important factor is the lack of awareness and Action. Without a clear idea of the extent of the counterfeit problem, it is difficult to come with the appropriate intervention strategies. The awareness of the problem is very low in many of those countries even though it is beginning to become an important factor for policymaking. In places where there is some awareness, there is still

very little knowledge of the extent of the problem (Cockburn, Newton, Agyarko, Akunyili, & White, 2005).

Finally, a big problem is the disease burden in these developing countries, combined with extreme poverty, bad health care systems (Wang et al., 2014). People have no choice but to go for cheap medication, cut corners, which opens patients up to counterfeits drugs. Socioeconomic factors play a major role in this (Krefis et al., 2010).

Assessment of the Global Counterfeit Antimalarial Drug Problem

The extent of counterfeit drug globally is not known since there has not been a study that looks at this problem globally. Nevertheless, it is a problem that affects almost every country rich or poor; but, it has a worse adverse effect on poorer countries (Caudron et al., 2008). According to the CDC (2013), it is estimated that 10% to 30% of all medicines sold in the developing world are counterfeit. This is estimated to be 1% in the industrialized countries. One question that begs asking is whether the problem with counterfeit drugs has either been ignored or underestimated because it is becoming crucial public health problem for malaria and other diseases (Newton et al., 2008). Financially, even though it creates a burden on these countries, the manufactures have lots to gain because it is very lucrative with an estimate of >15% of pharmaceutical sales worldwide with most of it (>60%) in developing countries (Newton et al., 2006)

A report from the Institute of Medicine (2013) says that according to a consortium of major drug companies, counterfeit drugs were sold in more than 124 countries in 2011 alone. Several studies on counterfeit drugs have been conducted in many countries mostly in Africa and Asia as these continents have the highest prevalence of counterfeit

medications. Majority of these studies were on antimalarial medication and antimicrobials in general (Newton et al., 2011). Majority of these counterfeit medications are in sub-Saharan Africa ranging from about 12% to 50 %. South eastern Asia follows very closely with range with about 10 to 40% (Almuzaini, Sammons, & Choonara, 2013).

Amin and Kokwaro (2005) studied the quality of sulphadoxine-pyrimethamine (SP) and lumefantrine (LMFT) drugs given as over the counter medication (OEM) communities Kenya. These drugs are OEM because most people self-medicate after infection. They found that about 45% of SP and 33.0% of LMFT were counterfeit (Amin, Snow, & Kokwaro, 2005). A cross sectional survey to access pharmacies selling antimalarial drugs in Southeast Asia (Laos, Myanmar, Vietnam, Thailand and Cambodia) found that 53% of the tablets did not contain the right antimalarial medications. Four years later, collaborative investigation into the counterfeit artemether in South East Asia was carried out involving countries including Vietnam, Laos, Cambodia, Thailand and Myanmar. Several professionals were involved including chemists, palynologists, police, healthcare personnel and criminologists with the coordination from International Criminal Police Organization (INTERPOL). Using High Pressure Liquid chromatography, the investigators confirmed that almost 50% of artemether drugs were counterfeit (Newton et al., 2008). This is a huge problem in mainland Asia and the same issue applies in Africa, as most of these counterfeit drugs are shipped from Asia (Newton et al., 2011).

Developing countries like Ghana lack well established regulatory organizations; these countries also tend to have high poverty and are endemic to infectious diseases like

malaria (Barimah & Mensah, 2013; Kassebaum et al., 2014). Ghana has grappling challenges in healthcare with millions of people lacking access to health care and most people relying on local stores, medicine men and women, pharmacies and licensed chemical sellers for medical advice and treatment. The lack of effective heath care makes the system very vulnerable and easy for counterfeit medication to infiltrate the market. In recent years, there has been some coverage about counterfeit antimalarial dugs in Ghana, and the awareness was raised because it directly affected an influential person. (Daily Guide, 2013). It is believed that majority of the counterfeit medication comes from South east Asia (Bate & Hess, 2010). But the extent of counterfeit medication is not known except for a few publications in a few small towns in Ghana (Asuamah et al., 2013; Bate & Hess, 2010).

Previous Work on Counterfeit Medication in Ghana

There have been very few studies looking at the quality of the medication in Ghana. A pilot study conducted in 2013 looked at the quality of artemether and Lumefantrine tablets in a fishing village in an attempt to look at the quality in fishing villages in Ghana (Affum et al., 2013). The researchers randomly sampled blister packs of antimalarial tablets from a small fishing village. They used protocols from the International Pharmacopoeia and Global Pharma Health Fund Minilab (IPGPM) to assess the quality of the tablets, and the analytical procedure used was High Pressure Liquid Chromatography (HPLC). They found that 17% of the drugs they tested had quality issues (Affum et al., 2013). The advantage of doing this is that it was pilot project, so they focused on a small little village. However, the caveat is that it hardly tells us

anything about the counterfeit problem in Ghana as a whole. In the assessment of counterfeit medication in Ghana, the different outlets have to be taken into considerations. The main outlets include drugs sold by the government hospitals, the large pharmacies and the small scale licensed chemical sellers (FHI360, 2013). The demographics of fishing and non-fishing communities may be different, so it may be important to have a larger size sample covering different groups and demographics. There are studies that show that the antimalarial behaviors between different regions are different. For instance, behavior between urban centers and villages were different, and this could affect the extent of counterfeit medication (Gardiner, Biggar, Collins, & Nkrumah, 1984). Another study looked at substandard and falsified anti-tuberculosis drugs in 19 cities in Africa, Asia and South America. Ghana was one of the countries in Africa that was tested. This study was not focused on Ghana so the sample size in Ghana was very small, which does not inform us about the whole country. Once again, it did not take into consideration the different ways that people acquire their medication in Ghana (Bate, Jensen, Hess, Mooney, & Milligan, 2013). Bate, Coticelli, Tren, and Attaran (2008) also studied the quality of antimalarial medication in six countries including Ghana, Kenya, Nigeria, Rwanda, Tanzania and Uganda. They studied several antimalarial drugs and found that on the average 35% of the drugs were counterfeit. Because they were using many countries and several antimalarial drugs, they had very few samples in each cohort. They sampled only 37 tablets from Ghana, which is quite small. No statistical reason were given for choosing 37 tablets (Bate et al., 2008).

Stanton et al. (2012) looked at the quality of uterotonic drugs in Ghana. Ampules were purchased from three districts with different characteristics in Ghana; these were coastal, forest and savannah districts. They found that most (86% to 100%) of the different drugs did not meet the quality standards set by WHO. This study did not take into consideration the vast difference in the demography within these regions, the population differences and difference between the various points of sales (Stanton et al., 2012). Bate and Hess (2010) looked at the quality of antimalarial drug quality in Accra and Lagos, which are the capital cities of Ghana and Nigeria respectively. In this study, the percentage of counterfeit drugs in Ghana ranged from 54% to 94% depending on the method used to check the quality of the drug. The researchers used what they called a visual method and analytical tests using Raman spectrometer. The problem with this study is that they focused their sampling at the capital city only and their sampling method was only from private pharmacies. Only 18 pharmacies were sampled in Ghana (Bate & Hess, 2010). There are 429 pharmacies and 9210 licensed chemical sellers in the country (FHI360, 2013), any study being done in Ghana should statistically represent these outlets. Most of these studies used high pressure liquid chromatography (HPLC) as the analytical techniques used to measure the concentration of the drug.

Conclusions

Malaria is still endemic in many places especially in the sub-Saharan region of Africa. There are several medications that can be used for the treatment and prevention the disease. Unfortunately, there are studies and reports that show that some of these countries are infiltrated with counterfeit antimalarial medication. Several studies have

been done to check the quality of drugs especially antimalarial drugs. Ghana is one of the countries with very high rates of malaria infection. A literature review shows very few studies attempting to assess the quality of drugs in Ghana. Majority of these studies were not comprehensive enough. The data were not comprehensive, most were pilot studies, which focused on very small populations. Sampling seemed arbitrary with no statistical basis on how the populations were selected. Most of the research studies were all focused on small regions in the country, which did not tell us much about the quality of drugs in the whole country. The previous studies showed vast variability of the results, which did not substantiate a systematic pattern for arriving at a conclusive state. They range from hardly any counterfeit drugs to almost 90% of the drugs being counterfeit. Most of the sampling done for these studies was from samples collected from retail outlets. None of studies considered the different kinds of retail outlets used in Ghana. Therefore, there is a need for a more comprehensive study that provides a quantitative and systematic approach and address the extent of counterfeit antimalarial drugs in Ghana.

Chapter 3: Research Method

Introduction

In this chapter, I will address the research design, rationale of the research, and the study variables. I will also evaluate the target population, sampling procedure, and the instrument for analysis in addition to providing operationalization of variables and assessing the data analysis and threats to validity. Next, I will identify the software for analyses and evaluate possible ethical concerns. Finally, I will summarize the design and methodology.

Study Purpose

There are several medications in the market used for malaria treatment. It is believed that most of these drugs are counterfeit. Unfortunately, the areas suffering most from malaria seem to have a higher prevalence of counterfeit medication. Any eradication program will have to include reducing or eliminating counterfeit medication in the systems. Because there is no data quantifying the percentage of these drugs that are counterfeit, the purpose of this study was to empirically assess the poor quality of antimalarial drugs in Ghana. I did this by investigating the most popular or prescribed antimalarial tablet artemether-lumefantrine, as this tablet is recommended by the Ghana Ministry of Health (2009) as the first line for uncomplicated malaria.

Research Design and Rationale

This was a cross sectional correlational study that qualifies as quasi-experimental due to lacking a control group, which is a part of what makes a study experimental. The rationale of the study was to determine the quality of antimalarial medication and to

investigate possible sources of the variation in quality in Ghana. The actual amount of active ingredients of the two most prescribed antimalarial drugs, artemether and lumefantrine, were compared to the expected or labeled amount. This study required systematic measurement of study samples in the lab using validated analytical techniques. As Fowler (2009) describes, the quantitative method is the best way to assess a situation or problem analytically, which is why it was used in this study. According to Creswell (2009), one of the hallmarks of quantitative methodology is the analytical part of the study; for this study, the analytical part was the quantitative measurements used to determine the relationship among the variables. It is also important to point out that this study was not intended to prove a causal relationship; rather, it is descriptive. The aim of the study was to empirically define the problem with the quality of antimalarial drugs in Ghana, as empirical knowledge of the problem can provide a sustainable way of finding a solution.

Study Variables

The study variables were the concentration of artemether and lumefantrine, which is measured in milligram per milliliter of solution. These were the dependent variables as shown in Table 1. The independent variables are the pharmacies, LCS, and their locations. This includes those acquired from private and government run pharmacies in cities, small towns, and wholesale companies (Table 1). It was also important to see if the cost of the drugs was different and if it had an effect on the other study variables. This was also considered as a possible covariate (Table 1).

Table 1

Study Variables

Dependent	Concentration of artemether (mg/ml) Concentration of lumefantrine (mg/ml)
Independent	Private pharmacies Cities that the private pharmacies are locates Small towns and villages that the private pharmacies are located Government Pharmacies LCS Cities that the LCS are located Small towns and villages are located mPedigree scratch-off panel
Covariate	Cost of Drugs

Target Population

I examined artemether-lumefantrine combination tablets, which in Ghana can be obtained in two formalized ways: traditional pharmacies with a trained pharmacist and licensed chemical sellers (LCS). LCS sell drugs mostly in suburbs small town and villages, with no supervision of a pharmacist, but are licensed by the government to sell over-the-counter medication and common medications authorized by the government. Because these are not well controlled or monitored, the LCS sells almost the same medications sold by the pharmacies.

The tablets were obtained from a variety of locations in Ghana. A majority of the pharmacies are in the major cities within ten regions. According to the Ghana Pharmacy Council, there are 430 Pharmacies and 9,210 Licensed Chemical Sellers throughout the country. A majority of the pharmacies are located in four major cities: the city of Accra

has about half (233), Kumasi has (79) pharmacies, and 40 are in the other 2. The LCS are more spread out as they serve more remote and rural communities.

Sampling Procedures

Stratified sampling was used to group and sample the population of the town or city based on the pharmacies per population density. For the sampling of the licensed chemical sellers, simple random sampling was used. In addition, for the pharmacy stores, after the stratification method was done, simple random sampling was used. The goal of the study was to have a power of .08 (80%), with a Cohen specification of a large effect size of 0.5 for pharmacies and medium effect size of 0.3 for LCS. For each hypothesis, a 95% confidence with the alpha level (type 1 error) set to 0.05 (5%) was assumed. Using Gpower 3.1 software, the total number of observation in this study was 141. This represented 32 pharmacies and 109 LCS. The numbers of samples that represented pharmacies and LCS found in the cities were 16 and 39 respectively. The numbers of samples that represented pharmacies and LCS found in small towns/villages were both 16, and the number samples for local and imported drugs were 141 each. The total number of samples representing local and government sources was 141 and 16 (from 10 regional and 6 district capital towns) respectively.

Table 2 below shows the number of pharmacies with their samples for each stratum and Table 2 and Table 3 show the towns that were randomly picked for sampling of the pharmacies. Half of the samples were from the cities and the other half from small towns/villages, as LCS are more spread out as they serve more remote and rural communities. Half of the LCS sampling was from towns that were already sampled for

pharmacies (Table 3 and Table 4), and the other half was from towns/villages with no pharmacies (Table 5). Inclusion criterion for pharmacies was that they were stores run by registered pharmacists as defined by the Ghana pharmacy board; exclusion criterion for pharmacies was that they were LCS and stores without registered pharmacists. Inclusion criterion for LCS was that they were stores without registered pharmacists; exclusion criterion for LCS was that they were pharmacies and stores with pharmacists. The government-run pharmacies are located in mostly in the cities and the bigger towns. Each Region has an average of four government-run hospitals or clinics; sampling was done from two of the hospital pharmacies in each region. Cities like Accra and Kumasi with many pharmacies and LCS will have their sampling done by taking samples from every 10th pharmacy and LCS going from North to South.

Table 2

Number of Private Pharmacies in Ghana by Town/City

Town/City	Number of Pharmacies
Accra	233
Adenta	1
Aflao	1
Agogo	1
Agona Swedru	1
Akim Oda	1
Anloga	1
Asamankese	1
Ashiaman	1
Bawku	1
Berekum	1
Bolgatanga	1
Cape Coast*	10
Dome	1
Effiakuma	1
Ejura	1
Ho	1
Kintampo	1
Koforidua	8
Konongo	1
Kumasi	79
Lashibi	1
Madina	1
Mampong	1
Nkawkaw	1
Nsawam	1
Nungua	1
Obuasi	4
Oduponkpehe	1
Prestea	1
Savelugu	1
Sekondi-Takoradi	20
Suhum	1
Sunyani	8
Taifa	1

Tamale	5
Tarkwa	2
Techiman	3
Tema	24
Teshie	1
Wa	1
Wenchi	1
Winneba	1
Yendi	1
Total	**429**

Table 3

Number of Pharmacies and LCS Sampled by City

City	Number of Pharmacies	Number of LCS
Accra	7	23
Cape Coast	1	1
Koforidua	1	1
Kumasi	3	10
Sekondi-Takoradi	1	1
Sunyani	1	1
Tamale	1	1
Tema	1	1

Table 4

Number of Pharmacies and LCS Sampled by Small Town/Village

Small Towns /Villages	Number of Pharmacies	Number of LCS
Agogo	1	1
Agona Swedru	1	1
Akim Oda	1	1
Anloga	1	1
Bawku	1	1
Bolgatanga	1	1
Effiakuma	1	1
Kintampo	1	1
Konongo	1	1
Mampong	1	1
Nkawkaw	1	1
Savelugu	1	1
Suhum	1	1
Wa	1	1
Wenchi	1	1
Yendi	1	1

Table 5

Number of LCS in 10 Regions in Ghana with No Pharmacies

Region	Towns	Number of LCS
Greater Accra Region	Ashaiman	1
	Adafoah	1
	Taifa	1
	Dome	1
Western Region	Bobiani	1
	Half Assini	1
	Dunkwa	1
	Kumenda	1
Ashanti Region	Tepa	1
	Bibiani	1
	Agogo	1
	Pekyi	1
Northern Region	Bole	1
	Zabzugu	1
	Nyankpala	1
	Bimbilla	1
Upper East Region	Navrongo	1
	Garu	1
	Zebila	1
	Winkogo	1
Upper West	Yala	1
	Nabolo	1
	Jirapa	1
	Hamale	1
Volta Region	Denu	1
	Jasikan	1
	Kpandu	1
	Hoehoe	1
Brong Ahafo Region	Tuobodom	1
	Jema	1
	Brumasi	1
	Jema	1
Eastern	Asene	1
	Kpong	1
	Kade	1
	Oda	1
Cape Coast	Saltpond	1
	Praso	1
	Brakwa	1
	Komenda	1

Research Questions and Hypotheses

It may not be possible at this time to detect all the counterfeit medication in Ghana, and we may not be able to detect it for ATMT and LMFT either. However, we can find out the minimum percentage of artemether and lumefantrine in Ghana that is counterfeit, and which are good predictors of the quality antimalarial medication. Four research questions and hypothesis were used to investigate this:

RQ1: Is there a difference between the percentage of counterfeit medication in pharmacies found in the cities and those found in the rural areas?

Ho1: There is no significant difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

Ha1: There is a significant difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

RQ2: Is there a difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers?

Ho2: There is no significant difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers.

Ha2: There is a significant difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers.

RQ3: Is there a significant difference in the percentage of counterfeit drugs between those drugs imported and drugs locally manufactured?

Ho3: There is no significant difference in the percentage of counterfeit drugs between those drugs imported versus drugs locally manufactured.

Ha3: There is a difference in the percentage of counterfeit drugs between those drugs imported versus drugs locally manufactured.

RQ4: Is there a correlation between the mPedigree scratch-off panel on the packaging and percent of counterfeit drugs?

Ho4: There is no significant difference between the mPedigree scratch-off panel on the packaging and percent of counterfeit drugs.

Ha4: There is a significant difference between the mPedigree scratch-off panel on the packaging and percent of counterfeit drugs.

Instrumentation and Operationalization of Constructs

Operationalization

In order test the hypotheses, the variables had to be identified and defined. The operational definitions of the variables are in Table 6.

Table 6

Variable Type	Variable	Operational Definition
Dependent	Concentration of artemether (mg/ml)	The concentration of the artemether and lumefantrine represents the amount of drug per unit volume of water. This will allow us to compare the various amounts on the drugs on the same scale and units.
	Concentration of lumefantrine (mg/ml)	
Independent	Private pharmacies	Private pharmacies (stores run by at least one registered pharmacist) in cities.

Continued on next page

Variable Type	Variable	Operational Definition
Independent	Cities	Cities are defined as urban communities that have utilities, public transportation, modern sanitation, large population density, and businesses.
	Small towns and villages	Small towns and villages lack some or all utilities like pipe born water, public transportation, modern sanitation and businesses.
	Licensed chemical sellers (LCS)	Licensed chemical sellers (stores not run by registered pharmacists) in cities
	mPedigree scratch-off panel	The mPedigree scratch-off panel, is intended to protect against counterfeit medication by labeling medication using unique codes, which are verified by SMS. The code is sent via SMS to a global hotline for verification. A response is sent back within seconds to confirm or deny the authenticity of the drug
Covariate	Cost of Drugs	The cost of the medication may affect the quality of the drug. The cost of every table will also be recorded and tracked to see if it is a possible covariate.

Data Collection

In order to test samples, data was collected from the various kinds of retail stores described in the hypotheses and transferred into an excel sheet.

Determination of the concentration of artemether and lumefantrine

The concentration of artemether and lumefantrine was determined using High Performance Liquid Chromatography (HPLC). This was performed at the Mayo Clinic Pharmacology Shared Resource Center in Rochester, MN. This lab is a certified lab that pharmacologic expertise, methodologies, and services especially for phase I and II trials funded by the National Cancer Institute (NCI). This removed the complication of dealing with customs and shipping these drugs to the US for measurement. They have several years of experience developing, approving, and validation methods for testing the concentration of drugs for clinical trials. HPLC is an analytical method used for separating mixtures and quantitation the amount of the analytes in the mixture. It is the method recommended by the US Food and Drug Administration (USFDA) for checking drug concentration, and it is used by pharmaceutical companies, toxicologists, and pharmacologists. The basic principle of chromatography is the separation of mixtures based on the speed of movement through a medium. After the sample goes through the medium, a detector will measure the fluorescence, or the wavelength emitted by each of the analytes, which is quantified. These tests are confirmed using standards and controls and quantified using calibration curves from these standards. The assay was based on validated assays used by others and implemented by the African National Quality Control Laboratories (Gaudin et al., 2009; Gu, Li, Melendez, & Weina, 2008). The separation of the mixtures was achieved by using column (100 × 4.6 mm, 3μm) as a stationary phase and a binary gradient using a liquid phase (aqueous phase) containing phosphate buffer at pH 3 (10 mm) and acetonitrile. The liquid phase will move the solubilized drugs through

the stationary phase, which allows the drugs to separate based on the chemical properties, the partition coefficient between the drugs and the column bed. These processes and methodology were validated and has been accepted by the USFDA as the guideline in order to ensure its robustness, specificity, accuracy and precision are achieved (Geditz et al., 2014; Houstoun et al., 2014). HPLC grade (>99%) artemether and lumefantrine were be purchased from Fisher Scientific to create standards and quality controls (Fischer Scientific, 2016). This dissolved in fixed volumes of 20% water and 80% acetate buffer PH 4.5 (buffer A) to make the calibration standards. The concentrations were measured in mg/ml. The tablets were also dissolved in 10mls buffer A. These were vortexed and centrifuged at 3500 rpm for 5 mins. The supernatant was decanted into a 96 well filter plate before he samples were analyzed. These samples also included standards and controls per good lab practice based on the code of federal regulations title 21 (U. S. Food and Drug Administration, 2016) and the Guidance for Industry, Analytical Procedure and Methods Validation for Drugs and Biologics (U. S. Food and Drug Administration, 2001).

Analysis Plan

After all the data is collected, and the samples have been evaluated, the data was imported into the Statistical Package, SPSS version 21, for further analyzes. The data was exported from the instrument and verified to maintain the integrity and validity of the data. The data collected from analyzing the concentrations of artemether and lumefantrine in the lab using the HPLC system was entered into the SPSS spreadsheet to determine the correlation between the pharmacies and LCS. Generally, analysis was

conducted using descriptive statistics. Categorical variables were described using frequencies and the continuous variables were examined using means and standard deviations (Table 7). Possible Relationships between categorical independent variables was tested using cross-tabulations with Pearson's $\chi 2$ (Table 7). Multiple linear regressions will also be used to assess the associations between the variables. The probability of the distribution of the concentration of artemether and lumefantrine concentrations was described using histograms.

Table 7.

List of Variables and Analyses

Type of Variable	Descriptive	Covariance
Concentration of artemether (mg/ml) in private pharmacies in Cities	Means and SDs	ANOVA's
Concentration of artemether (mg/ml) in private Small towns and villages	Means and SDs	ANOVA's
Concentration of artemether (mg/ml) in LCS in Cities	Means and SDs	ANOVA's
Concentration of artemether (mg/ml) in LCS in Small towns and villages	Means and SDs	ANOVA's
Concentration artemether (mg/ml) in Wholesale stores	Means and SDs	ANOVA's
Concentration of lumefantrine (mg/ml) in private pharmacies in Cities	Means and SDs	ANOVA's
Concentration of lumefantrine (mg/ml) in private Small towns and villages	Means and SDs	ANOVA's
Concentration of lumefantrine (mg/ml) in LCS in Cities	Means and SDs	ANOVA's
Concentration of lumefantrine (mg/ml) in LCS in Small towns and villages	Means and SDs	ANOVA's
Concentration lumefantrine (mg/ml) in Wholesale stores	Means and SDs	ANOVA's

Continued on next page

Type of Variable	Descriptive	Covariance
Cost of Drugs	Means and SDs	ANOVA's
Correlation between Cost of Drugs and pharmacies in Cities	Correlation coefficient (r)	ANOVA's
Correlation between Cost of Drugs and LCS in Cities	Correlation coefficient (r)	ANOVA's
Correlation between Cost of Drugs and pharmacies in small towns/villages	Correlation coefficient (r)	ANOVA's
Correlation between Cost of Drugs and LCS in small towns/villages	Correlation coefficient (r)	ANOVA's
Number (Percent) of counterfeit Drugs in Cities	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in Cities	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine Cities	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in Cities	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in Cities	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in Cities	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit Drugs in all Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in all Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine all Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in all Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in all Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in all Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit Drugs in all LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in all LCS	Frequencies	Crosstabs With Pearson's $\chi 2$

Continued on next page

Type of Variable	Descriptive	Covariance
Number (Percent) of counterfeit lumefantrine all LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in all LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in all LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in all LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit Drugs in whole sale stores	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in whole sale stores	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine in whole sale stores	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in whole sale stores	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in whole sale stores	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in whole sale stores	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit Drugs in Small towns and villages	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in small towns and villages	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine in small towns and villages	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in small towns and villages	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in small towns and villages	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in small towns and villages	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit Drugs in City Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in City Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine City Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in City Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$

Continued on the next page

Type of Variable	Descriptive	Covariance
Number (Percent) correct lumefantrine concentration in City Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in City Pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit Drugs in City LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in City LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine City LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in City LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in City LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in City LCS	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit artemether in government pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of counterfeit lumefantrine government pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) of Drugs with Correct concentration in government pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct lumefantrine concentration in government pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$
Number (Percent) correct artemether concentration in government pharmacies	Frequencies	Crosstabs With Pearson's $\chi 2$

Below is a summary of the research questions:

1) RQ1 - Is there a difference between the percentage of counterfeit medication in pharmacies found in the cities and those found in the rural areas? Was tested using Crosstabs with Pearson's $\chi 2$.

2) RQ2 - Is there a difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers? Was tested using Crosstabs with Pearson's $\chi 2$.
3) RQ3 - Is there a significant difference in the percentage of counterfeit drugs between those drugs imported and drugs locally manufactured? Was tested using Crosstabs with Pearson's $\chi 2$.
4) RQ4 – Is there a significant difference in the percentage of counterfeit drugs between drugs with scratch codes and those without scratch codes? Was tested using Crosstabs with Pearson's $\chi 2$.

Threats to Validity

There is the need for an evidence of validity and reliability for the study especially during interpretation phase (Trochim, 2006). Therefore, a very specific and sensitive assay to ensure the data accuracy was used as well as using a logical approach to explain the problem and any dependent resolution to the problem statement. One of such methodologies is the use of Construct validity. Construct validity addresses whether the results are what they are supposed to be for the research or if what was done was what it was intended to do (Fowler, 2009). It deals with how the variables were operationalized and if they are related to the theory of the study. This was prevented from happening with the use a validated HPLC assay, which is also the assay used for similar studies. Another problem is the possibility of Internal validity issues, which mainly deals with how the experiment was conducted and if it has an effect on the outcome (Fowler, 2009). There could be a flaw in the study because if sample collection and allocation of

variables is not performed correctly, this could lead to the wrong conclusions. Consequently, it could raise questions about conclusion validity. With a power of .08 (80%), the goal is to reduce this possibility. Another threat to external validity is the fact that the conclusions drawn from this study should hold for the whole country. The goals are to use the correct statistics to prevent this from happening. A limitation of this study is that it is not providing any relationship or possible cause and effect between the variables (Creswell, 2007).

Ethical Procedures

Approval from the Walden University Institutional Review Boards (1-06-15-00041987) was obtained prior to data collection. I will observe all research ethics during the primary data collection of this research. I will follow the ethical principles of the Belmont Report. The confidentiality of the pharmacies and LCS was protected by not revealing their names when the data is being processed. Each store was given a unique identification code, and this code will in a separate, secure location from the data files. All data was kept under password protection. Because these drugs could cause harm to the patients that buy them, any retail store that is found to have counterfeit drugs was reported to the Ghana food and drug administration (GFDA). The GFDA for the quality of all drugs distributed in Ghana. It has the right to prosecute and arrest perpetrators. It has been on high alert due to the incidence suspected counterfeit drugs in the Ghanaian market. It was my ethical duty to report any such occurrences especially because I will have the quantitative evidence.

Summary

This chapter focused on the use of quantitative experimental research methodology in this research investigation. The rational of the study is to assess the quality of antimalarial medication in Ghana by empirically comparing the actual amount of active ingredients of the two most prescribed antimalarial drugs, artemether and lumefantrine, to the intended or labelled amount. These drugs were purchased from retail stores in Ghana from various towns and cities, and measured using a HPLC to compare the actual versus expected concentrations. The various topics included in this chapter were study design, rational, study variables, target population, sampling and sampling procedures, eligibility criteria, research questions and hypothesis, study variables description and instrumentation, determination of the concentration of artemether and Lumefantrine, sampling, ethics and threats to validity. Included in this chapter is a description of my statistical analysis of the data. In Chapter 4, the results the study was processed and discussed.

Chapter 4: Results

Introduction

The purpose of this quantitative study was to explore the extent of antimalarial counterfeiting by looking at the percentage of ATMT and LMFT in drugs sold in retail outlets in Ghana that is counterfeit. The following are the research questions of this study:

RQ1 - Is there a difference between the percentage of counterfeit medication in pharmacies found in the cities and those found in the rural areas?

Ho1: There is no significant difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

Ha1: There is a significant difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

RQ2 - Is there a difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers?

Ho2: There is no significant difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers.

Ha2: There is a significant difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers.

RQ3 - Is there a significant difference in the percentage of counterfeit drugs between those drugs imported and drugs locally manufactured?

Ho3: There is no significant difference in the percentage of counterfeit drugs between those drugs imported versus drugs locally manufactured.

Ha3: There is a difference in the percentage of counterfeit drugs between those drugs imported versus drugs locally manufactured.

RQ4 – Is there a correlation between the MPedigree scratch-off panel on the packaging and percent of counterfeit drugs?

Ho4: There is no significant difference between the MPedigree scratch-off panel on the packaging and percent of counterfeit drugs.

Ha4: There is a significant difference between the MPedigree scratch-off panel on the packaging and percent of counterfeit drugs.

In this chapter, I will present the results of the study and descriptive statistics of each variable, relationships among variables, and analyses conducted to examine the research questions and hypotheses. In this study, alpha was set to .05, which means that p-values less than .05 were considered statistically significant.

Data Collection

Divergence in data collection from the research plan presented in Chapter 3 is presented here in the results section. The timeframe for this data collection was from February 4, 2016 to June 7, 2016. I went to Ghana to collect the samples from all over the country based on what was described in Chapter 3. There were no issues with quickly purchasing products from the outlets, as there was no reason for the outlets not to sell the drugs. As mentioned in Chapter 3, stratified sampling was used to group and sample the population of the town or city based populations. Simple random sampling method was used for sample collection. The goal of the study was to have a power of .08 (80%), with a Cohen specification of a large effect size of 0.5 for pharmacies and

medium effect size 0.3 for LCS. For each hypothesis, a 95% confidence with the alpha level (type 1 error) set to 0.05 (5%) was assumed.

Out of the outlets and demographics, nearly all carried the medication except for government hospitals, which will not sell the mediation without prescription. The total number of outlets in this study was 145. Demographics of pharmacies and license chemical sellers are shown in Table 8; a majority of the drugs were purchased from LCS.

Table 8.

Descriptive Statistics of Location of Outlets

Outlets	**Frequency**	**Percent**
Big city pharmacies	23	28.0
Whole sale pharmacies	6	7.3
Small town pharmacies	17	20.7
Big city LCS	19	23.2
Small town LCS	46	20.7

Analytical Results

The mobile phase was made up of an aqueous solution composed of 0.05% Trifluoracetic Acid (TFA) and acetonitrile 40:60 (v/v), adjusted a pH to 3 and filtered through 0.45 µ membrane filter and sonicated before use. Flow rate of mobile phase was maintained at 1.5 ml/min. The column temperature maintained was ambient temperature. The detection was carried out at 210nm. Injection volume 20 µl and total run time was 3.5 min. Column was Zorbax SB-CN HPLC column (150 × 4.6 mm, 3.5 µm, Agilent). Pyrimethamine was used as an internal standard. An example of the chromatogram is shown on Figure 5.

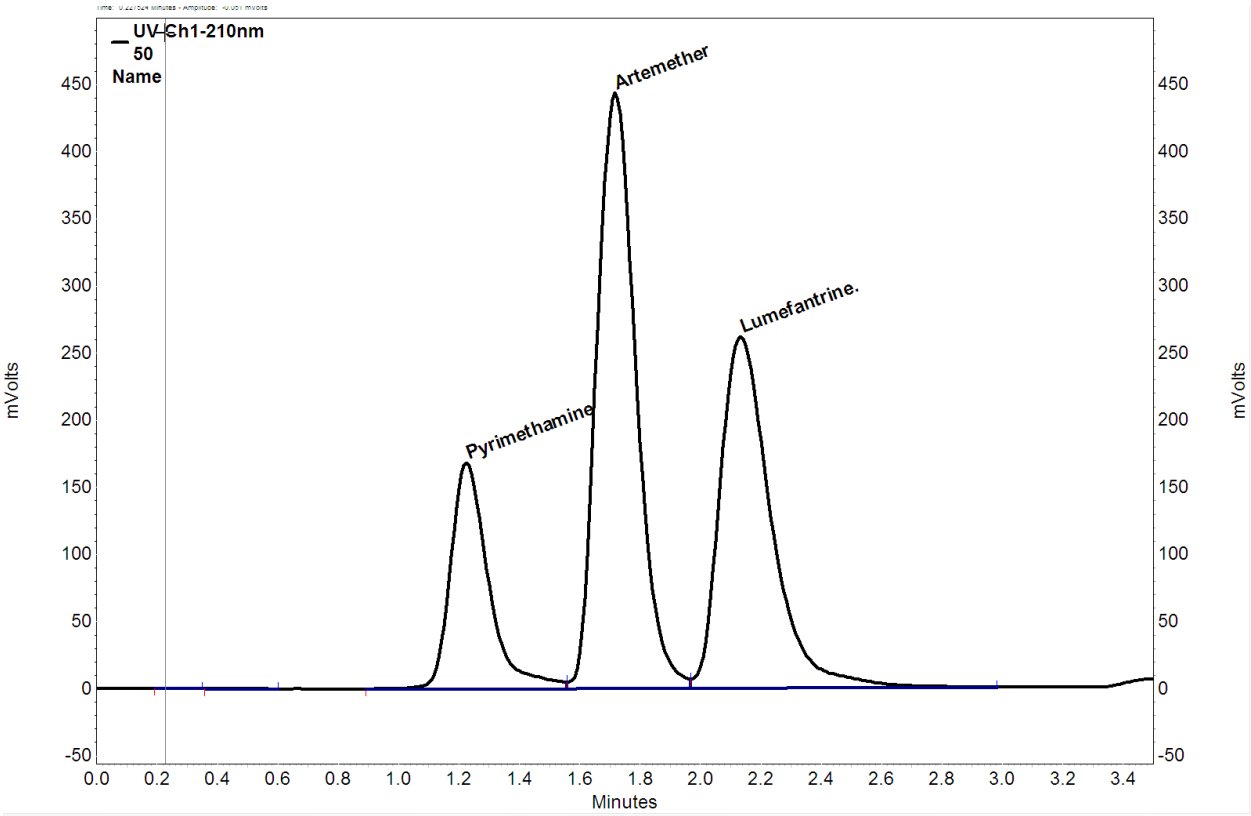

Figure 5. Example of Chromatogram obtained for 50 ug/ml of artemether and 50 ug/ml of lumefantrine.

A calibration curve was calculated and fitted by 1/x weighted regression of the peak-area ratios of peak height of drug to the peak height of the internal standard. The standard used for the calibration were 0, 1, 5, 100, 500 and 1000 ug/ml. The quality control samples were 1, 40, 80 and 800 ug/ml. The concentration of the artemether and lumefantrine in the tablets were calculated using the linear curve and multiplied by 1000 to represent the 1:1000 dilution for each tablet. The final concentration was therefore in mg/ml. The accuracy of the method was determined by using known concentrations of standard after it had been added to fixed concentration of the preanalyzed tablet solution. Percent recovery was calculated by using the peak area before and after the addition of

the known standards. The recovery studies were performed in triplicate using standard addition method based on 10%, 100%, 1000% level and after which the recovery was calculated. Based on this, average recovery was 99.2% for artemether and 99.4 lumefantrine, which confirms accuracy of the assay. Since some of the tablets had different amounts, all of them were standardized to 20mg/ml for artemether and 120 mg/ml for lumefantrine. Summary of the descriptive statistics of the samples is shown in Table 9. On average the mean (SD) was 15.8 (5.5) and 102.5 (5.5) for all locations except for wholesale stores that did not have counterfeit drugs.

Table 9

Descriptive Statistics of Drug Concentrations

	N	mean	sd	min	max
Concentration of artemether (mg/ml)					
Private pharmacies in cities	16	16.2	5.7	0	20
Wholesale stores	6	16.1	5.6	4.75	19
Private pharmacies in small towns and villages	17	15.5	0.5	14.8	19
LCS in cities	46	15.6	5.3	1	19.8
LCS in small towns and villages	65	15.6	5.1	0	20.8
Concentration of lumefantrine (mg/ml)					
Private pharmacies in cities	16	104.8	34.6	0	120
Wholesale stores	6	117.3	1.8	115	120
Private pharmacies in small towns and villages	17	96.3	34.6	26	118.5
LCS in cities	46	100.1	29.8	17.5	119
LCS in small towns and villages	65	100.6	29.5	15.75	119.3

When the drugs were purchased the prices were also recorded to see if this could affect the quality of these drug being purchased. Of the 150 drugs that were purchased, the

mean (sd) was 8.0 (3.8) Ghana Cedis. (1 dollar on the average at the time of purchase was equivalent to 3.7 Ghana Cedis). The summary is shown on Table 10.

Table 10

Summary of Cost for Purchasing the Drugs

Location	Mean	N	Std. Deviation
Big city pharmacies	9.44	16	5.5
Wholesale pharmacies	5.83	6	1.6
Small town pharmacies	9.00	17	5.7
Big city LCS	7.72	46	2.9
Small town LCS	7.78	65	3.3
Total	8.00	150	3.8

I next determined the definition of counterfeit drugs based on the concentration. The nominal value for artemether and lumefantrine were 20mg/ml and 120mg/ml respectively. Generally, FDA considers these drugs as counterfeit (substandard) if the concentration is less than 20 % of the expected values. In this case, all concentrations less than 16 ng/ml and 96 ng/ml of artemether and lumefantrine respectively were considered. Table 11 shows a summary of counterfeit drugs based on the locations.

Table 11

Summary of Quality of all Drugs based on Location

	Counterfeit		Non- counterfeit	
Location	Number	%	Number	%
Big city pharmacies	1	6.3	15	93.8
Whole sale pharmacies	0	0.0	6	100.0
Small town pharmacies	3	17.6	14	82.4
Big city LCS	11	23.9	35	76.1
Small town LCS	15	23.1	50	76.9
Total	**30**	**20.0**	**120**	**80.0**

Table 12.

Summary of Quality of artemether and lumefantrine on Outlet

	Counterfeit		Non- counterfeit	
Outlet	number	%	Number	%
Population	30	20.0	120	80.0
Pharmacy	4	10.3	35	89.7
LCS	26	23.4	85	76.6

Table 13.

Summary of Quality of artemether and lumefantrine based on Presence or Absence of Scratch

	Counterfeit		Non- counterfeit	
Outlet	number	%	number	%
No-Scratch	30	34.5	57	65.5
Scratch	0	0	63	100

Table 14.

Summary of quality of artemether and lumefantrine only based on import or local manufacture

	Counterfeit		Non- counterfeit	
Outlet	number	%	number	%
Local	0	0	23	100
Imported	30	23.6	97	76.4

Out of 150 drugs that were purchased, 30 (20%) of them were counterfeit. Small town LCS had the highest percentage of counterfeit medication, while wholesale pharmacies had no counterfeit medication. Comparing both drugs, the trends were

exactly the same. Any tablet that had counterfeit lumefantrine also had counterfeit artemether. Comparing pharmacies and LCS, LCS had more counterfeit drugs (about 14% more) than pharmacies (Tables 12). None of the locally manufactured medications were counterfeit (Tables 14). All the counterfeit medications were imported drugs and had no mPedigree scratch-off panels on them (Tables 13).

Analysis of Research Questions

A few steps were taken in the analysis of research: several initial democratic variables were lumped (collapsed) to generate other relevant variables, nonparametric Pearson's Chi square (χ^2) tests were the primary analysis used to test the hypotheses, and other tests used linear regression to determine the correlation between the cost of medication and the quality of medication.

RQ1 - Is there a difference between the percentage of counterfeit medication in pharmacies found in the cities and those found in the rural areas?

Ho1: There is no significant difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

Ha1: There is a significant difference between the percentages of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

Based on the results below, the p value (0.512) is > 0.05, (Table 15) the null hypothesis cannot be rejected. There is no significant difference ($\chi^2 = 0.430$, $p = 0.512$) between the quantity of counterfeit medication in pharmacies found in the cities versus those found in the rural areas.

Table 15

Comparing the Quality of Drugs in Cities versus Rural Areas

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.430	1	.512		
Continuity Correction[b]	.203	1	.652		
Likelihood Ratio	.433	1	.510		
Fisher's Exact Test				.545	.327
Linear-by-Linear Association	.428	1	.513		
N of Valid Cases	150				

RQ2 - Is there a difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers?

Ho2: There is no significant difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers.

Ha2: There is a significant difference in the percentage of counterfeit drugs between pharmacies and Licensed Chemical Sellers.

Based on the results below, the p value (0.077) is > 0.05, (Table 17) the null hypothesis was not rejected. There is a no significant difference ($\chi 2 = 3.127$, $p = 0.077$) between the quantity of counterfeit drugs from pharmacy versus LCS.

Table 16

Comparing the Quality of Drugs in Pharmacy Versus LCS

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	3.127	1	.077		
Continuity Correction[b]	2.358	1	.125		
Likelihood Ratio	3.484	1	.062		
Fisher's Exact Test				.103	.057
Linear-by-Linear Association	3.106	1	.078		
N of Valid Cases	150				

RQ3 - Is there a significant difference in the percentage of counterfeit drugs between those drugs imported and drugs locally manufactured?

Ho3: There is no significant difference in the percentage of counterfeit drugs between those drugs imported versus drugs locally manufactured.

Ha3: There is a difference in the percentage of counterfeit drugs between those drugs imported versus drugs locally manufactured.

Based on the results below, the p value (0.009) is < 0.05, (Table 17) the null hypothesis was rejected in lieu of the alternative hypothesis. There is a significant difference ($\chi 2 = 6.791$, $p = 0.009$) between the quantity of counterfeit drugs from locally made versus imported drugs.

Table 17

Comparing the Quality of Drugs in Locally Made Versus Imported

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	6.791	1	.009		
Continuity Correction[b]	5.395	1	.020		
Likelihood Ratio	11.263	1	.001		
Fisher's Exact Test				.008	.004
Linear-by-Linear Association	6.746	1	.009		
N of Valid Cases	150				

RQ4 – Is there a correlation between the MPedigree scratch-off panel on the packaging and percent of counterfeit drugs?

Ho4: There is no significant difference between the MPedigree scratch-off panel on the packaging and percent of counterfeit drugs.

Ha4: There is a significant difference between the MPedigree scratch-off panel on the packaging and percent of counterfeit drugs.

Based the results below, the p value (0.000) is < 0.05, (Table 18) the null hypothesis was rejected in lieu of the alternative hypothesis. There is a significant difference ($\chi 2$ = 27.155, p = 0.000) between the quantity of counterfeit drugs from mPedigree scratch-off panel boxes versus those that were not scratched.

Table 18

Comparing the Quality of Drugs based on Use of mPedigree Scratch-off Panel

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	27.155	1	.000		
Continuity Correction[b]	25.043	1	.000		
Likelihood Ratio	38.032	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	26.974	1	.000		
N of Valid Cases	150				

Using multiple regression analysis, it was found that the kind of store (Beta = .027, p = .714) and the location in a city or small town/village (Beta = -.021, p = .143) are not predictors of the quality artemether. Checking the same for lumefantrine the kind of store (Beta = -.008, p = .898) and the location (Beta = -.027, p = .682) were also not predictors of the quality of drugs. For both artemether (Beta = -.521, $p < .05$) and lumefantrine (Beta = -.639, $p < .05$) the origin of the drug (local or imported) predictors for drug quality. This was also true for the present of mPedigree scratch-off panel on boxes. For both artemether (Beta = -.110, $p < .01$) and lumefantrine (Beta = -.151, $p < .023$), having the scratch was a predictor of the quality if the drugs. Regression results are shown on Table 19 and Table 20 for LMFT and ATMT respectively.

Table 19.

Multiple linear regression results from comparing dependent and all independent variables for lumefantrine

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	299.029	34.823		8.587	.000	230.204	367.855
	imported or Local drug	-181.569	18.676	-.639	-9.722	.000	-218.481	-144.657
	Location Pham &LCS	-1.949	15.139	-.008	-.129	.898	-31.870	27.972
	Location City&Small Town/Village	-5.522	13.468	-.027	-.410	.682	-32.141	21.098
	Scratch	31.312	13.625	.151	2.298	.023	4.384	58.241

a. Dependent Variable: Lumefantrin_Mean

Table 20.

Multiple linear regression results from comparing dependent and all independent variables for artemether

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	43.639	6.825		6.394	.000	30.149	57.129
imported or Local drug	-26.192	3.661	-.521	-7.155	.000	-33.427	-18.957
LocationPham&LCS	.806	2.967	.020	.272	.786	-5.058	6.671
LocationCity&SmallTownVillage	-.493	2.640	-.014	-.187	.852	-5.710	4.725
Scratch	4.020	2.670	.110	1.505	.134	-1.258	9.298

a. Dependent Variable: Artemether_Mean

The cost of each of these drugs were recorded. A correlation analysis was performed to check if there was c relation between the cost of drug and the quality of the drug. Cost of drug and the quality or he drug were correlated for both (Kedell's: artemether r= .243, p <0.05 and Spearman's: artemether r= .298, p <0.05) and lumefantrine (Kedell's: artemether r= .190, p <0.05 and Spearman's: r= .258 p <0. Results for correlation analysis is on Table 19 and Table 20 for artemether and lumefantrine respectively.

Table 21.

Correlation results from comparing cot of drugs and artemether concentration

			Price_in_GHS	Artemether_ Mean actual
Kendall's tau_b	Price_in_GHS	Correlation Coefficient	1.000	.243**
		Sig. (2-tailed)	.	.000
		N	150	150
	Artemether_Mean actual	Correlation Coefficient	.243**	1.000
		Sig. (2-tailed)	.000	.
		N	150	150
Spearman's rho	Price_in_GHS	Correlation Coefficient	1.000	.298**
		Sig. (2-tailed)	.	.000
		N	150	150
	Artemether_Mean actual	Correlation Coefficient	.298**	1.000
		Sig. (2-tailed)	.000	.
		N	150	150

**. Correlation is significant at the 0.01 level (2-tailed).

Table 22.

Correlation results from comparing cost of drugs and lumefantrine concentration

			Price_in_GH S	Lumefantrin_ Mean actual
Kendall's tau_b	Price_in_GHS	Correlation Coefficient	1.000	.190**
		Sig. (2-tailed)	.	.002
		N	150	150
	Lumefantrin_Mean actual	Correlation Coefficient	.190**	1.000
		Sig. (2-tailed)	.002	.
		N	150	150

Spearman's rho	Price_in_GHS	Correlation Coefficient	1.000	.258**
		Sig. (2-tailed)	.	.001
		N	150	150
	Lumefantrin_Mean actual	Correlation Coefficient	.258**	1.000
		Sig. (2-tailed)	.001	.
		N	150	150

**. Correlation is significant at the 0.01 level (2-tailed).

Conclusions

Pearson Chi-Square analyses were conducted to examine relationships among variables. These tests were conducted to investigate the quality of antimalarial medication. Overall, results revealed that about 20% of the antimalarial medications tested were counterfeit. Even though the percent of counterfeit medication in LCS was higher than pharmacies, this was not statistically significant. The same applies to differences between cities and small towns/villages, this was not statistically significant. Statistically significant differences were found between imported and locally made drugs. The results form comparing drugs with mPedigree scratch-off panel boxes versus drugs those without were similar. Cost of the drug was also correlated with the quality of the drug. The implications of these findings as well as suggestions will be discussed in Chapter 5.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The main goal of this quantitative study was to explore the extent of antimalarial counterfeit medication by looking at the quantities of ATMT and LMFT sold in retail outlets in Ghana that is counterfeit. Fake and substandard drugs need to be addressed due to the threats to patients: failure to provide effective treatments, adulteration with toxic chemicals, and substandard drugs that can lead the parasites to become resistant to the medications (Attaran et al., 2012). The amount of ATMT and LMFT purchased from retail outlets in Ghana was determined using validated analytical methods and compared to the expected amounts. Overall, results revealed about 20% of drugs purchased were counterfeit. The findings and conclusions of this study are discussed in the following section.

Interpretation of the Findings

Difference between Locations

The first set of findings about counterfeit medication relates to the following question: Is there a difference between the percentage of counterfeit medication in drug stores found in cities and those found in the rural areas? Results revealed no statistical difference between cities and rural areas (see Table 18). Despite this study's results, according to Gasmelseid (2016), not only is there a huge variation between geographic regions when it comes to the prevalence of counterfeit medications, variations can also exist between rural and urban centers. There is no difference in Ghana based on this data

likely because these medications in the rural areas are purchased from the cities, and they may have the same sources.

Difference between Pharmacies and LCS

The next set of findings about counterfeit medication relates to the following question: Is there a difference in the percentage of counterfeit drugs between pharmacies and licensed chemical sellers? Results show some difference between pharmacies and LCS, with pharmacies exhibiting higher quality, but this difference was not statistically significant (Table 19). Because of the structure of pharmacies compared to LCS, it was expected to have a significantly higher. LCS are usually independently owned by nonpharmacists, usually by pharmacy technicians at best, and no training is required to obtain a license (FHI360, 2013). This means LCS are prone to illegal practices such as sale of prescription medication, which is illegal but overlooked by authorities in Ghana. The fact that there is no significant difference also shows that they likely purchase from similar sources.

Difference between Imported and Locally Manufactured Drugs

The next finding relates to the following question: Is there a significant difference in the percentage of counterfeit drugs between those drugs imported and drugs locally manufactured? Results revealed that there is a statistical difference between the qualities of drugs that were manufactured locally compared to import ones (Table 20). Ghana has a well-established and developing pharmaceutical manufacturing base, and this report provides profiles of six of the major Ghana pharmaceutical manufacturers. The profiles provide some interesting contrasts in manufacturing strategy against the background of

many common constraints for local pharmaceutical manufacturing development in Ghana. Locally manufactured drugs make about 30% of drugs in the Ghanaian pharmaceutical market. A majority (70%) of medication used in Ghana is mostly imported and they are mostly Southeastern Asia (India and China). There is generally the presumption that I imported goods including medication have higher quality that locally manufactured goods. The locally manufactured medication also tends to be higher in prices. Unfortunately, most of the 750 million counterfeit drugs seized in Africa by World Customs Organization (WCO) since 2012 were from India and China (Barbiere, 2017). It is also important to mention that cost of the drug was also found correlated with the quality of the drug.

Effect of mPedigree Scratch-off Panel

The final finding relates to the following question: Is there a correlation between the mPedigree scratch-off panel on the packaging and percent of counterfeit drugs? Results revealed that there is a statistical difference between the qualities of drugs with the mPedigree scratch-off panel compared to those without (Table 21). This was the largest decider of the quality of drug as all counterfeit medication found in this study had no mPedigree scratch-off panel. This was expected because drugs with this mPedigree scratch-off panel are supposed to be good quality and from the manufacturer.

Findings in Relation to Theoretical Framework

The use of explanatory theory in the study is supported by the results of the study that 20% of drugs are counterfeit, which empirically defined the scope of the problem. Using receptor occupancy theory, the concentration of the drugs was determined to assess

the quality of the drugs. The concentration of the drugs correlated with the amount of drug that will occupy the receptors which correlated with response/efficacy. The total efficacy can only be achieved if all the receptors needed to destroy the plasmodium parasite are occupied. In this case 20% of the drugs will not achieve total efficacy. It also means that there will be no difference in efficacy if we compared location (cities and rural) and LCS versus pharmacies. On the other hand, there will be differences in efficacy between imported versus locally manufactured and the presence versus absence of the mPedigree scratch-off panel.

Limitations of the Study

Limitations for this study include generalization and whether the results are valid and reliable. Examining two antimalarial medications in Ghana may not provide a complete representation of all antimalarial medication in Africa. One way to overcome this in future research is to study other medications and include other countries in the sub region. Another limitation of this study is that the study may not capture all possible outlets. The data was based on data for a country that lacks good data collection systems. The presence of possible illegal outlets is also a limitation, because these are not being counted. Some of these were solved by making sure the data collection process is done based on statistics, using random sampling and other research methods.

Recommendations

A recommendation for future researchers is to include different countries and different experimental designs as a part of their studies. A recommendation to healthcare personnel, government, and patients is to be aware of the 20% counterfeit antimalarial

mediation in the system and eliminate it. From this study, all drugs with the mPedigree scratch-off panel were of good quality, leading to a recommendation to promote only drugs with a mPedigree scratch-off panel. Another recommendation is to promote locally manufactured medication; all drugs imported from India and China should be scrutinized to make sure they are not counterfeit. The government will need to hold companies who are selling and marketing counterfeit medication accountable to deter others.

Implications

The results from this research can help the Ghana standard boards, the Ghana health service, other stakeholders, and policymakers understand the scope of counterfeit antimalarial medication in Ghana. Government/nongovernment organizations and the society at large will benefit from this information. With a better understanding of how much antimalarial medication is counterfeit in Ghana, organizations can create interventions to minimize the effects of counterfeit antimalarial medication in Ghana. Some of the findings may also have a positive impact on public health. The results show that there is no difference between the quality of the medication between cities and rural areas of the country, which implies they likely have similar sources. The results also inform the public on the quality of medication based on mPedigree scratch-off panels; none of the drugs in this study with mPedigree scratch-off panel were counterfeit, which indicates the public should purchase only drugs with mPedigree scratch-off panel and locally manufactured instead of imported medication. With these results, there can be advocacy to get the government to provide subsidies to local companies to help drive the cost down, which will make the medication more affordable comparable to the cost of

buying imported drugs. Finally, the names of the companies with the fake/counterfeit drugs will be given to the authorities for further investigation, so the sources of these counterfeit drugs can be cut off.

Conclusions

The outcomes, the results, and the lessons learned from the results of this study have many implications that can lead to positive social change (e.g., awareness of ways to acquire quality medication, understanding of the distribution of counterfeit medication and possible reduction, or eradication of the sources of these counterfeit medications) not only in Ghana but also in other sub-Saharan African countries. The results from this study can be used by all stakeholders to effectively control the amount of counterfeit medication in the Ghana which is a public health issue. For example, the findings of this study suggest drugs with mPedigree scratch-off panel are likely to be of high quality, so stakeholders should work together to create awareness and to educate people about how this works and why it is important to purchase only drugs with these panels. Results also reveal that all counterfeit drugs were imported. Therefore, stakeholders should also work together to make locally manufactured drugs more assessable and encourage/educate the public to use locally manufactured drugs.

Malaria is still an epidemic in many parts of the world and it still affects millions of people worldwide. Malaria can be treated with several drugs and these drugs work well if used appropriately and contain the right amounts of the active ingredient. In this study, 20% of these drugs were found to be counterfeit. This study begins to help us address the counterfeit problem by empirically finding out the distribution of the

counterfeit medication. Knowing the distribution will help with the initiation of programs to help address this problem.

In summary, in the attempt to eradicate of malaria, secondary prevention plays a pivotal role, which means that people infected by the parasite need to be treated quickly and efficaciously to curb the spread of the disease. All medications therefore need to have the correct active ingredients, the correct regimens adhered to, and the correct use for the right disease. Tackling the issue of counterfeit medication and making quality drugs assessable is very important aspect of this process.

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