

**TREATMENT SEEKING BEHAVIORS AMONG CARETAKERS OF
CHILDREN WITH SUSPECTED MALARIA IN EASTERN UGANDA**

by
Katrina A. Berg, MA

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Abstract

Malaria is the single, biggest cause of childhood mortality in Uganda. Efforts to increase access to first-line treatment, artemisinin-based combination therapies (ACTs), for uncomplicated malaria have had a significant impact on their uptake. However, many people continue to engage in self-treatment and rely on non-ACT antimalarials. This dissertation aims to explore the facilitators and barriers to appropriate treatment-seeking behaviors and outcomes for childhood malaria in eastern Uganda.

A synthesis of existing literature indicates that self-treatment is the preferred first step in the illness resolution process for suspected malaria, including treating suspected malaria with drugs stored at home or from a local drug shop. Initiating treatment in the formal sector is associated with receiving first-line treatment for malaria. Illness severity emerges as a primary determinant of seeking immediate care in a formal healthcare facility. Access and local illness concepts are identified as significant barriers to seeking appropriate, timely treatment. Overall, there existed a lack of complexity in the types of predictors used in previous research.

A quantitative analysis was conducted to understand determinants of seeking care at various levels of the healthcare system. Attitudes and knowledge were associated with seeking care outside of the household. Illness severity and access were the most salient predictors of initiating care at a formal healthcare facility.

A multilevel analysis explored the determinants of treatment outcomes for uncomplicated malaria, mainly use of first-line, nationally-recommended drugs. Caretakers continue to rely on non-ACT antimalarials for severe illness, children under

five, and confirmed malaria. High levels of malaria knowledge and perceived efficacy in malaria-related services were associated with ACT-use.

Findings from this research indicate that caretakers of young children continue to rely on self-treatment for non-serious malarial illness. Efforts should continue to maintain increased access to ACTs, especially in rural areas. National malaria control strategies and behavior change campaigns must target consumers to increase consumer utilization of formal healthcare facilities where diagnostics are available and encourage their sale in local drug shops. Education campaigns are recommended to increase treatment guideline awareness, malaria knowledge, and perceived efficacy in ACTs as well as malaria-related services within the healthcare system.

Advisor: Stella O. Babalola, PhD

Readers: William John Moss, MD, MPH

William Brieger, DrPH, MPH

J. Douglas Storey, PhD, MA

Alternates: Carol R. Underwood, PhD, MA

Cynthia Schaffer Minkovitz, MD, MPP

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Chapter 1: Introduction

In 2012, there were an estimated 207 million cases of malaria world wide, and 627,000 deaths (WHO, 2013). Although more than 40% of the world's population is at risk for malaria, the disease disproportionately affects people living in Africa and children under five years of age. In 2012, 80% of all cases and 90% of all deaths occurred in Africa, and 77% of deaths occurred in children under five (WHO, 2013).

In Uganda, malaria is the leading cause of childhood mortality. Uganda has one of the highest malaria burdens in the world, and is one of five African countries that make up 50% of all global deaths, and 47% of all malaria cases (Roll Back Malaria Partnership [RBMP], 2012). In 2012, Uganda reported more than 13.5 million cases, and almost 100,000 deaths due to malaria (WHO, 2013).

In order to assist in the development of national policies and guidelines, the World Health Organization [WHO] (2010) recommends that all suspected cases of uncomplicated malaria are confirmed diagnostically prior to prescribing treatment, and recommends the use of artemisinin-based combination therapies (ACTs) as the first-line drug. Although testing behaviors have increased in recent years, overall rates remain low. In 2012, it was estimated that 60% of all suspected cases of malaria in the public sector in Africa received a diagnostic test (WHO, 2013). However, this does not include the cases that sought treatment from the informal, private sector, which caretakers frequently rely on in many malaria endemic countries in Africa.

When a child presents with febrile or malarial symptoms, caretakers may treat children at home or take their child to a health facility. Treating at home includes providing western drugs stored at home or purchased over the counter, using local herbal

supplements, engaging in fever-reduction methods such as tepid sponging. The most common first step in the illness-seeking process for suspected malaria is to engage in self-treatment by giving febrile children western drugs stored at home or purchased from a local drug shop (Abuya et al., 2007; Littrell, 2011; Tobin-West & Babatunde, 2011).

Unfortunately, drug shops rarely offer diagnostic testing, and do not always stock the recommended first-line treatments for malaria. In Uganda the testing rates appear to be much lower than reported for the rest of the continent. It is estimated that only between 18% and 26% of children under five received a malaria test during their last fever episode (ACTwatch Group & PACE/Uganda, 2013; UBOS, 2012). Several studies report extremely high rates of self-treatment with close to 80% of suspected malaria cases being treated in local drug shops where both recommended and non-recommended antimalarials may be purchased over-the-counter (Mukanga et al., 2012; UBOS, 2010).

Self-treatment presents two challenges to malaria control. The first is that without a diagnostic confirmation, caretakers and health workers are forced to rely on presumptive treatment, which is based on the presence of fever. However, fever is indicative of many other common childhood illnesses such as pneumonia, diarrhea, and measles. Several studies estimate that only between 25% and 50% of children under five in Africa who present at healthcare facilities with fever are likely to have malaria (Gething, et al., 2010; Mazigo, Meza, Ambrose, Kidenya, & Kweka, 2011; Nankabirwa, et al., 2009). As a result, the reliance on presumptive treatment leads directly to high rates of overtreatment.

Presumptive treatment wastes expensive resources, exposes children to unnecessary side effects of the medication, and fails to identify the true illness, which

may result in severe illness. Widespread reliance on presumptive treatment has been suggested to lead to the development of drug resistance (Bloland, 2001; Wongsrichanalai, Pickard, Wernsdorfer, & Meshnick, 2002). Selective use of antimalarials may reduce overall drug pressure, and assist in the control of antimalarial resistance (Farooq & Mahajan, 2004). Furthermore, without the advice or guidance from a trained health worker, caretakers may not give the correct dose or complete the full regimen, which may lead to artemisinin resistance (Bloland, 2001).

The second challenge to malaria control produced by the over-utilization of self-treatment is the rate of inappropriate treatment outcomes. Through the Affordable Medicine Facility – malaria (AMFm) the cost of ACTs has been reduced significantly, increasing access to these life-saving drugs to the most vulnerable populations (Roll Back Malaria Partnership [RBM Partnership, 2008). Despite international treatment guidelines endorsing the use of ACTs, and increased access due to subsidized prices, many people throughout the African region continue to take non-ACT antimalarials that are ineffective. In many cases, more than half of all suspected malaria episodes are treated with a non-ACT antimalarial (Aborah, et al., 2013; Mangham, et al., 2011; Watsierah, Jura, Oyug, Abong'o, & Ouma 2010). Among children under five in Africa, the most vulnerable population, non-ACT antimalarials, namely chloroquine, quinine, and sulphadoxine/pyrimethamine (SP), are frequently the top choice (Buabeng, Duwiejua, Dodoo, Matowe, & Enlund 2007; Littrell, et al., 2011).

The Malaria Development Goals (MDGs) have prioritized improving child healthcare and reducing mortality rates. A significant focus has been placed on malaria, the most significant cause of childhood mortality. Over the past decade significant efforts

have been made in both the prevention and treatment of malaria that has greatly reduced malaria incidence rates, globally and in Africa. However, several immediate challenges pose threats to maintaining these positive trends, and realizing the MDG goals. First, international funding for malaria control is falling short of the estimated required amounts to reach international control goals. Secondly, current treatment-seeking patterns not only waste valuable resources, but also may speed up the development of artemisinin resistance in Africa.

Large sums of money have been dedicated to scaling up resources and services within healthcare systems. However, these services are wasted unless people access them. It is critical that efforts are made to increase consumer utilization of the healthcare system. In order to do this, more complex understandings of the consumer culture for malaria-related services and treatment is necessary. Therefore, this research aims to understand treatment-seeking patterns and outcomes for childhood malaria in Africa, and to identify the determinants that lead to high rates of self-treatment and inappropriate drug use. In addition, this research aims to assess how caretakers engage in treatment-seeking behaviors for younger and older children as most of the current literature focuses on children under five.

Study Aims

The overall aim of this research is to explore how to increase appropriate treatment-seeking behaviors and treatment outcomes for children under ten years of age with suspected malaria in Uganda.

Specific Study Aims:

1. To critically review the current scientific understanding of treatment-seeking patterns and determinants of behavior for suspected malaria in children in Africa.
2. To identify facilitators and barriers to seeking treatment for febrile children under ten years of age at various levels of the health care system in Uganda.
3. To identify determinants of appropriate treatment outcomes for suspected malaria in children under ten years of age.

Dissertation Overview

This dissertation is divided into six chapters that present the rationale for this research, the theoretical framework that guided this research, three individual manuscripts that address the three study aims above, and overall conclusions.

Chapter 1: Introduction. The first chapter presents a brief introduction into the rationale for this research including a summary of malaria trends, identification of the most salient challenges for malaria control, and the specific aims of this study

Chapter 2: Background and Theoretical Framework. Chapter 2 provides more in-depth background information about global and national trends in malaria, international guidelines, antimalarial resistance challenges, and concerns about current malaria treatment-seeking practices for children under five years of age. The theoretical framework that guides this research is outlined.

Chapter 3: Manuscript 1. The third chapter presents a comprehensive summary of peer-reviewed literature. The literature reviews focuses on the current level of malaria knowledge among caretakers of children under ten years of age, how treatment-seeking behavior affects treatment outcomes, treatment-seeking patterns for children with malaria, and predictors of treatment-seeking patterns.

Chapter 4: Manuscript 2. The fourth chapter addresses the second research question, and implements quantitative methods to explore potential predictors of treatment-seeking behaviors. Specifically, this chapter looks at how attitude and knowledge predictors affect treatment-seeking decisions at various levels of the healthcare system.

Chapter 5: Manuscript 3. The fifth chapter utilizes quantitative methods to address the third research question. Determinants of appropriate antimalarial outcomes are assessed and discussed.

Chapter 6: Conclusions. The sixth and final chapter summarizes the main finding of this dissertation and presents recommendations for future research.

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Chapter 2: Background And Theoretical Perspective

Malaria remains a significant global health concern that puts more than 3 billion people at risk each year. In 2012, there were an estimated 207 million cases of malaria world wide, and 627,000 deaths (WHO, 2013). There are more than 100 malaria-endemic countries globally, 97 of which are categorized as having ongoing malaria transmission (WHO, 2013). While these countries are spread across six WHO regions, the morbidity and mortality burden disproportionately affects the Africa Region, and an overwhelming majority of the disease burden is concentrated in sub-Saharan Africa. In 2012, about 80% of all cases world wide, and 90% of all deaths, occurred in Africa. The WHO has identified 10 high-burden countries, which account for 60% of all malaria deaths in Africa: Burkina Faso, Cameroon, Cote d'Ivoire, the Democratic Republic of the Congo, Ghana, Mozambique, Niger, Nigeria, Uganda, and Tanzania (WHO, 2013). These ten countries bear the majority of the global malaria impact.

Malaria is caused by *Plasmodium* parasites, and is spread through the bite of the female *Anopheles* mosquito. Five types of *Plasmodium* species affect humans including *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi*. The two most common species are *P. falciparum* and *P. vivax*, but *P. falciparum* is by far the greatest cause of malaria mortality. About 30-40 *Anopheles* species are capable of transmitting malaria to humans. The dominant vector species most commonly found in Africa, *An. gambiae* and *An. arabiensis*, have longer life spans and display higher rates of biting humans, which are some of the factors contributing to the high rates of malaria deaths in Africa (Sinka et al., 2010). In Africa, 98% of all malaria cases are caused by *P. falciparum*, and 93% of *P. falciparum* cases worldwide occur in sub-Saharan Africa (RBM Partnership, 2008).

In addition to causing high rates of morbidity and mortality, malaria impacts the economic growth in the countries most affected. Costs incurred by individual families include the purchase of treatment, transport expense to reach health facilities, absence from school, caretaker time lost due to traveling to health facilities and caring for sick children, and burial expenses. Government-incurred costs include providing treatment, diagnostics, and staff to health facilities as well as managing prevention interventions. These individual and national-level impacts contribute significantly to the ongoing cycle of poverty. Direct losses due to malaria illness are estimated to be \$12 billion each year in Africa alone (RBM Partnership, 2008).

Vulnerable Populations

Beyond geographical residence, children under five, pregnant women, and poor people are at an increased risk for developing severe malaria symptoms and death. Children are the most vulnerable to malaria; 77% of the deaths attributed to malaria worldwide occurred in children under five (WHO, 2013). Malaria is one of the leading causes of child deaths; every minute a child in Africa dies from malaria. In areas of high malaria transmission, people develop immunity over time, which reduces the risk of death from infection. However, young children have not developed immunity, and are at the highest risk of developing severe malaria symptoms and dying.

During pregnancy, women experience decreased immunity, thereby increasing their risk of developing severe malaria symptoms, putting both the mother and her unborn child at risk (WHO, 2014). Pregnant women without partial immunity to malaria are at an increased risk of having a miscarriage or dying (WHO, 2014). Malaria during

pregnancy increases the likelihood of the mother developing maternal anemia, which contributes to low birth weight and infant mortality (WHO, 2014). The malaria risks inherent with pregnancy not only endanger the mother, but also put young children further at risk by being born underweight.

Poorer people are more susceptible to malaria infection as well. Households in lower SES strata are more likely to get malaria as compared to households in highest SES stratum (Castillo-Riquelme, McIntyre & Barnes, 2008; WHO, 2013). One reason for this difference is that poorer people are more likely to live in rural areas where malaria infection rates are the highest (RBM Partnership, 2008). In addition, rural dwellings are constructed of simple materials, providing little or no protection at night, when *An. gambiae* mosquitoes are active. The lack of access to inexpensive and effective treatment is another significant driver of higher mortality rates among the poorer segment of the population. People living in the highest SES stratum are more likely to get antimalarials as compared to the people in the lower strata (Njau, et al., 2006). Poorer people are also more likely to buy antimalarials that are ineffective, and that may promote resistance (RBM Partnership, 2008). In order to reduce malaria morbidity and mortality, it is critical that programs and policies highlight the need to ensure necessary treatments reach the poor, especially children under five and pregnant women in the ten most affected countries in Africa.

Malaria Control Goals and Progress to Date

The Roll Back Malaria Partnership (RBM Partnership, 2008) was formed in 1998 with the intention of increasing international collaboration in fighting malaria. Utilizing

information and research from more than 65 international institutions and 250 experts, the RBM created the Global Malaria Action Plan (GMAP) - a comprehensive global strategy that lays the groundwork to first achieve malaria control, and then elimination (RBM Partnership, 2008). Current objectives aim to reduce the malaria burden by 2015. These goals include reducing global malaria cases by 75% (from 2000 levels), to reduce global malaria deaths to near zero, and to eliminate malaria in 10 new countries by 2015 (RBM Partnership, 2008). The final stage looks beyond 2015, and addresses maintaining near zero mortality rates, universal coverage, and achieving elimination in countries in the pre-elimination stage.

Significant progress has been achieved to date due to widespread interventions including indoor residual spraying, insecticide-treated bed net distribution, and increased access to rapid diagnostic tests (RDTs) for malaria and artemisinin-based combination therapies (ACTs). Overall, malaria-related mortality rates have dropped by 45% worldwide, by 49% in Africa, and by 54% among children under five in Africa (WHO, 2013). Although these rates are shy of reaching the goal to reduce deaths to near zero, it is important to note that the greatest improvements have been reported among the most vulnerable populations. It is estimated that more than 3 million lives were saved among children under five in Africa (WHO, 2013). Of the 103 countries worldwide with ongoing transmission in 2000, 59 have started to reverse the malaria incidence rates (WHO, 2013). Furthermore, 52 of these countries are on track to meet the targets of reducing malaria incidence rates by 75% (WHO, 2013).

Unfortunately, the trends are not as promising in the Africa Region. Only 8 of the 44 countries with ongoing transmission have achieved 75% reduction rates in malaria

incidence (WHO, 2013). An additional challenge is that there has been a decrease in international financial support in recent years (WHO, 2013). While global achievements in malaria control deserve recognition, efforts must be focused now in order to continue prevention efforts and to manage drug supplies in order to continue these positive trends that have been achieved and continue to decrease malaria mortality rates.

Malaria Trends in Uganda

Uganda has one of the highest malaria burdens in the world, and it is one of the leading causes of infant mortality in the country (WHO, 2013). Malaria is endemic throughout the year in 90-95% of the country, with *P. falciparum* accounting for all malaria cases (WHO, 2013). Ninety percent of the population experiences high malaria transmission year round, and the remaining 10% experiences low transmission (WHO, 2013). In Uganda, malaria accounts for between 30 and 50% of all outpatient care cases, between 15% and 20% of all admissions, and between 9 and 14% of inpatient deaths (UBOS, 2010). About 11 million cases of malaria are reported each year in Uganda (UBOS, 2010). However, between 60% and 80% of suspected malaria cases are treated in the informal sector, making the estimated number of actual cases to be as high as 60,000,000 per year (UBOS, 2010). In children under five years of age, malaria is the leading cause of mortality; between 70,000 and 100,000 children die each year in Uganda due to malaria (UBOS, 2010).

Access to Effective Treatment

Appropriate and effective treatment is essential to reducing malaria mortality rates. Currently, the WHO recommends artemisinin-based combinations therapy (ACT) as first-line treatment for uncomplicated *P. falciparum* malaria, and more than 85 countries have adopted this recommendation into their national policies (WHO, 2010). Since malaria was initially discovered, various drugs have been used for its treatment. Widespread resistance to most of these drugs has greatly reduced their efficacy; however, many are still commonly available for over-the-counter purchase in malaria endemic areas. The WHO has defined antimalarial drug resistance as “the ability of a parasite strain to survive and/or multiply despite the proper administration and absorption of an antimalarial drug in the dose normally recommended” (WHO, 2011). A brief overview of the most common antimalarials available is presented below.

Chloroquine was developed for the treatment of non-falciparum malaria. Chloroquine resistance independently emerged on the border of Thailand and Cambodia border as well as Columbia, and is now widespread throughout Southeast Asia, South America, and Africa (Wongsrichanalai, Pickard, Wernsdorfer, & Meshnick, 2002). Both Amodiaquine and Sulphadoxine-pyrimethamine (SP) were recommended for the treatment of non-severe malaria that was thought to be chloroquine resistant (Bloland). Resistance to SP was first seen along the Thailand-Cambodia border, and high-level resistance has been documented throughout Southeast Asia, southern China, the Amazon Basin, and Africa (Wongsrichanalai et al., 2002).

Mefloquine is used for the treatment of non-severe malaria thought to be chloroquine and SP-resistant. It is also used as a prophylaxis in areas where chloroquine-

resistance is high (Bloand). Quinine is the oldest drug used to treat malaria. It continues to be used for the treatment of severe malaria, and malaria during a woman's first trimester of pregnancy (Bloand). Resistance to quinine was first seen along the Thailand-Cambodia border, and has been reported in South America and Africa (Wongsrichanalai et al., 2002). Tetracycline and doxycycline are most commonly used as a prophylaxis, but may be used with quinine to increase its efficacy (Bloand).

Artemisinin-based combination therapies may include an artemisinin derivative combined with various other single agent antimalarial drugs. Artemisinin-resistance has been identified already in Cambodia and Thailand, but has yet to be seen in the Africa Region (Phyo et al., 2012). The WHO prioritizes artesunate (an artemisinin derivative) combined with amodiaquine, and artemether (an artemisinin derivative) combined with lumefantrine. Other recommended combinations include artesunate plus mefloquine, and artesunate plus sulfadoxine-pyrimethamine (WHO, 2010).

Unfortunately, the full cost of a single ACT dose is economically out-of-reach to many of the people who need them. Artemether Lumafantrine (AL), a fixed-dose ACT, has been the recommended first-line treatment for uncomplicated malaria in Uganda since 2004. Although AL is provided for free in government health centers, drugs are often unavailable due to stock outs and more than 80% of caretakers initiate treatment from a private facility (USAID, 2011). Within a few years of its roll-out, only half of private facilities had any first-line treatment, AL was sixty times more expensive than other treatment, and only 50% of patients were able to purchase a full dose (USAID, 2011). In 2009, ACT Watch reported ACT prices to range between \$2.27 and \$6.06 per dose in the private sector (Palafox et al., 2012). Recommended ACTs make up a small

percentage of antimalarials sold in the private sector when compared to other non-artemisinin based medicines, such as chloroquine, quinine, and SP that are much cheaper (Palafox et al., 2012). Subsequent research indicated that the price of the ACTs presented a significant barrier. A pilot project that greatly subsidized the cost of ACTs in Uganda resulted in an increase in the number of caretakers of children who were able to purchase and use these front-line, effective treatments (Talisuna et al., 2012). The findings of this study suggest that eliminating the cost barrier increases ACT-uptake in Uganda; however, the determinants of continued non-ACT use are not well known.

One of the more significant achievements undertaken by the international community in attempts to reach the RBM goals has been to increase access to life-saving drugs for everyone who needs them by eliminating the cost barrier. The Affordable Medicine Facility – malaria (AMFm) is a financing mechanism hosted by the Global Fund with the primary goal of increasing universal access to affordable ACTs in all sectors (RBM Partnership, 2008). Through the AMFm, the cost of ACTs has been drastically reduced, and the drugs widely distributed, increasing access for millions of people. Uganda, along with seven other countries, were included in the AMFm Phase I launched in 2009 (RBM Partnership, 2008).

Although increased access to appropriate treatment is necessary to meet malaria control goals and save lives, it raises new public health and policy concerns. ACTs have been made available for sale in informal health facilities, including local drug shops, which many people rely on as their first point of care. However, these informal facilities rarely have diagnostic capabilities or a professionally trained health worker available for consultation. As a result, patients and caretakers may purchase medicines without a

prescription, and often rely on presumptive treatment for malaria. Presumptive treatment leads to an excessive use of ACTs, which results in wasted resources, mistreatment of the true illness, and exposure to side effects from needless treatment. It is essential that international and national policies emphasize the need to closely monitor and support ACT prescribing and purchasing behaviors in order to balance the provision of life-saving drugs to people who need them, while preserving the integrity of these drugs.

Presumptive Treatment Concerns

In order to preserve limited resources and to ensure children receive appropriate treatment, diagnostic confirmation must become a priority. The main concern with clinical diagnosis for malaria is that it relies predominantly on the presence of fever, which has been shown to be a poor predictor of malaria in a variety of settings. Compiling national-level data from 41 African countries, Gething et al. (2010), estimate that less than half of children under-five with a history of fever who seek treatment from the public sector are likely to have malaria. Studies in Tanzania and Uganda have shown confirmed malaria rates in children who present at health facilities with fever to be as low as 12 – 25% (Mazigo, Meza, Ambrose, Kidenya, & Kweka, 2011; Nankabirwa, et al., 2009). While clinical diagnosis and presumptive treatment ensure that very few true cases of malaria are missed, it results in high rates of overtreatment, and a waste of limited resources. Furthermore, the true cause of illness has not been detected in children who have been falsely diagnosed with malaria, and remains untreated.

Malaria testing has become a key step in conserving ACTs. The WHO recommends that all suspected cases of malaria among all age groups receive a diagnostic

confirmation before prescribing an antimalarial, and that health professionals should rely on clinical diagnosis only when it is impossible to complete a blood test (WHO, 2010). Current behavior patterns in Africa indicate that a significant proportion of suspected malaria cases are self-treated at home or at informal health facilities where malaria diagnoses are rarely available (Abuya et al., 2007; Littrell, 2011; Tobin-West & Babatunde, 2011). Testing rates in Africa have increased in the last few years, but are the lowest in comparison to all the other WHO regions (WHO, 2013). In 2010, 37% of suspected cases in the public sector were blood-tested, and 61% of suspected cases were tested in 2012 (WHO, 2013).

There exist two immediate goals in order to reduce malaria morbidity and mortality, especially in children. First, children with malaria need access to ACTs, the recommended first-line drugs for the treatment of malaria. Second, in order to preserve the limited quantities of ACTs and to slow resistance to these drugs, diagnostic confirmation must be scaled up. The widespread reliance on the informal sector presents the biggest barrier to achieving these two goals. Caretakers frequently purchase antimalarials of their choice, and often without a blood confirmation. Significant portions of malaria funding have been dedicated to increasing the availability of both diagnostic tests and ACTs in the healthcare system. However, these resources are wasted if consumers do not access them.

Therefore, this research focuses on the demand-side of malaria management: the caretakers of children. As ACTs become more widely available, it is essential to monitor the uptake and appropriate usage of ACTs as well as caretaker understanding of the national recommendations. Malaria control goals include ensuring all children who need

antimalarials receive first-line treatment while preserving the supply of ACTs through increased diagnostic confirmation. In order to encourage malaria testing as a part of routine treatment-seeking behaviors for febrile illness and to increase appropriate treatment outcomes, it is critical to understand how caregivers understand malaria, blood confirmation, and the antimalarial treatments as well as the complex factors that facilitate and inhibit care-seeking behaviors.

Theoretical Perspective

The use of a theoretical framework provides a strategic plan for designing this dissertation research. The conceptual framework included in this dissertation illustrates the relationships among hypothesized factors that affect caregivers' decisions about seeking health care for suspected malaria in children. The decision to seek care, as well as the place where care is sought, is guided by numerous factors interacting on various levels. The proposed conceptual framework is based on the illness decision model that has been modified to include the theoretical concepts of attitudes and beliefs from the Theory of Reasoned Action (TRA), and the concept of outcome expectancy from Social Cognitive Theory (SCT).

Illness Treatment Decisions

The illness treatment decision model is a healthcare utilization model developed by James C. Young while completing ethnographic studies in a rural Mexican village (Young, 1980). This model assesses the various types of information people utilize to make treatment choices for various illnesses. It also looks beyond determinants of simply

seeking any care, and considers various types of traditional and modern treatment options. The benefit of this model is that it is ideal for understanding recurrent behavior patterns, and not engaging in a single behavior. As malaria is a common child illness in Uganda, previous experiences shape preferences and future behaviors.

The model identifies four conditions, or types of information, that influence treatment choices. Various combinations of these four conditions predict nine pathways of treatment-seeking behavior options. The predictability of the model depends on the recurrent nature of illness, and the fact that people establish patterns for various situations that are based on these four general conditions. The original model was developed to understand treatment-seeking decisions for illness in general. The model for this research has been modified to address treatment-seeking choices specifically for suspected malaria, a recurrent disease with behavioral patterns that can be mapped. The original four conditions are gravity, knowledge of a home remedy, “faith,” and accessibility.

This research utilizes this choice-making model, and includes measures of knowledge and attitudes to better understand how different types of factors affect treatment seeking on various levels. Beliefs and attitudes are individual-level theoretical constructs that assist in determining the likelihood of engaging in a particular behavior. Fishbein & Ajzen (1975) define attitudes as overall evaluations of how a person feels about an object, and are measured in terms of favoring and not favoring something. The modified conditions are explained here and presented in Figure 2.1.

Gravity includes the perceived severity of the individual illness as well as the locally understood seriousness of the disease in general. The explanatory variables associated with the first condition include perceived illness severity of the individual

malaria episode and perceived malaria prevalence in the community. The second condition is the ability to engage in a home treatment. For this condition to be applicable, the patient (or the caretaker of the patient) must be aware of a home treatment for the specific ailment, and the treatment must be available. Home treatment includes herbal remedies as well as drugs available for purchase in the village. In the modified model, this condition includes malaria-related knowledge variables.

The third condition is called “faith.” The third condition applies to the perceived efficacy of the available treatment options. For each illness, the patient or caretaker typically believes that either a traditional cure or a modern cure is more effective. Preferences largely depend on the individual, the specific illness, and previous experiences with the illness and various providers. In this adapted model, this condition is referred to as outcome expectancy, which is a psychological determinant of behavior from the Social Cognitive Theory (SCT). Outcome expectations are beliefs about the behavioral outcomes that will happen if the person engages in a certain behavior (Bandura, 1986). This condition focuses on the outcome expectancy that the child will get better based on the perceived quality of the services and treatments available from various healthcare facilities. The fourth condition is accessibility, and includes both the cost of the treatment (the services and/or the drugs), the location of various facilities, and transportation expenses.

Based on the possible combinations of the presence of these four conditions for each illness episode, nine possible pathways, or “rules,” are delineated for initial treatment-seeking behaviors in the original model. In the community where this research was conducted there were four treatment options: home treatment with herbs or locally

bought remedies, a local curer who relies on folk or herbal remedies, a *practicante* who is a local practitioner of modern medicine, or a physician practicing in either a private clinic or a government-run facility.

A non-serious illness with a known remedy results in home treatment. If there is not a known remedy and the patient believes modern treatment is the most efficacious for that illness, then they will seek treatment at a *practicante*. If the person believes local remedies are more efficacious, they will seek treatment at a curer. At the other end of the model, someone with a grave illness who believes traditional remedies are the most efficacious for that specific case will seek treatment at a curer. If someone believes modern medicine is the best possible option, and the health facilities are accessible, they will seek treatment from a physician.

The modified version presented here, includes various measureable factors within each condition that are hypothesized to affect behavioral outcomes. The healthcare facility options have been modified to mirror the healthcare system in Uganda.

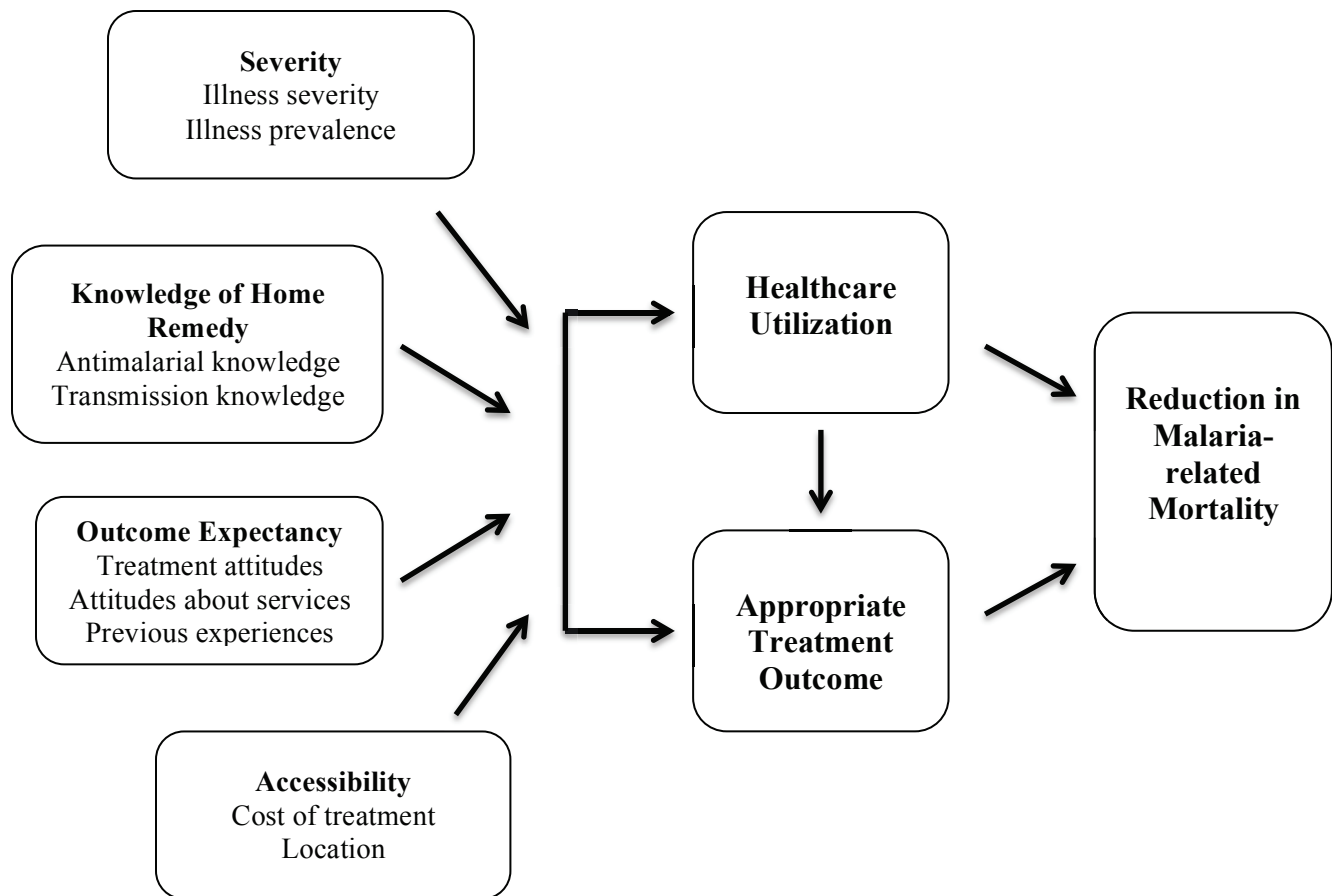
Rationale for Research

As access to recommended antimalarial treatments becomes a significant focus of malaria control, the timing of this research is essential in understanding both the patterns of ACT-uptake among caretakers of children as well as the determinants of non-ACT use. The results of this research will contribute to public health efforts to increase appropriate treatment-seeking behaviors among caretakers of young children. While basic patterns of treatment-seeking have been described in previous studies, this work will add significantly to the literature by providing a richer understanding of the drivers and

barriers to seeking appropriate health care services. These results will assist the Government of Uganda (GOU) and non-governmental organizations in understanding the barriers to ACT-use in order to effectively target caregivers who continue to use non-ACT treatments.

Understanding the barriers and facilitators to treatment-seeking is necessary to increase appropriate treatment outcomes, and reduce the malaria burden. With the results of this research, the malaria control community in Uganda will be able to design appropriate behavior change campaigns aimed at increasing consumer utilization of the healthcare system. Furthermore, the results may help guide the development of appropriate training for health care providers to take advantage of their role in local communities to increase knowledge about malaria testing and antimalarial efficacy. Finally, policy makers can use this information to develop policies to increase support in lower-level health centers and in the informal sector to scale-up malaria testing and treatment.

Figure 2.1: Conceptual Framework



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CHAPTER 3: MANUSCRIPT 1

Health-seeking behaviors for childhood malaria in Africa:

A review of the literature

Katrina Berg, MA

Johns Hopkins School of Public Health

Department of Health, Behavior and Society

Abstract

Background. The global malaria burden continues to disproportionately affect people living in Africa and children. Understanding the treatment-seeking process for suspected malaria is essential to the development of behavior change campaigns and policies that aim to reduce malaria-related morbidity and mortality. This review focuses on to what extent the current literature addresses malaria knowledge among caretakers of children under ten years of age, the overall treatment-seeking patterns for febrile children, how seeking care at different types of health facilities affect appropriate treatment outcomes, and the determinants of seeking care at a various levels of the health care system.

Methods. Systematic methods were employed to identify peer-reviewed articles that focused on treatment-seeking patterns for fever or malaria in children between the years 2003 and 2013.

Results. Awareness of malaria and fever as the main symptom was high. Caretakers often initiated self-treatment for suspected malaria, and relied on formal healthcare facilities as the second point of care. Children whose caretakers engaged in self-treatment were more likely to receive inappropriate treatment. Socio-demographic variables, structural barriers, perceived illness severity, local illness concepts, and perceived quality of service were all identified as predictors of seeking care in the formal sector.

Conclusion. The current understanding of treatment-seeking behavior is limited to mostly access, perceived severity, and socio-demographic predictors. Few studies assess determinants at more than two levels of the healthcare system. More research is needed to understand how knowledge and malaria affect treatment-seeking decisions.

Background

Although both the number of cases and deaths due to malaria have decreased since 2000, malaria continues to pose a significant health burden globally. In 2012, there were an estimated 207 million cases of malaria, and 627,000 malaria-related deaths worldwide (WHO, 2013). Malaria disproportionately affects those living in the Africa region and young children. An estimated 80% of all malaria cases worldwide and 90% of the deaths due to malaria occurred in Africa (WHO, 2013). Approximately 77% of all malaria deaths occurred among children under five years of age (WHO, 2013).

In response to these high morbidity and mortality rates, the international health community has proposed aggressive malaria control goals for 2015. The Millennium Development Goals, developed through the United Nations, aim to reduce the mortality rate among children by two-thirds and to reverse malaria incidence rates (WHO, 2011). The Roll Back Malaria Partnership's main objectives are to reduce malaria deaths to near zero, to reduce malaria incidence by three-quarters, and to eliminate malaria in ten countries by 2015 (RBM Partnership, 2008). Despite recognized achievements over the past decade, including vast distribution of insecticide-treated nets (ITNs), increased availability of first-line malaria treatment, and a reduction in reported malaria cases and deaths, these targets remain a challenge to achieve by 2015.

The World Health Organization (WHO) currently recommends artemisinin-based combination therapy (ACT) as first-line treatment for uncomplicated *P. falciparum* malaria, which accounts for 98% of all malaria cases in Africa (WHO, 2013). However poorer people frequently buy antimalarials that are ineffective, and that may promote resistance (RBM Partnership, 2008). The Affordable Medicine Facility – malaria

(AMFm) is a financing mechanism hosted by the Global Fund with the primary goal to increase universal access to affordable ACTs in all sectors (RBM Partnership, 2008).

Although increased access to appropriate treatment is necessary to meet the malaria control goals, it presents two challenges. The first is to make sure all children with malaria receive the appropriate treatment within 24-48 hours of symptom onset.

Consumers have become accustomed to the previously recommended treatments, and widespread use of ACTs is not currently the norm in all endemic countries.

The second, and probably more difficult, challenge is to decrease presumptive treatment with ACTs. Presumptive treatment occurs when ACTs are given to a child based on the presence of symptoms, and without confirmation of parasite presence. Presumptive treatment may occur at all levels of the healthcare system, but is most common within the informal sector, which includes self-treatment at home or at a local drug shop. At home, caretakers typically diagnose their children based on the presence of fever, and self-treat with medicines stored in the house. In local drug shops, caretakers purchase any available drug of their choice without a prescription. Presumptive treatment may also occur at local health facilities when diagnostic capabilities are not available, but there is a professional health worker present to make a more informed diagnosis. It is important that children with malaria receive the recommended first-line drugs for uncomplicated malaria, but it is also necessary to limit the use of these drugs to confirmed malaria cases whenever possible.

Fever Prevalence in Children Under Five

Fever is a regular occurrence among children under five throughout Africa. Many of the studies included in this literature review measured a two-week period prevalence for fever in children under five. In areas of low malaria transmission, period prevalence fever rates for children under five ranged between 12% and 23% (Guyatt & Snow 2004; Elmardi et al., 2011). However, in areas with at least moderate malaria transmission, the fever period prevalence rates were much higher, and ranged between 21% and 63% (Abuya et al., 2007; Deressa, Ali, & Berhane 2007; Mbonye, Bygbjerg, & Magnussen, 2008; Mota, Lara, Kunkwenzu, & Lalloo, 2009; Tobin-West & Babatunde, 2011). At least a fifth of the households interviewed reported a child under five with fever in just the previous fourteen days, although in some areas, more than half the children experienced fever symptoms in the previous two weeks. These results indicate that many caretakers of young children in moderate to high transmission areas care for a child with fever on a regular basis.

Although fever is commonly associated with malaria, fever has been shown to be a poor predictor of malaria in a variety of settings. Less than a quarter of children in Uganda presenting at health facilities with fever or history of fever had malaria (Nankabirwa, et al., 2009). In Tanzania, only 12% of children under five with fever or history of fever had a positive blood slide for malaria (Mazigo, Meza, Ambrose, Kidenya, & Kweka, 2011). Fever is indicative of many other common childhood illnesses such as pneumonia, diarrhea, and measles. Although symptoms vary for childhood diseases, clinical diagnosis based on symptoms alone presents significant challenges.

When considering how often children under five years of age in many African countries have fever, and how frequently the fever may be the result of a non-malarial illness, it is clear how presumptive treatment for malaria may result in a significant number of children who are over treated. In addition to wasting limited resources, presumptive treatment unnecessarily exposes young children to harmful side effects of the ACTs. Furthermore, the true illness remains unknown and untreated, putting the sick child at risk for the development of a more serious condition. For the reasons discussed here, the WHO recommends that all children under five who present with fever should be tested for malaria whenever possible before providing antimalarials (WHO, 2010).

Testing rates in public facilities have increased dramatically in just a short period of time, from 37% in 2010 to 61% in 2012 (WHO, 2013). However, these testing rates are from formal facilities, and do not include all the cases that go untested in informal facilities. In order to improve diagnostic confirmation for all suspected malaria cases, and therefore, increase appropriate treatment, it is necessary to encourage caretakers to seek care at higher levels of the health care system where accurate diagnostic tests and appropriate treatment are available.

The first step in shifting the typical treatment-seeking patterns is to understand how caretakers perceive febrile and malaria illness and how they select treatment, to map out illness resolution patterns, and to identify which determinants are the most salient in guiding their treatment-seeking choices. This will illuminate what is currently known about treatment-seeking behavior for suspected, uncomplicated malaria. Once behavioral patterns and determinants are outlined, it will be possible to identify specific subpopulations to target interventions. Furthermore, gaps in understanding about

treatment seeking can be identified to guide additional research that will improve already targeted interventions.

Research Aims

The aim of this systematic literature review is to describe the current scientific understanding of treatment-seeking patterns among caretakers of febrile children younger than ten years of age in Africa. More specifically, this literature review addresses what has been studied, and what is already well understood about the following questions: 1) What is the current level of malaria knowledge among caretakers of children under ten years of age? 2) What are the overall treatment-seeking patterns for febrile children under ten years of age? 3) How does seeking care at different types of health facilities affect appropriate treatment according to international guidelines? 4) What are the determinants of seeking care at a various levels of the health care system?

Methods

Search Strategy

Systematic methods were employed to identify peer-reviewed articles that focused on treatment-seeking patterns for fever or malaria in children. PubMed, Scopus, PsychInfo, and Embase databases were searched for articles published in English in the last 10 years, between 2003 and 2012. An additional search was conducted to update the literature to include articles published in 2013. Additional search requirements included studies that were conducted in an African country, that focused on children under ten years of age, and that included one of the three main search concepts.

Database Search Criteria

A Public Health Informationist was consulted in the development of the search concepts for this literature review. Databases were searched according to a list of terms that focused on three main concepts. Each concept was an individual theme that focused on different aspects of the treatment seeking for suspected malaria process. These themes included the illness itself, the behavior of interest, and the outcome of the behavior. The search terms included within each theme, as well as the development of each theme, are described below.

The first theme identified the most general topic of the literature review: the health issue itself, malaria. This theme was defined before initiating the search, and search terms related to this concept included, “malaria”, “fever,” and “febrile illness.”

The second theme focused on the treatment-seeking behavior or patterns of seeking care for suspected malaria or fever. Key words were included that would recover articles that focused on any part of the illness resolution process such as self-treatment and testing. Words that described the overall process such as management and illness resolution were also included. Verbs that described the main behavior such as treatment-seeking, practice, and choice were added to the list of search terms. These initial terms were selected in order to address the study questions. During the initial stages of the literature review, additional key terms were added to the development of this theme. The final list of search terms related to the second theme included “treatment-seeking,” “health-seeking,” “information,” “knowledge, attitude, practice,” “health,” “care,” “testing,” “management,” “home management,” “home-based management,” “perception(s),” “diagnosis,” “presumptive diagnosis,” “self-treatment,” “seek,”

“seeking,” “practice,” “prevention,” “behavior,” “pattern(s),” “resolution,” “choice(s),” and “strategies.”

The third concept focused on the intended outcome of the treatment-seeking process: the acquisition of drugs for the treatment of malaria. These drugs include western medicines that are either purchased over-the-counter or provided from a health facility. This theme was defined based on the study questions, and according to the background research on antimalarial utilization and recommendations. Search terms related to the third concept included both general and specific medicines known to treat malaria: “drug(s),” “antimalarials,” “ACT,” “artemisinin,” “artemisinin-based therapy,” and “artemisinin combination therapy.” Terms that describe drugs and treatments used to treat other childhood illnesses were excluded in order to limit the literature to malaria-specific treatment-seeking behaviors.

Article Evaluation

The selected articles were read thoroughly, summarized, and analyzed for specific topics. First, each article was read briefly and summarized according to basic research categories for ease of future reference. A spreadsheet was maintained that listed each article’s title, authors, methods, country of study, sample population, purpose, validity, and overall findings.

Next, the articles were read in greater detail to analyze the results and findings in order to address the proposed study questions. During this step, articles were read for four specific themes: malaria knowledge, treatment-seeking behaviors, treatment outcomes, and determinants of place of treatment-seeking initiation. The database was expanded to

indicate whether or not each theme was discussed, and to describe the results. Within each theme, sub-themes were generated and described based on the findings within each theme. Within the malaria knowledge theme, sub-themes included type of malaria knowledge measured as well as general knowledge results. Examples of malaria knowledge sub-themes include malaria awareness, symptom knowledge, and knowledge of cause of malaria.

The second theme focused on the treatment-seeking process. Sub-themes that emerged included the number of places the caretaker sought care during the illness resolution, the place that care was initiated, the sequence of places where caretakers sought care, the treatment obtained, whether the child was blood-tested for malaria, test type, and wait times to initiate treatment. Many sub-themes were identified in the first stage of the analysis, although several sub-themes emerged during the thorough reading of the articles. These additional themes were included, and previously read articles were re-read to look for the newly defined sub-themes.

The third theme included treatment outcomes. The following sub-themes were recorded: types of antimalarials taken and association between place of treatment-seeking initiation and outcome. The final theme focused on determinants of the first place the caretaker sought care. This theme was divided into two sub-themes: 1) comparing caretakers who engaged in home-treatment compared to caretakers who sought any type of care and 2) comparing caretakers who initiated treatment at various levels of the healthcare system, including the home, drug shops, public health centers, and private clinics. Within both sub-themes, all identified determinants associated with place of

initial treatment were recorded. Examples of determinants include local illness concepts, SES, child's gender, and location.

Results

Article Selection

Initial search results yielded 126 articles. The abstracts were read for inclusion into the final sample to be reviewed. Articles were excluded if they were outside Africa, did not focus on children under ten, focused on other non-malarial childhood diseases, focused the analysis to a single stage in the treatment-seeking process or restricted the sample to children who had completed specific treatments. Other literature reviews were also excluded. Upon completion of this process, 46 articles were selected for in-depth analysis and inclusion in this literature review.

Of the 46 articles included in the final analysis, 35 discussed treatment-seeking patterns, while only 29 included information about determinants of treatment seeking. Seven of the articles were qualitative studies, 30 were quantitative studies, and 9 of the articles relied on mixed methods. Fourteen African countries were represented among all the articles.

Caretaker Knowledge about Malaria

Among the reviewed articles, malaria knowledge was addressed in various ways. Many of the qualitative articles included a discussion about how caretakers understand the terms malaria and fever. Local concepts and vocabulary often refer to specific sets of symptoms. In Ghana, malaria is often defined as paleness or weight loss, while fever

refers to a child exhibiting signs of weakness or loss of appetite (Ahorlu, Koram, Ahorlu, de Savigny, & Weiss, 2006). In Burkina Faso, *sumaya* most closely resembles uncomplicated malaria and is described as fever, weakness, loss of appetite, and vomiting (Beiersmann et al., 2007). *Knono* is a local word used to describe a person with convulsions or who is in a coma, and most closely represents severe malaria (Beiersmann et al., 2007). In some communities malaria is defined in various ways based on a scale of severity. In Tanzania, *malaria ya kawaida* is mild malaria, *malaria kali* is severe malaria, and *degedege* is a condition based on the presence of convulsions.

When measuring malaria knowledge, quantitative studies focused on two main themes: the recognition of fever as a primary symptom, and the cause of malaria. In general, caretaker awareness of malaria and knowledge that fever is a primary symptom of malaria is quite high. Between 75% and 91% of caretakers assume febrile illness to indicate malaria (Ndo, Menze-Djantio, & Antonio-Nkondjio, 2011; Okeke & Okeibunor, 2010; Watsierah et al., 2011). Through focus group discussions, caretakers indicated that either “fever” or “hot body” means that a child has malaria (Chibwana, Mathanga, Chinkhumba, & Campbell, 2009). In some cases, malaria is defined in local language simply as fever, or fever with other symptoms such as a headache or restlessness (Malik, Hanafi, Ali, Ahmed, & Mohamed, 2006). When a child has fever, caretakers most often assume it is the result of malaria, and initiate treatment based on this.

These results indicate high rates of recognizing fever as the main symptom of malaria, but they do not accurately reflect caretaker knowledge of fever. What is unknown from these studies is whether or not caretakers are aware that fever is a symptom of other common childhood illnesses. It is important that caretakers quickly

recognize malaria symptoms, but assuming all fevers are malaria leads to presumptive treatment. Understanding that fever is a symptom of various childhood illnesses may affect where caretakers seek initial treatment, and may discourage caretakers from self-treating with antimalarials.

Knowledge about the cause of malaria is more variable. In some areas malaria knowledge is quite high. Between 63% and 86% of mothers and caretakers were able to state that the main cause of malaria is mosquitoes (Deressa, Ali, & Hailemariam, 2008; Ndo et al., 2011; Nsungwa-Sabiiti, Tomson, Pariyo, Ogwal-Okeng, & Peterson, 2005; Tobin-West & Babatunde, 2011). In other cases, mothers correctly identify mosquitoes as a cause of malaria, but they are not aware that they are the *only* cause, and they identify incorrect causes of malaria in addition to mosquitoes. For example, caretakers in Ghana most commonly reported both mosquitoes and heat from the sun as the main causes of malaria (Ahorlu et al., 2006). The misunderstanding that heat from the sun causes malaria may be due to the fact that a fever or hot body are often used to indicate malaria.

However, several studies indicate that some caretakers have overall poor knowledge of the cause of malaria. In Ethiopia, only a third of mothers were aware that mosquitoes transmit malaria (Hwang et al., 2010). In Nigeria, almost three-quarters of caretakers named strenuous work (Idowu, Mafiana, Luwoye, & Adehanloye, 2008) and exposure to the sun (Falade, 2005) as the main cause of malaria, but very few named mosquitoes.

Understanding fever as a primary symptom of malaria appears to be quite high throughout Africa. However, there is a gap in the reviewed literature about fever knowledge, and whether caretakers understand the various types of illnesses that may

cause fever in addition to malaria. Overall, the knowledge that mosquitoes transmit malaria is high in many places. However, other factors continue to be falsely blamed for causing malaria in some areas such as hot or cold conditions, hard work, and unsanitary conditions. How these differences in malaria knowledge affect treatment seeking will be explored further in this literature review.

Treatment-seeking Patterns for Febrile Children Under Ten

Treatment-seeking patterns for fever and malaria have been well researched throughout Africa. When a child has a fever or is suspected to have malaria, there are several treatment options including doing nothing, managing the fever with tepid sponging, visiting an indigenous healer, treating at home with herbal remedies or with biomedical drugs, purchasing biomedical drugs at a local store, seeking specialized advice from a private clinic or public health facility, or engaging in a combination of these activities.

Health systems can be divided into sectors based on various categories such as formal versus informal/community-level or public versus private. Although variations exist in some countries, for the purpose of this literature review, the following classifications are employed (see Table 3.1). Formal sector facilities provide higher quality and more diverse services such as diagnostic testing and typically involve consultations with a trained health professional. The formal sector may include public health centers, public hospitals, private clinics and pharmacies. The providers in the formal sector have been trained and follow government-supported guidelines for testing and prescription purposes. The informal/community-level sector includes community

health workers (CHWs), drug shops or patent medicine vendors, family members or neighbors, and traditional healers. Although CHWs are typically part of the free government-run health system, they are often community volunteers with limited ability to diagnose illness or provide treatment. In some cases, CHWs have been trained to use RDTs and provide ACTs (Yeboah-Antwi et al., 2010). However, most CHWs are able to dispense simple medicines, and are not trained to distinguish among various types of illnesses. Informal/community-level facilities do not require a prescription or examination by a health professional, and typically do not offer diagnostic testing for malaria. Not all formal sector facilities offer malaria testing, such as lower level health centers, but many of the higher-level facilities have the capacity to conduct blood tests.

Both private and public facilities exist in both the formal and informal/community-level sectors. The private sector includes facilities or services that are run by individuals or organizations for financial gain. Pharmacies, local drug shops, medicine vendors, and private clinics are all part of the private sector as they do not provide free health services and prices are determined by the shop owners. Public sector facilities provide free services, and typically are managed by the government. These include health posts, CHWs, health centers, and government-run hospitals.

Caretaker action. When a child has fever, most mothers engage in some type of behavior, whether it is to relieve symptoms or to provide curative medicine, as compared to doing nothing at all. Studies from areas of year-round high malaria transmission or peak seasonal transmission report action rates between 79% and 99% (Deressa, 2007; Mbonye et al., 2008; Tobin-West & Babatunde, 2011; Uzochukwu, Onwujekwe, Onoka, & Ughasoro, 2008). Reasons caretakers do not engage in any type of curative care

include perceived mild illness, cost of care, distance from a health facility (Deressa, 2007), rural residence, and having no formal education (Kazembe, Appleton, & Kleinschmidt, 2007). It appears that reported action rates tend to drop in areas of low transmission. In an area of low transmission in Sudan, only 44% of mothers took some action for their febrile child (Elmardi et al., 2011). Less than 20% of children under five had reported a fever in the previous two weeks, and the measured malaria period prevalence rate was less than 2% (Elmardi et al., 2011). It is possible that in low transmission areas caretakers do not assume fever to be malaria or do not perceive malaria as a serious threat, as it is not a common illness, and therefore do not engage in immediate curative care. Fever may be more indicative of other illnesses that are typically treated at home.

Overall, very few fevers go completely untreated. Most caretakers recognize malaria symptoms, and engage in some form of curative care. However, these rates do not provide any information on whether or not the action taken was appropriate or successful.

Treatment-seeking patterns. Treatment seeking patterns have been well researched and documented in the literature. Most of the articles analyzed addressed some aspect of treatment seeking pathways including reporting actual first places accessed or describing caretakers' preferred steps in the illness resolution process. While treatment-seeking patterns vary from country to country, and even region-to-region, a clear preference for self-treatment when fever symptoms appear in a child emerges as the predominant first step. Self-treatment occurs when caretakers treat fever symptoms at home without the guidance or recommendation from a health professional with the

intention of relieving symptoms or treating malaria with western drugs. Actions based on guidance and recommendations from non-health professionals such as neighbors and other family members are considered self-treatment practices. Parents may use local herbs, engage in tepid sponging, give medicine stored at home, or purchase medicine from a drug shop, mobile vendor, or market stall without a prescription.

Studies conducted in high transmission areas indicate that caretakers' first response is to engage in self-treatment in Kenya (Abuya et al., 2007), Malawi (Holtz et al., 2003), Uganda (Nsungwa-Sabiiti et al., 2005), Nigeria (Uzochukwu et al., 2008), Democratic Republic of the Congo, Madagascar, and Benin (Littrell, 2011). Although rates of self-treatment vary in each country, it appears that close to half or more of all suspected malaria cases are first treated at home. Many studies indicate that between 47% and 65% of caretakers engage in self-treatment first (Guyatt & Snow, 2004; Mbonye et al., 2008; Mota et al., 2009; Okeke & Okeibunor, 2010; Rutebemberwa et al., 2009b). Several studies indicated that self-treatment is much higher in some areas with about three-quarters of febrile illnesses treated at home initially (Müller, Traoré, Becher, & Kouyaté, 2003; Nonvignon et al., 2010).

It is important to note that initiating treatment for suspected malaria or febrile illness in a formal healthcare facility is the preferred first choice in some countries, but this pattern is not common. In Ethiopia, where rates of seeking any care for febrile children are high, it appears that home management of fever is almost non-existent. Three quarters of rural mothers with a febrile child sought care from a public health center or private clinic first rather than engaging in self-treatment at home or from a local drug vendor (Deressa et al., 2007). In Sudan, more than 70% of caretakers with febrile

children who sought treatment went to a government facility first, and the use of drugs shops is not common (Elmardi et al., 2011). What is not clear from these studies is how common or convenient drug shops are in these areas. Formal health facilities may be the only place to access any treatment.

Treatment-seeking patterns indicate that illness resolution for malaria may require multiple steps, actions or treatments. The number of places that caretakers visit during this process varies within a wide range. Between 13% and 56% of caretakers visit at least 2 different types of health facilities before the child's illness is resolved (Deressa, 2007; Guyatt & Snow, 2004; Littrell, 2011; Simba et al., 2010). Caretakers typically initiate self-treatment, and then seek care at a higher-level facility if the illness persists. In Kenya, although more than 80% of children who took a medicine from home did not engage in any further action, those who engaged in a second treatment action went to a formal healthcare facility (Abuya et al., 2007).

Facility-based studies focus on patients who did seek care at a formal healthcare facility at some point during the illness resolution process. As these studies enrolled participants at the health facilities, it is not possible to determine what percentage of febrile children sought care at all or to describe initial treatment preferences. However, these studies indicate that caretakers typically use formal facilities as the second point of care. Between 80% and 100% of children in Nigeria had received some type of treatment before reaching the facility, and of those who took action, more than 80% of caretakers treated their child at home or with over-the-counter drugs (Emeka, 2005; Olaogun, Ayandiran, Olasode, Adebayo, & Omokhodion, 2005). This pattern suggests that

caretakers prefer to engage in self-treatment, and rely on the use of formal healthcare facilities as the second point of care.

Caretaker explanations of their treatment-seeking preferences match the patterns seen in the quantitative studies. Home treatment is seen as a type of first-aid for commonly experienced symptoms, such as fever. In Malawi and Tanzania, mothers prefer to first treat their febrile child with antipyretics, and further manage the fever with tepid sponging, and then seek antimalarials if the fever persists (Chibwana et al., 2009; Kamat & Nyato, 2006). Similarly, in Nigeria, malaria is not considered life threatening, and mothers seek care at higher-level facilities when self-treatment fails (Falade et al., 2005; Idowu et al., 2008). This trial and error process acts as a home-based diagnosis. If the fever continues after the application of home-based fever reduction methods, then the caretaker presumes their child has a more severe case of malaria and seeks treatment in the formal sector.

Not all treatment-seeking processes are as linear as the pattern described here. Two studies discussed patterns of seeking traditional care if modern treatment fails. Although not as common, some caretakers would initiate self-treatment with biomedical drugs for suspected malaria, and then seek treatment from a local healer if that fails (Makundi, Malebo, Mhame, Kitua, & Warsame, 2006; Nsungwa-Sabiiti et al., 2004). Caretakers may go back and forth between traditional and modern remedies until the child recovers (Makundi et al., 2006; Nsungwa-Sabiiti et al. 2004).

Overall, the most common illness resolution pattern is to engage in self-treatment, using tepid sponging, and/or drugs stored at home or purchased over-the-counter. This step is intended to alleviate the symptoms and cure mild illness. If this step fails, and

symptoms persist, caretakers then seek care at a formal health facility. The following sections discuss how the place where children initiate care may affect the treatment received, and how caretakers decide where to initiate treatment.

How Choice of Health Care Affects Treatment Outcomes

It is recommended that febrile children are tested and treated appropriately with ACTs within 24 - 48 hours on symptom onset (WHO, 2010). As seen in the literature caretakers prefer to treat their child at home, and then seek care in a formal facility if the illness persists. Where caretakers initiate care affects not only the timeliness of treatment seeking, but the treatment outcomes. Several studies assessed how place of initial treatment affect the timeliness of seeking care. Caretakers who rely on providing home-stocked drugs or purchasing drugs from a local shop as the first step, are more likely to seek care within 24 or 48 hours as compared to those who initiate treatment in the formal sector (Deressa, 2007; Holtz et al., 2003; Nsungwa-Sabiiti, et al., 2005; Rutebemberwa, Kallander, Tomson, Peterson, & Pariyo 2009a, Smith et al., 2010). This is most likely due to the convenience of using home-stored drugs or going to a drug shop, which is more common in rural areas.

However, the type of place where caretakers initiate treatment affects the quality of the treatment the child receives. While relying on self-treatment is easier and more accessible, it is not typically effective if the child actually has malaria. Caretakers who seek treatment in the informal sector often receive inappropriate treatment. Even though the WHO advises that all cases of fever are blood tested for malaria before prescribing or taking an ACT, clinical diagnosis and presumptive treatment are still recommended if

testing is not available (WHO, 2010). In most cases in the informal sector, it is not possible to do a blood test, and therefore, presumptive treatment with ACTs would be recommended for suspected malaria. However, when caretakers seek treatment from a drug shop, they often receive an antipyretic to reduce the fever, not an antimalarial (Abuya et al., 2007; Guyatt & Snow, 2004). Children are more likely to receive the recommended first-line treatment if they seek care in the formal sector as compared to the informal sector (Holtz et al., 2003; Simba et al., 2010). In Malawi, less than 25% of children who initiated treatment in the informal sector received an antimalarial compared to more than 90% of children who sought treatment in the formal sector (Mota et al., 2009). When adequately stocked, formal health care facilities are more likely to carry the recommended first-line treatment. Although drug shops maintain regular stocks of supplies, they do not always have the recommended antimalarial treatment, and often provide antipyretics. Oftentimes, ACTs are more expensive than non-ACTs in drug shops, whereas they are typically free-of-charge at most public facilities. Caretakers who give ineffective treatments to their children risk more severe consequences.

Determinants of Seeking Treatment at Various Levels of the Healthcare System

In addition to understanding basic treatment-seeking patterns and preferences, the determinants of selecting certain health care facilities as the first point of care for childhood febrile illness have been studied throughout Africa. The reviewed articles discussed determinants on various levels. Three of the reviewed articles focused on determinants of seeking *any* care outside of the household, including both drug shops and formal healthcare facilities. Fifteen of the articles focused specifically on determinants of

seeking formal care versus informal care or self-treatment. Six of the articles considered various levels of the healthcare system, and discussed determinants of seeking home-treatment, over-the-counter treatment, or formal healthcare. Three studies concentrated on seeking traditional care versus modern care. Finally, two articles assessed seeking care in the private sector versus the public sector. First, the determinants of seeking any care outside the household are summarized. Then the next section discusses preferences and determinants of seeking care at various levels of the healthcare system, focusing predominantly on barriers and facilitators of seeking care immediately in the formal sector.

Seeking any care. Two of the three articles that focused on seeking any care discussed determinants of seeking care outside the household, and one discussed determinants of delaying seeking any care outside the household. In these studies, seeking any care includes going to a drug shop, medicine vendor, formal healthcare facility as compared to caretakers who engage in home-treatment by using drugs already stored in the house, herbal remedies or engaging in tepid sponging.

Caretakers in higher socioeconomic status strata (SES) were more likely to initiate treatment outside the home than engage in home-treatment (Hwang et al., 2010; Smith et al., 2010). Mothers having attended any level of school and living in an urban area were also associated with seeking care outside the house, while owning at least one insecticide-treated mosquito net (ITN) was associated with home-treatment (Hwang et al., 2010). Only one study assessed factors beyond socio-demographic variables, and looked at various knowledge variables. However, having any malaria knowledge, either knowing the causes, symptoms, or preventive measures, was not associated with seeking

care outside the home (Hwang et al., 2010). Children from lower SES strata, with less severe symptoms, and whose caretakers perceived the distance to a health facility was far were more likely to delay seeking care outside the household (Rutebemberwa et al., 2009a).

These studies suggest that household wealth and access are the strongest predictors of seeking any care outside the household for febrile illness. Other factors include perceived illness severity and mother's education. The association between ITN ownership and home-treatment may appear unusual as caretakers who engage in preventive measures may be thought to be more likely to seek timely, appropriate care. However, it may be possible that caretakers perceive their malaria risk to be lower because they use ITNs. It is important to highlight that few studies assessed seeking any care, and they focused predominantly on socio-demographic predictors.

Seeking care at various levels of the healthcare system. As presented in the description of treatment-seeking patterns, caretakers throughout Africa initially rely on self-management of fever, which typically occurs in the informal sector. Most of the literature assesses the determinants of seeking care in the formal sector versus the informal sector. Based on the literature reviewed, determinants of formal care-seeking behavior include local illness concepts, socio-demographic characteristics, structural barriers, illness severity, and perceptions of quality of services.

Local illness concepts. Local illness concepts often distinguish between types or levels of malaria based on the level of symptom severity or perceived cause. Some symptoms or causes of illness are commonly thought to be the result of local religious beliefs including witchcraft or evil spirits, and therefore require local or traditional cures.

For example, witchcraft in children often presents itself in the form of fever requiring traditional cures, and it is believed that the use of modern medicine may cause death (Chibwana et al., 2009; Nanyonjo et al., 2012). As previously discussed, convulsions prompt immediate treatment in the formal sector in some places, but they are thought to be caused by evil spirits in many parts of Tanzania, and require treatment by a traditional healer (Makundi et al., 2006).

Local terminologies also categorize febrile illness and malaria into levels based on perceived causes and illness severity. Terms that equate to the biomedical term uncomplicated malaria, are often seen as the result of natural causes, which can be treated by the caretaker with either traditional or modern medicine. For example, in Burkina Faso, *sumaya* means ordinary malaria, is caused by natural causes such as climate or food, and is treated by traditional or modern medicine from home (Beiersmann et al., 2007). Similarly, in Ghana, ordinary malaria is thought to be caused by mosquitoes or exposure to heat, and should be treated at home with local herbs or biomedical drugs (Ahorlu et al., 2006). In these cases, treatments may need to be purchased from drug shops, but caretakers view this less severe type of malaria as non-threatening, and easily managed without seeking assistance at higher-level facilities. However, some fevers are thought to be caused by worms or houseflies, and are considered much more serious, therefore requiring treatment from a formal health facility (Ahorlu et al., 2006). The cause and categorization of febrile illness according to local concepts helps identify the preferred treatment type, which in turns determines where caretakers seek care.

Socio-demographic characteristics. Socioeconomic status (SES) is an indicator used to measure and compare overall household wealth, and is one of the most significant

factors associated with seeking care. It has already been shown that higher SES is associated with seeking any care outside the house. In addition, households of higher SES strata access the formal sector as the first point of care more than households of lower SES strata when their child has fever (Nonvignon et al., 2010; Onwujekwe, Hanson, & Uzochukwu, 2011; Simba et al., 2010; Smith et al., 2010).

Gender of the sick child also has been associated with treatment-seeking behaviors in two of the reviewed studies. Caretakers of boys are more likely than caretakers of girls to initiate treatment at formal healthcare facilities (Diallo, Dos Santos, Lalou, & Le Hesran, 2012). Smith et al. (2010) found that girls were more likely to seek treatment at informal community-based facilities, while boys were more likely to utilize formal facilities further from the household.

Children under five years of age were more likely to attend a formal facility than children between 5 and 10 years of age (Diallo et al., 2012; Ewing et al., 2011; Smith et al., 2010). As they have not developed any immunity to malaria, younger children are at an increased risk for severe illness. It is possible that caretakers have experienced more severe illness and rapid development of serious symptoms in younger children in the past, and these experiences may explain why they are more likely to initiate treatment in formal facilities for younger children.

Caretaker education was assessed in various studies as a predictor of treatment seeking. One study indicated that mothers with at least post-secondary school education were more likely to initiate treatment in the formal sector for their febrile children (Kakai, Menya, & Ordero, 2009). However, these results are inconsistent with two other

studies that found that mothers' education was not associated with initial place of treatment (Getahum, Deribe, & Deribrew, 2010; Rutebemberwa et al., 2009b).

Structural barriers. Many studies assessed issues of access and how they affect initial treatment-seeking behaviors. Access to formal health facilities is a significant and common barrier for many people, especially those residing in rural areas. Both the distance and the cost to reach formal health facilities present challenges. Caretakers select health facilities based on location, and prefer to initiate treatment in facilities that are closer (Falade et al., 2005; Müller et al., 2003). In Uganda, caretakers who lived more than a kilometer away from a health center were more likely to visit a CHW as compared to caretakers who lived within a kilometer of a health center (Mukanga, et al. 2011). Urban areas are more likely to have a greater variety of all types of health care options, while rural communities may only have informal services such as a drug shop or CHW. Not surprisingly, caretakers of febrile children in urban areas are more likely to seek treatment in the formal sector, and caretakers of children who reside in rural areas are more likely to seek treatment at informal health facilities, namely drug shops or private medicine vendors (Diallo et al., 2012; Ewing et al., 2011; Okeke & Okeibunor, 2010; Onwujekwe et al., 2010; Uzochukwu et al., 2008).

Cost of reaching health facilities is a second type of access barrier. As they often do not require transportation fees, healthcare facilities that are closer to the house are easier to reach, which caretakers have identified as a key characteristic that influence where they initially seek care. In many places the cost of service is much cheaper in the informal sector (Deressa et al., 2008; Okeke & Okafor, 2008). The cost to reach formal health facilities can be significantly higher for people living in more remote villages than

for people who reside in urban centers (Ewing et al., 2011). The transportation expense is a main reason for initiating treatment in local drug shops or from patent medicine vendors (Mota et al., 2009; Okeke & Okeibunor, 2010). Although caretakers must pay for the medicine when they go to a drug shop, it remains cheaper than paying for transport to reach many formal health facilities.

Illness severity. Perceived severity is self-reported by the caretakers, and is typically described as extreme fever or fever coupled with one or more malarial symptoms, such as headache, sweats, and fatigue. In the reviewed literature, severity is one of the strongest and most common predictors of seeking immediate care in the formal healthcare sector. Caretakers are more likely to seek care in the formal sector if the child's illness is perceived to be severe (Ewing et al., 2011; Müller et al., 2003; Okeke & Okeibunor, 2010), additional serious symptoms are present with fever (Rutebemberwa et al., 2009b) or the fever continues for several days (Mota et al., 2009). These situations indicate an illness beyond ordinary or uncomplicated malaria. Symptoms such as mild fever or fatigue are often considered manageable at home or with locally purchased drugs. Of interest is how caretakers react to the presence of convulsions. They are seen as symptoms of severe illness, but prompt different behaviors. In some cases, caretakers will seek care in the formal sector immediately for convulsions (Dillip et al., 2009), while in other places caretakers take their children to a traditional healer (Makundi et al., 2006; Okeke & Okafor 2008).

Several studies utilized qualitative methods that provide additional insight and support for the findings that severity is a significant predictor of formal healthcare utilization. Mothers who describe their child's illness as "ordinary" (Kamat, 2006) or

“not serious” (Falade et al., 2005) prefer to initiate treatment at home. Mothers in Sudan described the main reason for seeking care at a health center was the “deterioration of the child condition” (Malik et al., 2006). In Malawi, rural mothers described levels of illness severity based on the child’s activity level. If the child can play, their illness is considered mild, but if the child cannot play, it is then considered severe and should be taken to a formal healthcare facility (Chibwana et al., 2009). Other explanations for severity overlap with local concepts about the cause of the disease, and are discussed in the next section.

Perceived quality of service. How caretakers perceive the quality of service that is provided in a health facility influences where they take their febrile child. Formal healthcare facilities are perceived as providing more services such as malaria testing (Okeke & Okeibunor, 2010) as well as trained and experienced doctors and personnel (Nanyonjo et al., 2012; Rutembemerwa et al., 2009b). These are the qualities that caretakers seek out when home-treatment fails or the initial symptoms are severe. On the other hand, drug shops are identified as maintaining a constant supply of medicines when government-run facilities often run out of basic drugs (Chibwana et al, 2009; Idowu et al., 2008; Nanyonjo et al, 2012; Rutebemberwa et al., 2009b). When caretakers believe they already understand the illness, they rely on places that they know will have the types of medicine they need.

Previous experiences in a health facility help to define how caretakers view the quality of the service and can affect future visits and decisions. Positive experiences that are created during a treatment-seeking episode encourage similar treatment seeking behaviors for subsequent febrile illnesses (Iwelunmor, Idris, Adalakun, & Airhihenbuwa, 2010). Caretakers who visited higher-level healthcare facilities cited the health provider’s

use of malaria diagnostics and the provision of effective treatment as the primary reasons for their positive experiences (Iwelunmor et al., 2010). Drug shops were often identified as having a constant supply of various drugs, timely service, allow patients to purchase medicines on credit, and took time to treat patients (Rutebemberwa et al., 2009b; Nanyonjo et al., 2012). These quality services encourage caretakers to return to the same drug shop the next time one of their children has fever or malaria symptoms as they are confident that needed drugs will be available.

Negative experiences can have the opposite effect, and dissuade caretakers from returning to a specific health facility. Long waiting times for see a trained health worker and the long treatment times encourage caretakers to rely on informal health facilities for subsequent fever episodes because they are faster (Nonvignon et al., 2010). Government facilities are often criticized for treating patients poorly, which can create negative experiences as well (Chibwana et al., 2009; Idowu et al., 2008). Any of these negative experiences may lead to different treatment-seeking decisions for future febrile illnesses.

These descriptions of facility qualities suggest that outcome expectations are developed primarily during previous encounters. Furthermore, outcome expectations play an important predictor of where caretakers seek care, although they do not necessarily predict utilization of the formal sector or informal sector. These studies used qualitative methods to provide detailed information about attitudes towards various levels of the healthcare system are formed and affect the treatment-decision process. However, none of the studies reviewed here have measured attitudes or outcome expectancies and assessed whether or not they are associated with treatment-seeking outcomes.

Malaria Knowledge and Attitudes

The studies reviewed here focused primarily on structural, socio-demographic, and cultural determinants of treatment-seeking behavior. Many of the studies measured different types of malaria knowledge, but generally presented the results as descriptive information, and few studies directly assessed how knowledge affects treatment-seeking behaviors. Qualitative studies assessed how local understanding of malaria encourages certain health-seeking behaviors. Malaria illness is often categorized into various levels of severity, with only the most severe illnesses requiring immediate treatment in the formal sector. This information is critical to understanding how caretakers view malaria, and can influence the development of health education programs. However, malaria knowledge such as antimalarial knowledge, fever knowledge, and treatment knowledge were largely ignored as determinants of where care is initiated.

Two studies considered the role of malaria knowledge and the timeliness of seeking treatment. Simba, et al. (2010) found that knowledge about recommended antimalarial treatment was associated with timely, ACT-use. Surprisingly, Ahorlu et al. (2006) found that knowledge of malaria cause was not associated with receiving timely treatment. However, neither of these studies assessed how knowledge affects where caretakers seek treatment initially. Hwang et al., (2010) measured if any malaria knowledge was associated with seeking any care, but did not consider specific types of knowledge. This lack of clarification does not illuminate types of education programs that are needed to increase care-seeking behavior. Furthermore, this association does not consider if knowledge was associated with seeking care in the informal or formal sector, which as previously discussed, affects the quality of treatment received.

Littrell (2011) found that knowledge of first-line drugs in multiple countries was poor, and suggested that this may affect appropriate treatment in the informal sector. While caretaker antimalarial knowledge most likely will have an effect on the drugs they chose to purchase, this information does not assist in understanding how knowledge affects the decision-making process in terms of where treatment is initially sought. To the best of the author's knowledge, the role of attitudes in the health-seeking process has only been described in terms of qualitative descriptions of caretakers' preferences.

Discussion

A systematic review of the literature reveals that treatment-seeking patterns for fever and suspected malaria have been well researched in Africa. Caretakers readily recognize febrile illness in their children, and frequently associate fever with malaria. However, none of the reviewed studies measured if caretakers could name other illnesses that result in fever symptoms. Knowledge about the causes of malaria were much more variable as many caretakers name incorrect ways that malaria can be transmitted.

Most caretakers initiate some type of treatment, but as malaria is often perceived as a non-life threatening disease, they initiate treatment in informal health facilities that are closer to home and cheaper, such as local drug shops and patent medicine vendors. Caretakers typically rely on the formal sector as the second point of care if the illness persists. This pattern is consistently reported throughout the literature, and often results in a delay of appropriate treatment for the child. The determinants of seeking care have been researched and discussed less frequently in the literature.

Households from higher SES quintiles and those who live in urban areas are more likely to initiate treatment in the formal sector. This is due to the cost and time required to reach formal health facilities, which are often located in urban town centers. However, illness severity is one of the strongest factors and one of the most commonly cited reasons for seeking care at a formal health facility immediately, regardless of location. Local illness concepts vary throughout Africa, but often categorize malaria into various types based on perceived causes or symptom. These cultural determinants aid in determining the potential severity of the illness and often dictate where the child should be taken for treatment. Fevers labeled as less severe or ordinary are treated within the community at informal facilities, while more serious types of malaria require children to be taken to a facility in the formal sector.

In addition to these determinants, caretakers have treatment preferences based on the perceived quality of the provider. Formal health care facilities such as public health centers, clinics, and hospitals are viewed as having qualified, trained medical staff and quality services such as diagnostics. However, these facilities are associated with long waits, lack of drugs, and poor treatment towards sick patients. Drug shops are closer to home and consistently stock medicines. Drug shop owners offer medicines on credit and are available to open their shops after government facilities have closed. Previous experiences, both positive and negative, influence caretakers where to seek treatment during subsequent illnesses in the household. Negative experiences at inaccessible formal facilities encourage caretakers to rely on local drug shops as the first step in the illness resolution process.

Knowledge and attitudes, as they affect decision-making, were not widely assessed in the reviewed articles. Future studies should consider malaria-related knowledge and attitudes about diagnostics, antimalarials, and various healthcare services and how they affect caretaker decision-making. As diagnostic confirmation becomes more common, the role and importance of testing may change how caretakers perceive the prevalence of malaria among children under five. It is also important to understand how caretakers perceive the effectiveness diagnostic testing as compared to typical trial and error methods of diagnosing malaria that are based on the treatment and management of fever symptoms. WHO guidelines can only be enforced once patients reach a health care facility. If caretakers do not utilize formal health care facilities, there is minimal likelihood of receiving a diagnostic confirmation. In order to encourage testing before treating, and appropriate treatment for childhood fevers, the role of the caretakers must be understood beyond issues of access and availability of drugs and services. As this literature review indicates, several qualitative studies have looked deeper into these barriers to seeking care in the formal sector, but more research is needed to understand how attitudes and different types of knowledge affect initial decision-making processes.

While the literature presents a clear understanding of treatment seeking patterns in general, several gaps in understanding the decision-making process remain. One of the largest gaps is the limited view most studies took in assessing behaviors. Most of the literature divided treatment seeking into only two categories: informal and formal. Health systems provide a variety of options, but only six studies considered three or more types of treatment seeking behavior. Two of these studies assessed multiple levels of the healthcare system including traditional healers, home treatment, patent medicine dealers,

public health centers, and private hospitals. However, each study only considered a single predictor: SES (Onwujekwe et al., 2010) and urban residence (Onwujekwe et al., 2011). While these studies provide a more detailed understanding of how these predictors act at various levels of the healthcare system, they omit all other potential determinants. The other four studies included additional predictors, but they are limited in only considering a few socio-economic factors (Deressa et al., 2007; Kazembe et al., 2007; Nonvignon et al., 2010; Smith et al., 2010). The lack of studies that assessed various types of determinants in general presents a limited understanding of behavioral decision-making.

The articles reviewed addressed socio-demographic, structural, cultural, and illness severity as barriers to seeking treatment. Very few of the studies included various types of determinants, with the majority focusing on issues of access. Most studies considered treatment seeking in terms of two options, while only a handful of studies included a complex model of treatment-seeking behavior and addressed more than two levels of the healthcare system. However, these studies were extremely limited in the type of determinants they assessed at the multiple levels.

Strengths and Limitations

The biggest limitation to this literature review was the variability in health sector definitions and treatment-seeking outcome. Many studies compared the informal and formal sectors. However, other studies focused on the private versus public sectors, or the traditional versus modern treatment. Most studies focused on determinants of seeking care in the formal sector, while a few focused on seeking any care, and a handful considered more than two levels of the healthcare system. These differences made

comparisons a challenge. Furthermore, there was a significant amount of variability in the range and types of predictors used in the analyses. Some studies considered one or two predictors, while others included several types of predictors. Despite these differences, clear patterns emerged, and the most salient determinants studied to date were identified.

This literature review was able to identify the well-known determinants of treatment-seeking behaviors for suspected malaria, and to highlight the gaps in current understanding. Despite the abundance of information available about treatment-seeking patterns and preferences for febrile illness, the majority of suspected malaria cases are still treated in the informal sector. In order to improve consumer utilization of formal sector services as well as provision of health services, more research is needed to understand how caretakers' knowledge and attitudes about malaria and the illness resolution process affect treatment-seeking behavior. Future research should include how knowledge and attitudes work at the various levels of the healthcare system, and not limit its focus to the formal sector, in order to present a more complex understanding of how decisions are made and patterns develop. The results of future research may be used to develop appropriate behavior change campaigns that target caretakers who continue to rely on the informal sector as well as to increase health worker training to improve perceived quality of service.

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Table 3.1

Health Sector Classifications

	Informal/Community Sector	Formal Sector
Private Sector	Indigenous Healer Drug Shop/PMVs Family/Friends Market Stalls/Stores	Pharmacy Clinics Private Hospitals
Public Sector	CHWs	Government Health Centers Government Hospitals Health Posts

CHAPTER 4: MANUSCRIPT 2

Determinants of health-seeking behaviors for childhood malaria in eastern Uganda: Implications for control

Katrina Berg, MA

Johns Hopkins School of Public Health

Department of Health, Behavior and Society

Abstract

Background: More than half of all suspected malaria cases in children under five in Uganda are treated in the informal sector where diagnostic capabilities are rare and facilities often lack appropriate treatment. This study aims to identify determinants of treatment-seeking behavior for children with suspected malaria in order to increase consumer-utilization of formal healthcare facilities.

Methods: Data from 946 caretakers of children under ten years of age were collected in a baseline survey and ten monthly follow-up interviews. Multinomial logistic regression analyses were used to identify determinants of engaging in home-treatment, purchasing over-the-counter drugs, and going to a formal facility.

Results: Twenty-four percent of respondents treated their children at home, 41% purchased drugs from a drug shops, and 35% initiated treatment at a formal health facility. Caretakers residing in urban areas were more likely to seek care in a formal healthcare facility than at home (OR: 1.62, 95% CI = 1.05-2.51) or from a drug shop (OR: 2.05, 95% CI = 1.38-3.04). Children with more severe illness were more likely to seek care from a formal healthcare facility than at home (OR: 1.16, 95% CI = 1.07-1.24) or from a drug shop (OR: 1.09, 95% CI = 1.02-1.16). Caretakers with more positive attitudes about seeking care at a formal facility were more likely to seek care at the highest level of the healthcare system (OR: 2.14, 95% CI = 1.37-3.34) or from a drug shop (OR: 1.66, 95% CI = 1.06-2.59) than at home. Caretakers with more antimalarial knowledge were more likely to initiate care at a formal facility than at home (OR = 1.18, 95% CI = 1.01-1.37).

Conclusion: Malaria-related knowledge and attitudes are associated with seeking higher levels of healthcare for suspected malaria. Interventions are recommended to increase caretaker knowledge about malaria transmission, recommended treatment guidelines, and the risk of not engaging in immediate treatment for uncomplicated malaria. Efforts should be made to increase perceived efficacy government-run facilities in order to increase consumer utilization of the formal healthcare sector for suspected malaria.

Background

Malaria poses a public health concern globally, as well as a significant economic threat to the countries most affected. In 2012, there were 207 million malaria cases, and 627,000 deaths worldwide (WHO, 2013). Although less than half of the malaria-endemic countries are in Africa, the continent bears the majority of the burden. In 2012, 80% of the estimated malaria cases and more than 90% of the estimated deaths occurred in the Africa region (WHO, 2013). More than three-quarters of all deaths attributed to malaria occurs in children under five years of age, making them the most vulnerable population to this infectious disease (WHO, 2013). It is estimated that in Africa direct economic losses due to malaria total \$12 billion each year (RBM Partnership, 2008). These losses result from treatment expenses as well as the inability to work due to traveling to reach a healthcare facility and caring for a sick family member.

Uganda is one of the ten high-burden countries as identified by the WHO, and has the highest reported number of malaria cases worldwide (WHO, 2013). Malaria is the leading cause of morbidity and mortality in Uganda, with an estimated 11 million cases of reported malaria each year (UBOS, 2010). Malaria is endemic throughout the year in 90-95% of Uganda, with *P. falciparum* accounting for all reported cases (WHO, 2013). According to hospital records, it is estimated that malaria accounts for between 30% and 50% of all outpatient care cases, and between 15% and 20% of all admissions (UBOS, 2010).

When a child has a fever or is suspected to have malaria, there are several treatment options including doing nothing, managing the fever with tepid sponging, treating at home with herbal remedies or with biomedical drugs, purchasing biomedical

drugs at a local store, seeking specialized advice from a private clinic or public health center, or engaging in a combination of these activities. Self-treatment occurs in the informal sector, where parents treat their children themselves with herbs or drugs either stored at home or purchased from a drug shop. When purchasing drugs from a local shop, anyone may go on behalf of the patient, and a prescription is not needed. Seeking care at a formal healthcare facility, such as a private clinic/hospital or a public health center/hospital, increases the likelihood of the availability of diagnostic capabilities and trained health professionals.

Self-treatment is the most commonly preferred first step for the treatment of febrile illness in children throughout Africa. Studies conducted in high transmission areas indicate that caretakers' most common first response is to treat their child at home with drugs stored in the house or bought over-the-counter (Abuya et al., 2008; Holtz et al., 2003; Uzochukwu, Onwujekwe, Onoka, & Ughasoro, 2008). In Uganda, self-treatment is also the preferred first step in illness resolution for suspected malaria in children. More than half of children under five with febrile illness are first treated at home (Littrel, 2011; Mbonye, Bygbjerg, & Magnussen, 2008). Other studies indicate that close to 80% of suspected malaria cases are treated in the informal sector (Mukanga et al., 2012; UBOS, 2010).

In the informal sector, suspected malaria is often treated presumptively, based on the presence of fever, due to the lack of diagnostic capabilities. However, fever is a common symptom of various childhood illnesses such as pneumonia and influenza. National-level data from 41 African countries indicate that less than half of children under-five with a history of fever who seek treatment from the public sector are likely to

have malaria (Gething et al., 2010). In Uganda, only 24% of patients presenting at health facilities with fever or history of fever had malaria (Nankabirwa, et al., 2009). These studies indicate that more than half of childhood fevers may be caused by something other than malaria.

The World Health Organization (WHO) currently recommends artemisinin-based combinations therapy (ACT) as first-line treatment for uncomplicated *P. falciparum* malaria (WHO, 2010). However, poorer people frequently use cheaper non-artemisinin based antimalarial that are ineffective, and that may promote resistance (RBM Partnership, 2008). The Affordable Medicine Facility – malaria (AMFm) is a financing mechanism hosted by the Global Fund with the primary goal to increase universal access to affordable ACTs (RBM Partnership, 2008). Through the AMFm, ACTs have been made widely available in both the public and private health sectors at a subsidized price. Although increased access to appropriate treatment is necessary to reduce the malaria burden, especially for people of lower economic backgrounds, it raises new public health and policy concerns. One of the most pressing issues is the overuse of ACTs due to the reliance on the informal sector and presumptive treatment.

Presumptive treatment directly contributes to the overtreatment of malaria, which results in wasted resources, mistreatment of the true illness, exposure to side effects from needless treatment, and parasitological resistance to ACTs. Although artemisinin resistance has only been reported in Southeast Asia so far, increased efforts to supervise drug dispersion is essential to stemming the spread to Africa (Wongsrichanlai, Varma, Juliano, Kimerling, & MacArthur, 2010). Malaria control programs and strategies are

faced with the dual challenge of increasing access of ACTs in order to reduce malaria mortality rates, while preserving the integrity of ACTs for future populations.

The most effective way to conserve is to increase blood confirmation for the presence of malaria parasites before administering treatment. The WHO has modified the Guidelines for the Treatment of Malaria to recommend parasitological confirmation for suspected malaria for all populations, and presumptive treatment should only be used when diagnostic confirmation is not possible (WHO, 2010). However, diagnostic ability is limited particularly in rural areas where caretakers rely on home treatment and local drug shops. Despite campaigns that encourage caretakers to get their child tested and treated within 24 hours, most caretakers continue to rely on presumptive treatment.

In order to preserve ACTs, and to increase appropriate treatment for childhood malaria in Uganda, it is necessary to increase caretaker utilization of the formal healthcare system. Several types of determinants have been found to be associated with health-seeking behavior for malaria. Demographic characteristics associated with treatment-seeking behaviors include higher SES (Deressa, 2007; Onwujekwe, Hanson, & Uzochukwu, 2011; Simba et al., 2010), gender of the sick child (Nonvignon et al., 2010; Smith et al., 2010), and caretakers' education (Kakai, Menya, & Ordero, 2009). Children from wealthier families, boys, and children whose mothers attended secondary school are all more likely to initiate care at a formal healthcare facility.

The distance to formal health facilities presents a significant structural barrier for many people, especially those residing in rural areas. Caretakers select health facilities based on location, and are more likely to initiate treatment in facilities that are closer to their homes (Falade, 2005; Müller, Traoré, Becher & Kouyaté, 2003). Febrile children in

urban areas are more likely to seek treatment in the formal sector compared to children who reside in rural areas (Ewing et al., 2011; Okeke & Okeibunor, 2010; Onwujekwe et al., 2010; Uzochukwu et al., 2008).

The cost to reach formal healthcare facilities is one of the main reasons distance presents a significant access barrier. Caretakers often initiate care in places where the anticipated cost of the overall visit is cheaper (Deressa, Ali, & Hailemariam, 2008; Okeke & Okafor, 2008). The transportation expense is one of the main reasons for initiating treatment in a place closer to home (Mota, Lara, Kunkwenzu, & Lalloo, 2009; Okeke & Okeibunor, 2010). The cost to reach the formal health facilities can be significantly higher for people living in more remote villages (Ewing et al., 2011). Although caretakers must pay for the medicine when they go to a drug shop, it remains cheaper than paying for transport to reach many formal healthcare facilities.

Illness severity has been found to be one of the most significant determinants of treatment seeking. Seeking care in the formal sector has been associated with perceived illness severity (Ewing et al., 2011; Müller et al., 2003), children exhibiting multiple symptoms (Dillip et al., 2009; Rutebemberwa, Pariyo, Peterson, Tomson, & Kallander, 2009b), and the length of illness (Mota et al., 2009). These situations indicate an illness beyond ordinary or simple malaria, and warrant immediate attention in the formal sector.

Local illness concepts categorize types of febrile and malarial illness, and also influence where treatment is initiated. Local concepts that equate to the biomedical term uncomplicated malaria are often seen as the result of natural causes such as the climate, food, exposure to heat, or mosquitoes, which can be treated easily at home with either traditional or modern medicine (Ahorlu, Koram, Ahorlu, de Savigny, & Weiss 2006;

Beiersmann et al., 2007). These types of fevers are viewed as non-threatening conditions that do not require going to a formal healthcare facility unless symptoms worsen.

How caretakers perceive the quality of service that is provided in a healthcare facility influences where they take their febrile child. In general, formal healthcare facilities are perceived as providing higher quality services such as malaria testing (Okeke & Okeibunor, 2010) and trained and experienced doctors and personnel (Nanyonjo et al., 2012; Rutebemberwa et al., 2009b). Drug shops are identified as maintaining a constant supply of medicines when the government-run facilities often run out of basic drugs (Chibwana, Mathanga, Chinkhumba, & Campbell, 2009; Idowu, Mafiana, Luwoye, & Adehanloye, 2008; Nanyonjo et al., 2012; Rutebemberwa et al., 2009b). In addition to these general perceptions, previous experiences in a healthcare facility define how caretakers view the quality of the service and can affect future visits and decisions. Drug shops were often identified as having a constant supply of various drugs, timely service, allow patients to purchase medicines on credit, and took time to treat patients (Rutebemberwa et al., 2009b; Nanyonjo et al., 2012). Long waiting times to see a trained health worker and the long treatment times encourage caretakers to rely on informal health facilities for subsequent fever episodes because they are faster (Nonvignon et al., 2010). These various services and characteristics result in perceived timelier and more efficient outcomes that encourage caretakers to return to the same drug shop the next time one of their children has fever or malaria symptoms.

The literature on treatment seeking for malaria focuses primarily on structural, socio-demographic, and cultural determinants of behavior. Very few studies have assessed the association between malaria knowledge or attitudes and the type of place

where caretakers seek initial treatment. Two studies considered how malaria knowledge affects timely treatment, but they did not consider how knowledge affects place of treatment (Ahorlu et al., 2006; Simba et al., 2010). Hwang et al. (2010) measured various aspects of malaria knowledge with seeking any care outside of the house, but did not consider if knowledge was associated with seeking care in the informal or formal sector. These studies suggest that malaria knowledge may affect the first place care is initiated for suspected malaria in children, although very little is known.

While the role of knowledge has been considered minimally, to the best of the author's knowledge, how various attitudes about treatment priorities, diagnostics, health facility effectiveness, and antimalarial treatments affect treatment-seeking decisions has been largely ignored. Therefore, the aims of this study are to 1) document the treatment-seeking patterns of febrile children in Uganda and 2) explore the association among knowledge, attitudes, and place of treatment seeking initiation.

Methods

Data Source

Secondary data analysis was conducted on the data collected through the study titled: "Evaluating the Feasibility of Introducing Malaria Diagnosis in the Private Sector in Eastern Uganda," Dr. Jessica Cohen, Principal Investigator.¹ The primary goal of this study was to assess under which conditions Drug Shop Vendors (DSV) can appropriately sell and implement RDTs in local drug shops in Uganda. Additional goals included

¹ Dr. Cohen is Assistant Professor at the Harvard School of Public Health and an affiliated researcher at the Clinton Health Access Initiative (CHAI).

understanding overall treatment-seeking and testing patterns for people of all ages with fever, measuring the effect of increased access to RDTs on testing outcomes, determining customer willingness to pay for RDTs, and evaluating the impact of a community-based Behavior Change Campaign (BCC) on testing outcomes. Baseline data were collected from all drug shops in the study area, and monitoring data were collected from drug shops participating in the study. Baseline and follow-up data were collected from sampled households over the course of the study. The DSV assessment, RDT acceptability, and BCC impact have been evaluated and reported on elsewhere. This dissertation focuses on determinants of caretaker utilization of the healthcare system for suspected malaria, and therefore, focuses on the data collected during the household baseline and follow-up surveys.

This was a longitudinal study conducted in six districts in Eastern Uganda between March 2011 and May 2012. Thirty households were randomly selected from 92 villages in the six districts to be approached for enrollment (n=2760). Study eligibility included being 18 years of age, the recognized female head of household, able and voluntarily willing to complete future follow-up interviews on a monthly basis, and able to speak one of the two main local languages. All surveys and informed consent forms were translated into Ateso and Luganda, the two most prevalent languages throughout the six districts. Interviews were conducted in either Ateso or Luganda, according to the participants' preferences. Respondents who could not speak Ateso or Luganda were excluded from participating in the study. Although the female head of household was purposefully recruited, the male head of household was recruited if an eligible female was not a member of the household. A total of 2560 heads of household were enrolled

and included in the baseline survey. Through face-to-face interviews, data were collected at baseline on demographic information, malaria knowledge, treatment-seeking behavior for malaria, and attitudes about malaria. Nine subsequent monthly follow-up rounds as well as an endline survey were completed with the same respondents. Interviews were conducted each month to gather information on treatment-seeking behaviors for all illnesses experienced by all household members since the previous interview.

Data sample. The selected sample included the most recent potential malaria case in a child under ten years of age in the household in the previous month. Although children under five are the most vulnerable population, children under ten were included in order to assess if caretakers engaged in different behaviors for younger children and older children. Data was used from follow-up round 3 including attitudes about self-treatment and test adherence, fever knowledge, perceived illness severity, and behavioral outcomes. This was the first point in the study that both behavioral outcomes and attitudes were measured simultaneously. Demographic information, knowledge of malaria cause, and antimalarial knowledge were not asked during any other data collection round, and therefore were taken from the baseline survey data.

At follow-up round 3, 2490 households completed the survey. Of these, 1596 households reported at least one sick person in the household in the previous month. Including all illness episodes in these households provided data on 3037 individual cases. All cases that included a household member ten years of age or older were excluded (n=1491), leaving 1546 illness episodes. Individuals who did not exhibit malaria symptoms (n=62) were also excluded. Seventy-eight of these illness episodes were missing data on the outcome of interest (first place of treatment sought) or the attitude

measures, and were removed from the dataset, leaving a total of 1406 fever episodes in children less than ten years of age. Many households reported more than one fever episode in children in the past month (n=460). The most recent fever episode was retained for a final sample of 946 fever episodes in children under 10 years of age in the previous month to be included in the analysis. Figure 4.1 displays the sample selection process.

Measures

Dependent Variable

The dependent variable was initial treatment seeking behavior for the febrile child. When discussing their child's illness, respondents were asked "What did you do first?" Three levels of treatment seeking behaviors were defined: 1) took herbs or medicines from home 2) went to a drug shop or pharmacy, and 3) went to a formal healthcare facility. "Took herbs or medicines from home" included taking herbs or biomedical drugs from home or from a neighbor. "Went to a drug shop or pharmacy" included going to a drug shop, mobile vendor or pharmacy to purchase drugs. Both drug shops and pharmacies are licensed and registered with the government, and sell all products over-the-counter. "Went to a formal healthcare facility" included going to public health centers or private clinics/hospitals.

Independent Variables

Independent variables included socio-demographic variables, attitudes, knowledge, and perceived severity of the child's illness. During the baseline survey,

caretakers were asked a variety of socio-demographic questions including their age, the age of the sick child, the highest level of school they completed, typical items they owned in the household, occupation, and religion. Caretakers also answered questions about the cause of malaria and antimalarial knowledge. During follow-up round 3, respondents were asked about attitudes and fever knowledge in addition to completing an illness roster for all illness episodes in the household that occurred in the previous month. The perceived severity of each illness was recorded on each illness roster.

Socio-demographic variables.

Age of respondent. A continuous variable was created that indicated caretakers' self-reported age in years.

Child's age. Caretakers reported the child's age at the time of the recorded illness. Child's age is a continuous variable from 0-9 years of age. All children between birth and 11 months of age are recorded as 0 years of age.

Child's gender. Children were recorded as male or female, as reported by their caretaker.

Marriage. Caretakers were asked their marital status. A categorical variable was created that included the following categories: monogamous, polygamous, and other. The "other" category includes caretakers who reported their marital status as widowed, divorced/separated, or never married/never cohabitating.

Education. Caretakers were asked the highest grade or level of education they had achieved. A categorical variable was created that included the following categories: no education, primary or less, and secondary or higher. Caretakers who had never

attended any formal school were categorized as no education. Caretakers who had attended any primary school grade were labeled as primary or less, regardless of whether or not they had completed this level. Secondary or higher included anyone who had attended any level of secondary school, vocational school, or university.

Work. Caretakers were asked what they did for their primary occupation or their main source of income. A categorical variable was created that included the following categories: unemployed, farmers, and formally employed. Anyone who was retired, did not have a formal job, or was a housewife was categorized as unemployed. Caretakers who reported farming (commercial or subsistence) as their primary occupation were categorized as farmers. All caretakers who reported formal employment (such as a shopkeeper, hairdresser, teacher, etc.) were categorized as being formally employed outside of the home.

Religion. Caretakers were asked about their religious affiliation. A categorical variable was created that included Catholics and Born Again Christians; Protestants and Seventh Day Adventists; and Muslims.

Urban. A binary variable was created based on the urban or rural location of the household's village. All villages that were located in a town council were categorized as urban. All other villages were categorized as rural.

Socioeconomic status (SES). SES was based on ownership of household items, land, and building materials of the house. Household items included mobile phones, adult bicycles, solar panels or electricity, radios, televisions, motorcycles, and vehicles. Caretakers were categorized as owning the land if they had a title, and did not rent the land, squat on the land, or use it free-of-charge from an employer or family member.

Household building materials included walls made from cement bricks, a finished floor, and an iron or tin roof. The household received a point for the ownership of each item listed. The number of items was then summed (range: 0-9). More than three-quarters of the sample (76%) owned 5 items or fewer. Therefore, a categorical variable was created that included low, medium, and high SES categories based on terciles. Respondents with two or fewer items were in the bottom third, and categorized as low SES. Respondents with three or four items represented the middle tercile, and were categorized as medium SES. Respondents with five or more items were considered to have high SES.

Self-treatment attitude. Caretakers were read the following statement: you should first try to treat malaria at home before going to a clinic. They were then asked if they strongly agree, sometimes agree, sometimes disagree, or strongly disagree with this statement. A univariate analysis revealed that the variable was bimodal, and a dichotomous variable was created based on agreement and disagreement.

Test adherence attitude. Caretakers were read the following statement: you should take antimalarial medicine, even if your malaria test is negative. Antimalarials were defined as medicines used to treat malaria. This statement addresses perceived efficacy in the malaria test. Regardless of which type of antimalarial the respondents prefer to use, or whether or not they are actual antimalarials, their response indicates their faith in the accuracy of the test. They were then asked if they strongly agree, sometimes agree, sometimes disagree, or strongly disagree with this statement. A univariate analysis revealed the test adherence attitude to be bimodal; therefore, a dichotomous variable was created based on agreement and disagreement.

Malaria knowledge. Caretakers were asked to freely name all the ways that someone could contract malaria. In the Luganda language, malaria is known as *omusujja gw'ensiri*, which is translated as “fever caused by malaria.” This is the term used by the Ministry of Health when referring to malaria. In Ateso, the word used for uncomplicated malaria is *eimidi*. This term is translated simply into malaria.

A categorical variable was created that included having no knowledge, low knowledge, and high knowledge. Caretakers who did not state the correct answer without prompting (mosquitos) were considered to have no knowledge. Caretakers who stated mosquitoes, but also provided at least one incorrect answer, were considered to have low knowledge. Caretakers who stated the correct answer only, mosquitoes, were labeled as having high knowledge.

Antimalarial knowledge. Caretakers were asked to freely list all antimalarials that they had heard of. Antimalarials were defined for the participants as drugs used to treat malaria. A discrete variable was created that summed all correctly identified antimalarial medicines.

Fever knowledge. Caretakers were read the following statement: fever is often caused by illnesses other than malaria. They were then asked if they strongly agree, sometimes agree, sometimes disagree, or strongly disagree with this statement. A dichotomous variable was created based on agreement and disagreement. Caretakers who agreed that fever is often caused by other illness were coded as having high knowledge, and those who disagreed were coded as having low knowledge.

Perceived illness severity. Caretakers were asked to rate how severe they thought the illness was on a scale from 0-10. A discrete variable was created based on caretakers' self-reported perception of the child's illness severity.

Data Analysis

Frequency and summary statistics were calculated for the outcome of interest and all explanatory variables. A description of all categorical variables, including the frequencies and percentages, and all continuous variables, including the mean and standard deviations, are presented. Next, bivariate analyses were conducted on all explanatory variables and the behavioral outcome, treatment-seeking behavior. For continuous variables, a one-way analysis of variance was conducted to test for significant bivariate associations. Separate bivariate associations between all categorical explanatory variables and the outcome were calculated using Pearson's χ^2 tests in order to determine which factors contributed to treatment-seeking decisions. Simple multinomial regression analyses were conducted to calculate unadjusted associations between all explanatory variables and the treatment-seeking behavior.

Multinomial multivariable logistic regression analyses were used to explore the adjusted associations among the demographic variables, the variables of interest, and the behavioral outcome. It was determined a priori that explanatory variables with a p-value $\leq .2$ were to be included in the development of the multivariable model. All analyses were conducted using Stata 12.1 Statistical Package (StataCorp 2012).

Results

Respondent Attrition

Respondents were lost to follow-up during each follow-up survey that was conducted. Reasons for respondents being lost to follow-up include moving out of the study area, death, and refusing to participate further in the study. During the first, second, and third follow-up rounds 37, 23, and 11 respondents, respectively, were lost to follow-up. A total of 71 households were lost to follow-up for an attrition rate of 2.7%.

Sample Characteristics

Socio-demographic characteristics. The majority of the caretakers were women (98.32%). Just over half (51%) of the children were male. The average age of the respondents was 33.44 years (SD: 10.56, range: 17-90). The mean age of the children was 3.35 years (SD: 2.76, range: 0-9). Almost 85% of the caretakers were married, and more than 60% were in a monogamous marriage. Just over 44% of the respondents were Catholic, 41% were Protestant, and 14% were Muslim. A quarter of the respondents were categorized as having a low SES status, while 37% were categorized as being in the middle SES strata, and 37% in the highest SES strata. Almost 85% had attended at least one year of formal schooling, with almost 20% having completed at least one year of secondary school. More than three-quarters of the respondents (77%) lived in a rural area. Just over 12% of the respondents claimed to be unemployed, and the majority (64%) relied on farming as their main occupation. Full sample characteristics are presented in Table 4.1.

Malaria attitudes. Two thirds (76%) of the respondents agreed that fever should first be treated at home. More than 60% of respondents agreed that it was acceptable to take an antimalarial drug when a diagnostic test has resulted in a negative test.

Knowledge variables. Respondents with low fever knowledge did not think fever was indicative of illnesses other than malaria, and 42% were categorized as having low fever knowledge. A third of the respondents (34%) had no malaria knowledge, and could not correctly identify how malaria is transmitted. Just less than half the sample (48%) had low malaria knowledge, and could identify mosquitoes as a cause of malaria, but also provided at least one incorrect cause of malaria. The antimalarial knowledge mean was 2.44 (SD: 1.21; range: 0-7), and 94% of the respondents could freely name at least one antimalarial. The most commonly cited antimalarials included Coartem (65%), quinine (64%), chloroquine (34%), SP (14%), Artesunate (14%), and ACT (7%). Just over 40% incorrectly stated Panadol as an antimalarial.

Perceived severity. The mean perceived severity of all illness episodes was 6.13 (SD: 2.40, range: 0-7).

Treatment-seeking behavior. Table 4.2 displays the first place caretakers sought care for their child. Just over three quarters of caretakers (76%) engaged in some type of treatment-seeking behavior outside of the household, while almost one-quarter of the respondents (24%) gave either herbs or medicines that were stored at home to their child. Of those who sought care, 41% went to a pharmacy or drug shop to purchase biomedical drugs. A little over a third of the caretakers (35%) initiated care at a formal health facility.

More than three-quarters of children went to one place (78%), and 20% went to more than one place to seek treatment. Less than 2% of all sick children did not seek any treatment of any kind. Three quarters of the children did not receive a blood confirmation, while one quarter were tested for malaria. Ninety-three percent of children received some type of western drug. The most common drugs received were fever reducers/painkillers (77%), a non-ACT antimalarial (57%), ACT (41%), antibiotic (38%), antihistamine (14%), and anti worming pills (7%). The majority of the children (82%) were given more than 1 drug in the course of the illness resolution. Almost 20% of children took a non-antimalarial drug first. More than 41% of children were given an ACT first, and just under 40% were given a non-ACT antimalarial first.

Bivariate Analyses

Bivariate analyses were conducted on all explanatory variables of interest and the behavioral outcome: treatment-seeking behavior. All variables, except for respondent's age ($p = .467$), child's age ($p = .343$), religion ($p = .635$), and child's gender ($p = .771$) had a p -value $\leq .2$ and were retained for further exploration in the multinomial analysis. All bivariate associations are presented in Table 4.3.

Simple multinomial logistic regressions were used to calculate the unadjusted odds ratios for the explanatory variables and the outcome of interest. All unadjusted odds ratios are presented in Table 4.4. Caretakers who were widowed, divorced, or never married were almost 40% less likely ($p = .045$) to seek care at a drug shop than treat at home as compared to caretakers in a monogamous marriage. Caretakers whose principal employment was farming were almost 50% less likely ($p = .003$) to visit a formal

healthcare facility than a drug shop, and 73% more likely ($p = .042$) to visit a drug shop than to treat at home as compared to caretakers who were unemployed. Caretakers who resided in an urban area were 2.21 times more likely to visit a health facility than at a drug shop ($p < .001$), but were 35% less likely to visit a drug shop than treat at home ($p = .042$). Education was significantly associated with behavior as caretakers who had completed at least one year of secondary school were 2.23 times more likely ($p = .002$) to visit a formal healthcare facility than a drug shop, and 58% less likely ($p = .003$) to visit a drug shop than treat at home as compared to caretakers with no education.

Perceived illness severity and antimalarial knowledge were associated with seeking care at formal healthcare facilities. For each unit increase in reported perceived severity, caretakers were 9% more likely to initiate care at a formal healthcare facility than at a drug shop ($p = .008$), and were 15% more likely to initiate care at a health facility than at home ($p < .001$). Caretakers were 18% more likely to seek care at a formal healthcare center than at a drug shop ($p = .008$) for each one unit increase in antimalarial knowledge, and were 17% more likely to go to a formal healthcare facility than treat at home ($p = .031$). Caretakers with high knowledge of fever sources other than malaria were almost 40% less likely to seek care at a drug shop compared to treating at home ($p = .004$).

Attitudes about self-treatment and adherence to test results were both associated with seeking initial treatment at a formal healthcare facility. Caretakers with more positive attitudes about not initiating self-treatment were 46% more likely to visit a formal healthcare facility than a drug shop ($p = .025$), and 2.22 times more likely to visit a health facility than to treat at home ($p < .001$). Caretakers with more positive attitudes

about test adherence were 57% more likely to go to a formal healthcare facility than to treat at home ($p = .012$). There were no significant bivariate associations between SES or malaria knowledge and initial treatment-seeking behavior.

Multinomial Multivariable Analyses

All adjusted odds ratios in the final model are presented in Table 4.5. When controlling for other variables, caretaker education is significantly associated with treatment-seeking choice. Caretakers who completed at least one year of secondary school were almost 70% less likely to visit a drug shop ($p = .001$) than to treat at home, and 78% more likely ($p = .047$) to initiate treatment in a formal health facility than in a drug shop as compared to caretakers with no formal education. Caretakers who resided in urban areas were 2.05 times more likely to visit a higher-level health facility than go to a drug shop ($p < .001$), and 62% more likely to go to a formal health facility than to treat at home ($p = .030$) as compared to caretakers who resided in rural areas. Formally employed caretakers were almost 50% less likely ($p = .020$) to visit a formal health facility than a drug shop as compared to unemployed caretakers. Caretakers who relied on farming as their main source of income were 41% less likely ($p = .036$) to visit a formal health facility than go to a drug shop as compared to unemployed caretakers.

Caretakers with higher levels of perceived illness severity were more likely to visit a formal health center than initiate treatment at home ($OR = 1.16$; $p < .001$) or visit a drug shop ($OR = 1.09$; $p = .009$). Caretakers who had more positive attitudes about seeking immediate care at a formal health facility were 66% more likely to go to a drug shop than treat at home ($p = .028$), and were 2.14 times more likely to go to a formal

healthcare facility than treat at home ($p = .001$). For every unit increase in antimalarial knowledge, were 18% more likely ($p = .034$) to initiate care at a formal healthcare facility than at home. Caretakers with high fever knowledge were 46% less likely to visit a drug shop than to treat at home ($p = .001$) as compared to caretakers with low knowledge. Attitudes about adhering to malaria test results and knowledge about the cause of malaria were not statistically significant in this model.

Discussion

This study contributes to the literature by assessing various determinants of initial treatment-seeking behavior at three different levels of the health care system in Uganda: at home, at a drug store, and at a formal healthcare facility. Few other studies considered more than two places of seeking treatment, and these articles focused primarily on access and socio-demographic variables. This multinomial analysis included socio-demographic variables, structural barriers, a perceived illness severity measure, as well as attitude and knowledge variables, which provide more detailed information about the barriers and facilitators to seeking care for suspected malaria at various levels of the healthcare system.

The results of this study support the previously well-documented findings that access and perceived illness severity are two of the strongest predictors of initiating treatment seeking in formal healthcare facilities. Children living in urban areas were more likely to be taken to a formal healthcare facility over both drug shops and home-treatment as compared to children living in rural areas. These findings are in consistent with previous research conducted in Malawi, Burkina Faso, and Nigeria (Ewing et al.,

2011; Mota et al., 2009; Okeke & Okeibunor, 2010). Urban areas provide more healthcare options, whereas rural areas typically have only informal facilities.

Caretakers who perceived their child's illness to be more severe were more likely to initiate care at a formal facility over purchasing drugs at a local shop or treating from home. This finding is not surprising, and has been well documented in numerous other studies (Kamat, 2006; Mota et al., 2009; Müller et al., 2003; Rutebemberwa et al., 2009b).

In this study, caretakers with the highest levels of education were more likely to initiate care in a formal healthcare facility than at a drug shop, which is consistent with other studies (Hwang, et al., 2010; Kakai et al., 2009). It is unclear, however, why caretakers with higher levels of education in this study were less likely to initiate care at a drug shop than at home. It is possible that people with higher levels of education are more likely to store various types of medicine in preparation for recurring illnesses.

An interesting finding was that caretakers who rely on farming as their main source of income as well as those who are formally employed were more likely to seek care at a drug shop than at a formal healthcare facility as compared to caretakers that were unemployed. A possible explanation for this finding is that caretakers who spend their day away from the household, whether it is in the fields or in an office or shop, often seek care at the end of the day, when they return home to find that their child is sick. Drug shops remain open in the evenings when most formal healthcare facilities are closed, providing increased access to drugs in terms of longer hours rather than in terms of geography.

Attitudes and knowledge appear to play a more significant role in encouraging caretakers to seek any care outside of the house. None of the attitude and knowledge variables were significant when comparing treatment seeking at formal healthcare facilities to drug shops. Knowledge that fever is a symptom of illnesses other than malaria was associated with an increased likelihood of initiating care at home instead of a drug shop. As seen in the literature, many caretakers describe their treatment seeking process for febrile illness to begin in the household with fever reducers, and they later seek formal care if the fever persists (Chibwana et al., 2009; Kamat & Nyato, 2010). If the symptoms are not severe, caretakers who are aware that fever is caused by a variety of childhood illnesses may engage in home-treatment in order to treat the fever symptoms. If the treatment fails, this is an indication of a more serious cause of the fever, or a more serious case of malaria, and then they seek care at a higher level of the healthcare system.

Caretakers with higher antimalarial knowledge are more likely to go to a formal healthcare facility than to treat at home. These caretakers may seek care at a formal facility as they are seeking ACTs specifically, which may be expensive or unavailable at local drug shops. This finding is consistent with another study that found knowledge of recommended first-line treatment was associated with ACT-use (Simba et al., 2010). These results suggest the need to increase public education about updates in the national treatment recommendations. If the guidelines are not understood, caretakers may simply continue purchasing and using drugs that they are used to, and that had been previously recommended.

Caretakers with more positive attitudes about not engaging in self-treatment for malaria were more likely to initiate treatment at both a drug shop and a formal healthcare facility than at home. As the survey question asked about malaria specifically, and not febrile illness in general, this may be an indication that caretakers understand that malaria must be treated with antimalarials. Caretakers with negative attitudes about self-treating may have more positive outcome expectancies from drug shops and formal facilities.

Attitudes about adherence to blood tests, although significant in the bivariate analysis, were not a significant predictor of behavior in the multivariate model. This is not surprising as testing is not yet a routine step in the illness resolution process. Overall, 26% of the children in this sample were blood-tested for malaria, which is similar to national testing rates for children under five. Other studies have shown testing rates between 18% and 26% for children under five years of age with fever (ACTwatch Group & PACE/Uganda, 2013; UBOS, 2012). As testing is not yet a common step, attitudes about testing accuracy may not influence where caretakers choose to seek initial care. However, increasing perceived efficacy in diagnostic confirmation and reducing efficacy in the typical trial-and-error technical employed in the household might increase appropriate treatment-seeking outcomes.

Knowledge of the cause of malaria was surprisingly low: while two-thirds of the sample could correctly identify mosquitoes as a cause of malaria, less than 20% of caretakers could identify mosquitoes as the correct and sole cause of malaria. However, malaria knowledge was not associated with health-seeking care at any level of the healthcare system. It appears that alleviating symptoms and accessing treatment are more important facilitators to seeking care than understanding the cause of malaria. As seen in

other studies, local illness concepts influence caretaker understanding of various causes of fever and malaria, and ultimately, the type of treatment taken and the place of treatment initiation (Ahorlu et al., 2006; Beiersmann et al., 2007). More research is needed to understand the influence of local illness concepts on treatment-seeking behaviors in Uganda.

Strengths and Limitations

There exist several limitations to this research that must be recognized. The first is survey fatigue. The third follow-up interview was the fourth interview at that point in time, and more than 70 households were lost to follow up. The people who either moved out of the study area or chose to end their participation in the study may be different than the rest of the population sample. The respondents who remained in the study may have been fatigued with answering the same questions about their family each month. As the data collection team utilized the same illness roster during each follow-up round, respondents may have been able to anticipate how to answer the questions in order to shorten the interview time. However, every effort was made to ensure that the same member of the data collection team visited the same caretakers in order to build a relationship and increase the likelihood that participants would dedicate an hour of their time. The enumerators may have also influenced responses about treatment-seeking behaviors. As the team became knowledgeable in malaria-related services and guidelines, it is possible that they subtly approved of seeking treatment outside the household. As the team developed a relationship with the respondents, they may have also fielded questions about malaria. In order to prevent enumerator influence, maintaining a neutral expression

and the importance of not encouraging or discouraging a specific response was emphasized during the enumerator training.

The second limitation deals with measurement of the explanatory variables of interest: attitudes. As explained in the methods section, respondents identified their attitudes and beliefs on a four-point scale of agreement. It was determined during the univariate analyses that many of the attitude variables were so highly skewed that it was not possible to include them in the final analyses. Social desirability may have influenced the general direction of one's opinion, but a larger scale (e.g. from 0-10) may have resulted in more variation among the sample. In this case, stronger beliefs and attitudes could be compared to weaker ones.

A third limitation is the fact that local illness concepts were not measured. Overall knowledge of the cause of malaria transmission was low. It is possible that local illness concepts and categorizations may have had a more significant effect on where caretakers initiate care.

Despite these limitations, this research provides additional information about treatment seeking behaviors for febrile illness than were identified in the literature. Previous studies focused primarily on behavior in terms of initiating care in the formal or informal sector. However, this study considers three levels of healthcare: home-treatment, the purchase of over-the-counter medications, and utilization of formal healthcare facilities. This type of analysis presents a much richer understanding of treatment-seeking behaviors. Furthermore, this research included various types of predictors, specifically attitudes and knowledge, whereas previous studies highlighted access and socio-demographic barriers to treatment seeking.

There is strong evidence that mild illness and limited access are not the only barriers to seeking care for possible childhood malaria. This research provides evidence that knowledge and attitudes contribute to health-seeking behaviors as well and assist in the formation of recurring patterns. Caretakers that are more knowledgeable about available antimalarials and who believe seeking care at higher levels of the healthcare system is more effective for treating malaria are more likely to initiate care at the highest levels of the healthcare system.

Policy Implications, Recommendations, and Future Research

The results of this study have several policy implications. Results indicate that caretakers of young child continue to rely on local drug shops and home treatment as the first point of care for non-serious illness. A policy that requires a blood confirmation before selling an ACT may greatly reduce presumptive treatment in local drug shops. While free diagnostic services should be promoted in formal healthcare facilities, laws that permit and encourage community-based facilities to sell and use RDTs will increase the accessibility of testing. Both drug shops and community health workers could be utilized to improve community-based management of childhood malaria. Finally, government-sponsored trainings for drug shop owners will increase their ability to understanding the dangers of mistreating childhood febrile illness. Many shop owners are well known within their communities, and may be in an ideal position to influence the behaviors of their customers.

Future research should focus on understanding local illness concepts for suspected malaria and febrile illness. Overall, accurate knowledge about malaria transmission was low. Identifying locally perceived causes of malaria will further the understanding of how

caretakers make the decision to self-treat versus seeking care in the formal health sector. This information will also assist in understanding how caretakers select specific drugs. Research could also focus on how caretakers develop attitudes about new malaria-related products and services in order to develop campaigns aimed at increasing perceived efficacy in the healthcare system.

Extensive health education campaigns are recommended that specifically target caretakers of young children with uncomplicated malaria or fever that is viewed as non-severe. Campaigns should focus on increasing malaria knowledge in terms of understanding of national treatment guidelines for malaria, and should highlight the risk of not treating malarial infections perceived as mild immediately with an ACT. Further emphasis should be placed on the fact that mosquitoes, and only mosquitoes, transmit malaria. Furthermore, malaria-carrying mosquitoes make very little noise. Campaigns should highlight this fact, and encourage caretakers to use bed nets every night, and not just when they hear mosquitoes.

A complimentary campaign is recommended that targets health workers that diagnose and treat malaria. These campaigns should encourage healthcare workers to adhere strictly to malaria test results, and not provide ACTs to negative patients. An additional focus should be to increase the quality of patient-provider relationships, and to capitalize on one-on-one interactions to explain national guidelines, other sources of fever, and the effectiveness of diagnostic confirmation. Healthcare workers should explain the child's diagnosis and the reasons for providing or prescribing certain treatments.

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Figure 4.1

Sample Selection Process

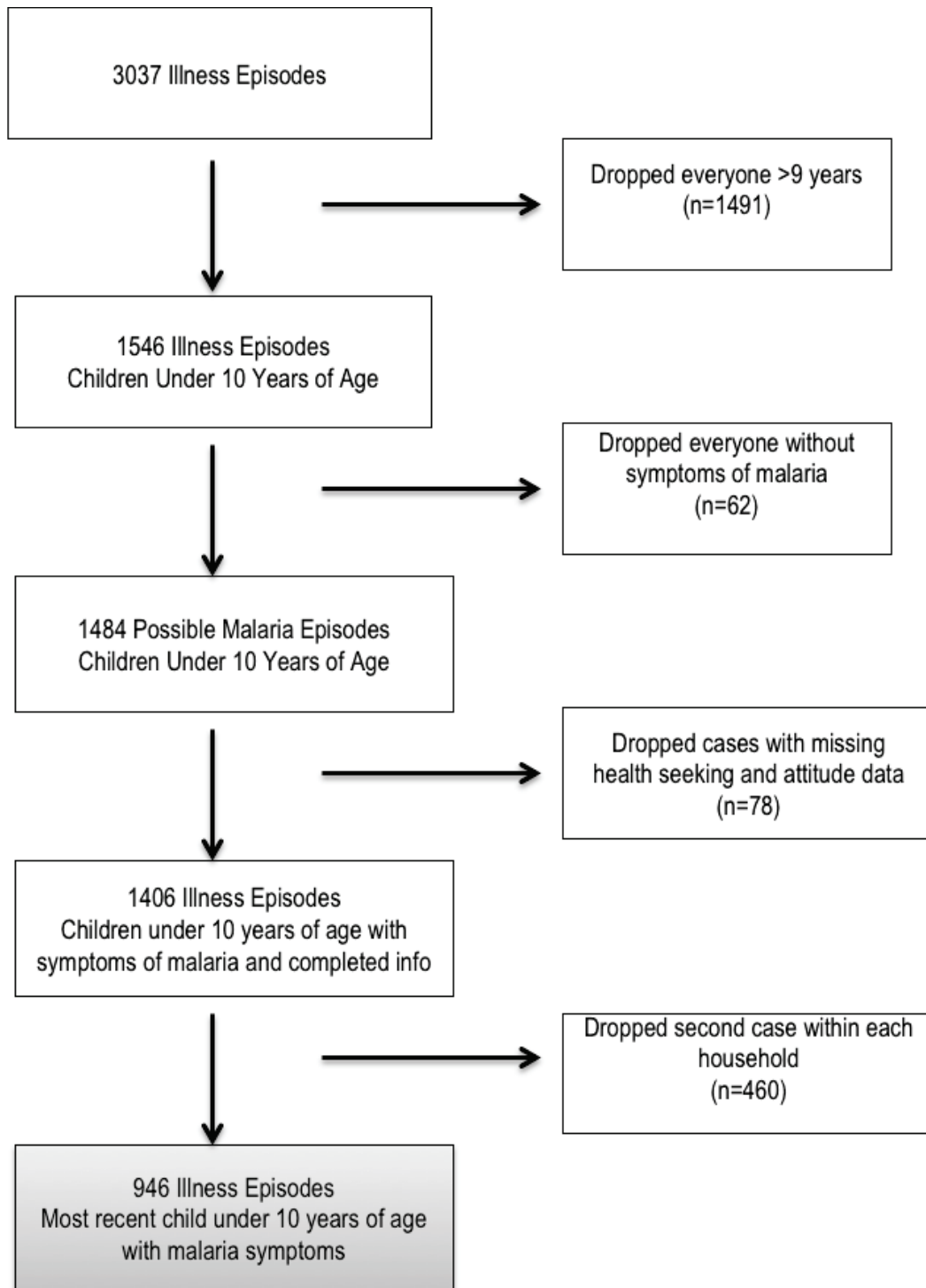


Table 4.1

<i>Sample Characteristics (n=946)</i>		
	N	%
Child's Gender		
Male	483	51.1
Female	463	49.0
Marriage		
Monogamous	585	61.8
Polygamous	217	22.9
Other	144	15.2
Education		
No education	148	15.6
Primary and Less	613	64.8
Secondary or Higher	185	19.6
Religion		
Catholic, Christian	424	44.8
Protestant, Adv	392	41.4
Muslim, Other	130	13.7
Work		
Unemployed	118	12.5
Farmer	602	63.6
Formally employed	226	23.9
Urban		
Rural	736	77.8
Urban	210	22.2
SES		
Low	243	25.7
Medium	352	37.2
High	351	37.1
Self-treatment Attitude		
Agree	715	75.6
Disagree	231	24.4
Test Adherence Attitude		
Agree	588	62.2
Disagree	358	37.8
Malaria Knowledge		
No Knowledge	317	33.5
Low Knowledge	449	47.5
High Knowledge	180	19.0
Fever Knowledge		
Low Knowledge	402	42.5
High Knowledge	544	57.5

Table 4.1A

<i>Sample Characteristics - Continuous Variables</i>					
	Median	Q1	Q2	SD	Range
Respondent's Age (years)	32	25	39	10.56	17-90
Child's Age (years)	3	1	5	2.76	0-9
Antimalarial Knowledge	2	2	3	1.21	0-7
Perceived Severity	6	4	8	2.40	0-10

Table 4.2

Behavioral Outcomes: Treatment Seeking Behavior (n=946)

Treatment Seeking Behavior	N (%)
Took herbs/medicines from home	253 (24.0)
Went to pharmacy or drug shop	385 (40.8)
Went to formal healthcare facility	334 (35.3)

Table 4.3

<i>Bivariate Associations between Predictors and Behavioral Outcome</i>				
	Home Treat	Drug Shop or Pharmacy	Formal Facility	P-value
	N (%)	N (%)	N (%)	
Child's Gender				0.771
Male	114 (23.6%)	202 (41.8%)	167 (34.6%)	
Female	113 (24.4%)	183 (39.5%)	174 (36.1%)	
Marriage				0.113
Monogamous	128 (21.9%)	251 (42.2 %)	206 (35.2%)	
Polygamous	60 (27.7%)	87 (40.1 %)	70 (32.3%)	
Other	39 (27.1%)	47 (32.6 %)	58 (40.3%)	
Education				0.001
No Education	33 (22.3%)	64 (43.2%)	51 (34.5%)	
Primary and Less	137 (22.4%)	275 (44.9%)	201 (32.8%)	
Secondary or Higher	57 (30.8%)	46 (24.9%)	82 (44.3%)	
Religion				0.635
Catholic, Christian	93 (21.9 %)	178 (42.0 %)	153 (36.1 %)	
Protestant, Adv.	97 (24.7 %)	157 (40.1 %)	138 (35.2 %)	
Muslim, Other	37 (28.5 %)	50 (38.5 %)	43 (33.1 %)	
Work				0.008
Unemployed	30 (25.4 %)	35 (29.7 %)	53 (44.9 %)	
Farmer	133 (22.1 %)	269 (44.7 %)	200 (33.2 %)	
Formally Employed	64 (28.3 %)	81 (35.8 %)	81 (35.8 %)	
Urban				<.001
Rural	176 (23.9%)	324 (44.0 %)	236 (32.1 %)	
Urban	51 (24.3 %)	61 (29.1 %)	98 (46.7 %)	
SES				0.072
Low	59 (24.3 %)	99 (40.7 %)	85 (35.0 %)	
Medium	74 (21.0 %)	162 (46.0 %)	116 (33.0 %)	
High	94 (26.8 %)	124 (35.3 %)	133 (37.9 %)	
Self-treat Attitude				0.001
Agrees	189 (26.4 %)	295 (41.3 %)	231 (32.3 %)	
Does Not Agree	38 (16.5 %)	90 (39.0 %)	107 (44.6 %)	
Test Adherence Attitude				0.042
Agrees	155 (26.4 %)	240 (40.8 %)	193 (32.8 %)	
Does Not Agree	72 (20.1 %)	145 (40.5 %)	141 (39.4 %)	
Malaria Knowledge				0.072
No Knowledge	72 (22.7 %)	139 (43.9 %)	106 (33.4 %)	
Low Knowledge	121 (27.0 %)	163 (36.3 %)	165 (36.8 %)	
High Knowledge	34 (18.9 %)	83 (46.1 %)	63 (35.0 %)	
Fever Knowledge				0.015
Low Knowledge	79 (19.7 %)	180 (44.8 %)	143 (35.6 %)	
High Knowledge	148 (27.27 %)	205 (37.7 %)	191 (35.1 %)	
	Mean (SD)	Mean (SD)	Mean (SD)	
Respondent's Age (years)	34.19 (11.16)	33.14 (10.05)	33.29 (10.72)	0.467
Child's Age (years)	3.40 (2.74)	3.48 (2.81)	3.18 (2.72)	0.343
Antimalarial Knowledge	2.37 (1.23)	2.35 (1.22)	2.60 (1.18)	0.016
Perceived Illness Severity	5.72 (2.47)	6.05 (2.35)	6.52 (2.35)	<0.001

Table 4.4

Unadjusted Odds Ratios between Socio-demographic Characteristics, Knowledge Scores, and Attitude Measures, and Behavioral Outcome

Variable	Home vs. Drug Shop	Home vs. Health Facility	Drug Shop vs. Health Facility
Unadjusted OR (95% CI)			
Marital Status			
Monogamous	1.00	1.00	1.00
Polygamous	.74 (.50–1.09)	.73 (.48–1.09)	.98 (.68–1.44)
Other	.62 (.38–.99)*	.92 (.58–1.47)	1.50 (.98–2.30)†
Education			
No Education	1.00	1.00	1.00
Primary or Less	1.04 (.65–1.65)	.95 (.50–1.55)	.92 (.61–1.38)
Secondary	.42 (.23–.74)**	.93 (.54–1.61)	2.23 (1.34–3.75)**
Work			
Unemployed	1.00	1.00	1.00
Farmer	1.73 (1.02–2.95)*	.85 (.52–1.40)	.49 (.31–.78)**
Formally Employed	1.08 (.60–1.95)	.72 (.41–1.25)	.66 (.39–1.12)
Urban			
Rural	1.00	1.00	1.00
Urban	.65 (.43–.98)*	1.43 (.97–2.12)	2.21 (1.54–3.16)***
SES			
Low	1.00	1.00	1.00
Medium	1.31 (.85–1.99)	1.09 (.70–1.69)	.83 (.57–1.21)
High	.79 (.52–1.20)	.98 (.65–1.50)	1.25 (.86–1.83)
Self-treat Attitude			
Agrees	1.00	1.00	1.00
Disagrees	1.51 (1.00–2.31)†	2.22 (1.46–3.37)***	1.46 (1.05–2.04)*
Test Adherence			
Agrees	1.00	1.00	1.00
Disagrees	1.30 (.92–1.84)	1.57 (1.10–2.24)*	1.21 (.90–1.63)
Malaria Knowledge			
No Knowledge	1.00	1.00	1.00
Low Knowledge	.70 (.48–1.01)†	.92 (.63–1.35)	1.33 (.95–1.85)
High Knowledge	1.26 (.78–2.06)	1.26 (.75–2.10)	1.00 (.66–1.51)
Fever Knowledge			
Low Knowledge	1.00	1.00	1.00
High Knowledge	.61 (.43–.85)**	.71 (.50–1.01)†	1.10 (.87–1.58)
Antimalarial			
Knowledge	.99 (.86–1.13)	1.17 (1.02–1.34)*	1.18 (1.05–1.233)**
Severity	1.06 (.99–1.14)†	1.15 (1.07–1.24)**	1.09 (1.02–1.16)**

Note. * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$; † $p \leq .10$

Table 4.5

Multinomial Logistic Regression of Socio-demographic, Attitude, and Knowledge Variables on Treatment-Seeking Behavior

Independent Variables	Home vs. DS Adj OR (95% CI)	Home vs. HF Adj OR (95% CI)	DS vs. HF Adj OR (95% CI)
Education			
No education	1.00	1.00	1.00
Primary or Less	1.01 (.62-1.63)	.84 (.51-1.39)	.83 (.54-1.27)
Secondary	.33 (.17-.61)**	.58 (.31-1.08)†	1.78 (1.01-3.14)*
Urban			
Rural	1.00	1.00	1.00
Urban	.79 (.50-1.25)	1.62 (1.05-2.51)*	2.05 (1.38-3.04)***
Work			
Unemployed	1.00	1.00	1.00
Farmer	1.45 (.83-2.53)	.86 (.46-1.31)	.59 (.36-.97)*
Formally Employed	1.17 (.63-2.16)	.60 (.34-1.08)†	.52 (.30-.90)*
Self-treat Attitude			
Agree	1.00	1.00	1.00
Disagree	1.66 (1.06-2.59)*	2.14 (1.37-3.34)**	1.29 (.90-1.85)
Test Adherence Attitude			
Agree	1.00	1.00	1.00
Disagree	1.11 (.71-1.60)	1.35 (.93-1.96)	1.22 (.89-1.68)
Malaria Knowledge			
No Knowledge	1.00	1.00	1.00
Low Know	.70 (.48-1.02)	.96 (.65-1.42)	1.37 (.97-1.94)†
High Know	1.37 (.83-2.28)	1.26 (.74-2.14)	.92 (.60-1.41)
Fever Knowledge			
Low Knowledge	1.00	1.00	1.00
High Knowledge	.54 (.38-.77)**	.72 (.50-1.04)†	1.32 (.97-1.81)
Antimalarial Knowledge			
Knowledge	1.08 (.93-1.25)	1.18 (1.01-1.37)*	1.09 (.95-1.24)
Severity	1.06 (.99-1.14)	1.16 (1.07-1.24)***	1.09 (1.02-1.16)**

Note. * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$; † $p \leq .10$

CHAPTER 5: MANUSCRIPT 3

Understanding antimalarial treatment outcomes for childhood malaria in Uganda: A multilevel analysis

Katrina Berg, MA

Johns Hopkins School of Public Health

Department of Health, Behavior and Society

Abstract

Background: Malaria is the leading cause of morbidity and mortality in children under five in Uganda. Artemisinin-combination therapy (ACT) is the recommended first-line treatment for uncomplicated malaria. However, children continue to receive non-ACT antimalarials that are less effective. The purpose of this study is to identify the determinants that affect appropriate treatment outcomes.

Methods: Data on 2106 cases of suspected malaria in children under ten years of age were collected in face-to-face interviews. Multilevel modeling was used to determine predictors of antimalarial treatment outcome: ACT versus non-ACT treatment.

Results: Although ACT use was common among caretakers of children under ten years of age, more than a third of children treated for suspected malaria received a non-ACT antimalarial (34%) such as quinine or chloroquine. Place of initial treatment-seeking, malaria knowledge, attitudes about malaria tests, and religion were associated with the child receiving an ACT. Children who were under five years of age, were tested for malaria, and whose caretakers perceived their illness to be more severe were more likely to receive a non-ACT antimalarial.

Conclusion: Interventions are needed to increase consumer awareness about treatment recommendations and malaria knowledge. More research is needed to understand how caretakers in Uganda perceive the efficacy of first-line ACTs as compared to the previously recommended antimalarials.

Background

More than 3 billion people are at risk for malaria each year. In 2012, there were an estimated 207 million malaria cases, and 627,000 deaths globally (WHO, 2013). However, malaria disproportionately affects sub-Saharan Africa. Almost 80% of the estimated malaria cases, and more than 90% of the deaths occurred in sub-Saharan Africa (WHO, 2013). Seventy-seven percent of all deaths worldwide occurred among children under five years of age, making them one of the most vulnerable populations (WHO, 2013). Due to a collaboration of international efforts, significant progress has been seen in the reduction of the malaria disease burden. Between 2000 and 2012 malaria mortality rates dropped by 42% in the world, and by 49% in Africa. In the same time period, mortality rates among children under five dropped by 51% in the world, and by 54% in Africa (WHO, 2013). Unfortunately, it appears that the decrease in malaria mortality has slowed down in recent years from 2011-2013 (WHO, 2013).

More than 90% of the population in Uganda lives in high transmission areas, and are at risk for malaria year round (WHO, 2013). *P. falciparum* is responsible for all of the malaria transmission in the country. Uganda has one of the highest malaria burdens in the world, and is one of five African countries that make up 50% of all global deaths, and 47% of all malaria cases (RBM Partnership, 2012). In 2012, Uganda reported more than 13.5 million cases, and almost 100,000 deaths (WHO, 2013). This presents a significant burden on both the formal and informal health care sectors. Malaria accounts for between 30% and 50% of all outpatient care cases, between 15% and 20% of all admissions, and between 9% and 14% of inpatient deaths (UBOS, 2010). Although the number of

reported cases of malaria has dropped by 50% in Uganda from 2006 to 2011, malaria remains the leading cause of childhood mortality (Republic of Uganda, 2013).

The WHO recommends artemisinin-based combination therapies (ACT) as first-line treatment for uncomplicated *P. falciparum* malaria (WHO, 2010). However, several antimalarials that are not recommended as first-line therapy for the treatment of uncomplicated malaria are still available at all levels of the health care system. In the public sector in Uganda, antimalarials are provided free-of-charge. Most public health centers stock and distribute government-recommended ACTs for malaria. In the informal sector, both government-recommended ACTs as well as non-ACT antimalarials are available for customers to purchase without a prescription. According to the Roll Back Malaria Task Force, poorer people frequently buy non-ACT antimalarials that are ineffective, and that may promote resistance (RBM Partnership, 2008). Through the Global Fund's financing mechanism, Affordable Medicine Facility – malaria (AMFm), ACTs have been subsidized to make them more affordable and to increase availability in both the informal and formal sectors (RBM Partnership, 2007).

Despite these recommendations, non-ACT use is still common. Previous studies indicate that non-ACT antimalarials continue to be the first treatment choice for suspected uncomplicated malaria. Studies conducted throughout Africa indicate that less than half of suspected malaria cases are initially treated with recommended ACT antimalarials (Aborah et al., 2013; Littrell, et al., 2013; Watsierah, Jura, Oyug, Abong'o, & Ouma, 2010). Studies in Nigeria and Ghana present ACT-use rates as low as 6 - 23% (Buabeng et al., 2007; Mangham, et al., 2011). In some cases, however, ACT-use rates are much higher. Studies in Nigeria, Cameroon, and Tanzania report that just over 50%

of patients follow recommended treatment guidelines (Cohen et al., 2013; Mangham-Jefferies, Hanson, Mbacham, Onwujekwe, & Wiseman, 2014). While these higher rates of appropriate antimalarial show promise for increased ACT uptake, the continued widespread use of non-recommended antimalarials including quinine, SP, and chloroquine, is concerning.

When children present with fever or other malarial symptoms, caretakers may engage in several behaviors including treating at home with herbs or medical drugs, purchasing drugs from local drug shops without a prescription, or seeking care at a higher-level health facility, including public health centers, private clinics, and hospitals. Self-treatment is the most common first step in the illness-resolution process with caretakers providing drugs to their children from home or a local shop (Abuya et al., 2007; Holtz et al., 2003; Mbonye, Bygbjerg, & Magnussen, 2008; Mukanga et al., 2012; Tobin-West & Babatunde, 2011).

In pharmacies and drug shops, consumer demand for specific drugs largely influence which medicines shopkeepers choose to stock (Palafox et al., 2014; Rusk et al., 2012). A qualitative study with medicine wholesalers indicated that consumers opted for drugs that had fewer side effects, came in a single dose to reduce long periods of side-effects, and that they were accustomed to using from previous experiences (Ringsted, Massawe, Lemnge, & Bygbjerg, 2011). The impact of consumer preferences for specific medicine is not limited to the private sector. Consumers may also influence public health care provider attitudes towards antimalarials, and ultimately which drugs they choose to prescribe (Mangham-Jefferies et al., 2014).

Recognizing the role that consumer culture plays on antimalarial-use in children is critical to increasing ACT uptake for all malaria cases. Previous research indicates that consumer preferences for specific antimalarial treatment are influenced by various factors. Children of caretakers who perceive ACTs to be affordable and effective (Palafox et al., 2014) and who are aware of ACTs (Ajayi, Soyannwo, & Akpa, 2013) are more likely to receive an ACT. Other determinants that affect ACT utilization include children in the highest SES stratum (Talisuna et al. 2012), children who are under five years of age, and children whose parents have completed higher levels of education (Mangham et al., 2011).

In Uganda, ACT-use has increased drastically in recent years, although reported rates vary. According to the Malaria Indicator Survey, just over half of the children who received an antimalarial took an ACT (UBOS, 2010). The most recent Demographic and Health Survey indicated an increase in ACT-use in recent years, and reported that 69% of febrile children who took an antimalarial, received an ACT (UBOS, 2012). However, according to Littrell et al., (2013), only 36% of children who took an antimalarial during their last febrile illness took an ACT. Although recent research report divergent rates in ACT-use, it is clear that caretakers of children under five continue to engage in widespread use of non-ACT antimalarial use.

Increasing access through wider distribution and subsidization of the cost of ACTs has played a significant role in increasing ACT-use. It is hypothesized, however, that access and price are not the sole barriers to appropriate antimalarial treatment. Understanding the various and complex influences on antimalarial treatment outcomes will be integral in informing interventions and national policies to increase uptake in

nationally recommended ACT-use for all children. The specific aims of this paper are 1) to document antimalarial use among children under ten years of age with suspected malaria, and 2) to identify salient determinants of appropriate antimalarial treatment.

Methods

Data Source

Data for this manuscript are from the study “Evaluating the Feasibility of Introducing Malaria Diagnosis in the Private Sector in Eastern Uganda,” which was a longitudinal study that monitored health-seeking behaviors for suspected malaria. Participating households completed a baseline survey, 9 monthly follow-up interviews as well as an endline survey between March 2011 and May 2012. In order to be eligible for the study, participants had to be 18 years of age, the recognized female head of household, able and voluntarily willing to complete future monthly follow-up interviews, and able to speak one of the two main local. All surveys and informed consent forms were translated into Ateso and Luganda, the two most prevalent languages throughout the six districts. Interviews were conducted in either Ateso or Luganda, according to the participants’ preferences. Respondents who could not speak Ateso or Luganda were excluded from participating in the study. In the event there was not a female head of household eligible for enrollment, the male head of household was recruited.

A total of 2560 heads of household were recruited to participate in the study during the baseline phase. All baseline and follow-up interviews were conducted face-to-face. Baseline interviews lasted about an hour, while follow-up interviews ranged between ten minutes and an hour depending on the number of sick people in the household. During the baseline survey, data were collected on demographic information,

household members, malaria knowledge, treatment-seeking behavior for the respondent and a child under five, and attitudes about malaria. The nine monthly follow-up interviews collected data on the treatment-seeking behaviors for all illnesses experienced by all household members since the previous interview. The endline survey captured the final round of behaviors, and measured malaria incidence through blood confirmation in order to measure malaria incidence in the study sample.

Data Sample

Data collected during follow-up rounds 8 and 9, the final two follow-up rounds of the study, were used for the analysis. At the time of the data collection for these rounds, the AMFm had made ACTs widely available at a subsidized rate. During earlier rounds, ACTs were not available for purchase in many of the local drug shops or they were much more expensive than non-ACT antimalarials. Data from the final two rounds were included in order to compare rates of antimalarial-use when appropriate treatment, ACTs, and sun-standard antimalarials were more equally available and similar in price. During these two rounds, a total of 5667 illness episodes were documented. Of these, 2570 cases involved household members 10 years of age or older, and were excluded from the analysis. Seventy-five of the children under ten years of age reported no signs of malaria or febrile illness, and were excluded as well. Of these 3022, 529 surveys were dropped due to missing information on attitudes or behavior. As the outcome of interest was antimalarial choice, children who had not taken an antimalarial treatment were excluded from the analysis (n=387). The final sample of respondents from follow-up rounds 8 and 9 who had a child with suspected malaria, provided complete behavioral information, and

took an antimalarial treatment at some point in the illness resolution process was 2106.

Figure 5.1 presents the sample selection process.

Measures

Dependent Variables

The dependent variable was type of antimalarial first taken by the sick child during the illness episode. Respondents were asked to list medicines taken during all steps of the illness resolution process. Children who did not take an antimalarial during any part of the illness resolution were excluded from this analysis. Responses were coded into two categories: artemisinin combination-based therapy (ACTs) and non-artemisinin combination-based therapy (non-ACTs). Non-ACTs antimalarials included both artemisinin monotherapies and any antimalarial treatment that does not contain artemisinin combined with another drug.

Independent Variables

Independent variables included socio-demographic variables, case-specific characteristics and behavior, as well as knowledge and attitude variables.

Socio-demographic variables. During the baseline survey, caretakers were asked a variety of demographic questions including their age, the age of the sick child, the highest level of school they completed, typical items they owned in the household, occupation, and religion.

Respondent's age. A continuous variable was created that indicated caretakers' self-reported age in years.

Child's age. Caretakers reported the child's age at the time of the recorded illness. A dichotomous variable was created with children under five years of age and children aged 5 to 9 years.

Child's gender. Children were recorded as male or female, as reported by their caretaker.

Education. Caretakers were asked the highest grade or level of education they had achieved. A categorical variable was created that included the following categories: no education, primary, and secondary or higher. Caretakers who had never attended any formal school were categorized as no education. Caretakers who had attended at least one year of primary school grade were labeled as primary, regardless of whether or not they had completed this level. Secondary or higher included anyone who had attended any level of secondary school, vocational school, or university.

Urban. A binary variable was created based on the urban or rural location of the household's village. All villages that were located in a town council were categorized as urban. All other villages were categorized as rural.

Socioeconomic status (SES). SES was based on ownership of household items, land, and building materials of the house. Household items included mobile phones, adult bicycles, solar panels or electricity, radios, televisions, motorcycles, and vehicles. Caretakers were categorized as owning the land if they had a title, and did not rent the land, squat on the land, or use it free-of-charge from an employer or family member. Household building materials included walls made from cement bricks, a finished floor, and an iron or tin roof. A continuous variable was created, and each household received a point for each item they owned.

Religion. Caretakers were asked about their religious affiliation. A categorical variable was created that included Catholics; Protestants and Born Again Christians; and Muslims.

Marriage. Caretakers were asked their marital status. A categorical variable was created that included the following categories: monogamous, polygamous, and other. The “other” category includes caretakers who reported their marital status as widowed, divorced/separated, or never married/never cohabitating.

Self-treatment attitude. Caretakers were read the following statement: you should first try to treat malaria at home before going to a clinic. They were then asked if they strongly agree, sometimes agree, sometimes disagree, or strongly disagree with this statement. A dichotomous variable was created based on agreement and disagreement.

Test adherence attitude. Caretakers were read the following statement: you should take antimalarial medicine, even if your malaria test is negative. They were then asked if they strongly agree, sometimes agree, sometimes disagree, or strongly disagree with this statement. A dichotomous variable was created based on agreement and disagreement.

Malaria test accuracy attitude. Caretakers were read the following statement: malaria test results at local health centers are accurate. They were then asked if they strongly agree, sometimes agree, sometimes disagree, or strongly disagree with this statement. A dichotomous variable was created based on agreement and disagreement.

Fever knowledge. Caretakers were read the following statement: fever is often caused by illnesses other than malaria. They were then asked if they strongly agree,

sometimes agree, sometimes disagree, or strongly disagree with this statement. A dichotomous variable was created based on agreement and disagreement.

Malaria knowledge. Caretakers were asked to freely name all the ways that someone could contract malaria. In the Luganda language, malaria is known as *omusujja gw'ensiri*, which is translated as “fever caused by malaria.” This is the term used by the Ministry of Health when referring to malaria. In Ateso, the word used for uncomplicated malaria is *eimidi*. This term is translated simply into malaria.

A categorical variable was created that included having no knowledge, low knowledge, and high knowledge. Caretakers who did not state the correct answer without prompting (mosquitos) were considered to have no knowledge. Caretakers who stated mosquitoes, but also provided at least one incorrect answer, were considered to have low knowledge. Caretakers who stated the correct answer only, mosquitoes, were labeled as having high knowledge.

Antimalarial knowledge. Enumerators elicited a free list of all antimalarials that the caretakers could name. Antimalarials were defined for the participants as drugs used to treat malaria. A discrete variable was created that summed all correctly identified antimalarial medicines.

Perceived illness severity. Caretakers were asked to rate how severe they thought the illness was on a scale from 0-10. A discrete variable was created based on caretakers' self-reported perception of the child's illness severity.

Perceived malaria prevalence. Caretakers were asked to ‘think about 10 adults that you know well in your neighborhood. How many had malaria in the last month (30 days)?’ The same question was asked about older children (age 5-14) as well as young

children (under five years of age). For each caretaker, an average of all three responses was calculated.

Malaria testing. At each point of care during the illness resolution process, caretakers were asked if their child was blood-tested for malaria. A dichotomous variable was created based on the child being blood-tested or not blood-tested for malaria.

Place of initial treatment. Respondents were asked where they initiated treatment for their child. Three levels of treatment seeking behaviors were defined: 1) took herbs or medicines from home 2) went to a drug shop or pharmacy, and 3) went to a formal healthcare facility. “Took herbs or medicines from home” included taking herbs or biomedical drugs from home or from a neighbor. “Went to a drug shop or pharmacy” included going to a drug shop, mobile vendor or pharmacy to purchase drugs. “Went to a formal healthcare facility” included going to public health centers or private clinics/hospitals.

Data Analyses

Frequency and summary statistics were calculated for the dependent variable as well as the predictor variables of interest. A description of all variables is presented, including the frequencies and percentages for all categorical variables, and the means and standard deviations for all continuous variables.

Bivariate analyses were conducted with the dependent variable and all explanatory variables of interest. A Student’s t-test was used to test for bivariate associations between continuous predictor variables and the outcome of interest. For all categorical variables, bivariate associations were calculated using Pearson’s χ^2 tests.

Simple logistic regressions were run to calculate unadjusted associations between all explanatory variables and antimalarial choice.

Many of the surveyed households experienced more than one potential malaria illness during the two follow-up rounds. It is hypothesized that caretakers engage in similar behaviors for illnesses with comparable symptoms. All surveyed participants reside in 92 individual villages. All of the villages are small communities, with most households in each one having the same access to various types of health facilities, drug shops, and medicine options. Therefore, it is hypothesized that behavior may cluster within both the household and the village. A multilevel logistic regression was employed to calculate the adjusted associations among predictor variables and antimalarial choice.

First, an empty model was estimated that contained a random intercept and no predictors. Then, all socio-demographic, behavioral, knowledge, and attitude variables with a $p\text{-value} \leq .20$ were retained to for inclusion in the final model. All analyses were conducted using Stata 12.1 Statistical Package (StataCorp 2012).

Results

Sample Characteristics

Socio-demographic characteristics. The mean age of the respondents was 33 years (SD: 10:08, range: 18-80). Just over half of the children (51%) were male. Almost 70% of the children were under five years of age, and 30% were five years or older. Of a maximum score of 10, the average SES score was 3.87 points (SD: 2.09, range: 0-10). More than 80% of the respondents lived in a rural area. Almost 65% of the respondents were in a monogamous marriage, 22% were in a polygamous marriage, and 13% were

widowed, divorced or never married. More than 85% of the respondents had completed some formal schooling with only 14% who had never attended school. Of the respondents who attended school, 67% completed at least one year of primary school, and 19% completed at least one year of secondary school. Almost 59% of the caretakers were Protestant, and 30% were Catholic. A little more than 11% of the caretakers were Muslim. Full sample characteristics are presented in Table 5.1.

Malaria attitudes and knowledge. More than three-quarters (78%) of the respondents disagreed that malaria tests at their local health facilities are accurate. About a third (32%) of the respondents were categorized as having no malaria knowledge, meaning that they were unable to freely state that mosquitoes transmit malaria. A little less than half the sample (47%) had low malaria knowledge, and 20% had high knowledge. Almost 62% of the respondents had high fever knowledge, while 38.15% were categorized as having low fever knowledge. The mean antimalarial knowledge score was 2.41 (SD: 1.17, range: 0-7).

Perceived severity and malaria prevalence. The mean perceived severity was 6.55 (SD: 2.31, range: 0-10). On average, respondents thought 5.30 of every 10 people had malaria in the last month.

Health-seeking behaviors. A little more than one-quarter of the children (28%) were blood-tested for malaria during their last suspected case of malaria. Almost a third (33%) of caretaker initiated treatment at home, and 36% went to a drug shop or pharmacy. Almost a third (31%) initiated care at a formal healthcare facility.

Type of antimalarial taken. The majority of the children (66%) received an ACT during their last suspected case of malaria, while more than a third of children with

suspected malaria (34%) received a non-ACT antimalarial. Of the children who received a non-ACT antimalarial, 81% took quinine, 10% took an artemisinin monotherapy, 6% took chloroquine, and 3% took SP.

Bivariate Analyses

Bivariate analyses were conducted on all potential predictor variables and the behavioral outcome: ACT use versus non-ACT use. All bivariate associations are presented in Table 5.2. Fever knowledge, perceived severity of the illness, the child getting blood-tested for malaria, attitude about malaria blood tests, religion, urban residence, SES, antimalarial knowledge, malaria knowledge, age of the child, perceived malaria prevalence, and place of initial treatment all had a p -value $\leq .2$ and were retained to use in building the multilevel model. Self-treatment attitude ($p = .859$), test adherence attitude ($p = .813$), respondent education level ($p = .269$), marriage ($p = .964$), and the child's gender ($p = .808$) were not significant at the bivariate level, and were excluded from the analysis.

Table 5.3 includes all the unadjusted odds ratios. Muslim caretakers were almost 40% less likely to give their child an ACT as compared to their Catholic counterparts ($p = .005$). Children five years of age and older were 24% more likely to receive an ACT during their last suspected malaria episode as compared to children under five years of age ($p = .033$). No other socio-demographic variables were significantly associated with the type of antimalarial given to the child.

Both attitude about malaria tests and malaria knowledge were associated with type of antimalarial given to the sick child. Caretakers with more positive attitudes about the accuracy of malaria blood tests were 27% more likely to give their child an ACT over

a substandard antimalarial ($p = .028$). Caretakers with high malaria knowledge were 58% more likely to give their child an ACT as compared to caretakers with no malaria knowledge ($p = .001$).

Two behaviors, getting tested for malaria and initiating treatment at a formal health facility, were significantly associated with type of antimalarial provided as well. Children who were blood-tested for malaria were 40% less likely to take an ACT as compared to those who were not tested ($p < .001$). Children whose caretakers sought care at a formal healthcare center were 49% less likely to get an ACT as compared to those who engaged in home-treatment ($p < .001$), and 70% less likely to get an ACT if they sought care at a drug shop as compared to treating at home ($p < .001$). Finally, for each unit of perceived severity, caretakers were 12% less likely to provide an ACT to their child ($p < .001$).

Multilevel Modeling

The empty model indicated that both the household and village-level variances are significant. The intraclass correlation (ICC) indicates that 7% of the total variance in antimalarial use is due to the differences across villages, and 49% is due to the differences among households. Results from the empty model estimation are presented in Table 5.4.

All adjusted odd ratios for the final model are included in Table 5.5. When controlling for all other variables, caretakers who initiated the treatment-seeking process at a formal healthcare facility were 40% less likely to get an ACT ($p = .013$) as compared to caretakers who initiated treatment at home. Caretakers who went to a drug shop first

were almost 80% less likely to get an ACT ($p < .001$) as compared to caretakers who treated at home. Muslim caretakers were almost 50% less likely to give their child an ACT as compared to Catholic caretakers ($p = .017$). There was no significant difference between antimalarial choice between Protestant and Christian caretakers ($p = .275$).

Both malaria knowledge and caretaker attitudes about malaria tests were significantly associated with appropriate antimalarial choice. Caretakers with high malaria knowledge, as compared to those with no malaria knowledge, were 78% more likely to give their sick child an ACT over a non-ACT antimalarial ($p = .022$). However, there was no significant difference in antimalarial treatment between caretakers with low malaria knowledge and no malaria knowledge. Caretakers with positive attitudes about the accuracy of malaria blood tests were 51% more likely to give their child an ACT over a non-ACT antimalarial ($p = .054$).

Surprisingly, caretakers who perceived their children to have a more severe illness, caretakers whose children received a blood test for malaria, and children under five years of age were less likely to get an ACT. Caretakers who perceived their child's illness to be more severe were almost 11% less likely to give their child an ACT ($p < .001$). Children who were blood-tested for malaria were 54% less likely to receive an ACT ($p < .001$). Children who were at least five years of age were 37% more likely to receive an ACT ($p = .030$) than children under five years of age. Neither SES level nor antimalarial knowledge had any effect on antimalarial choice.

Discussion

Children whose caretakers initiated care at home were more likely to receive an ACT. This is contradictory to what has been found in other studies where children who

were taken to a formal healthcare facility were more likely to receive an ACT (Buabeng et al., 2007; Littrell, et al., 2013). This finding is quite unexpected, but may be an indirect effect of the widespread availability of ACTs. It is well known that caretakers prefer to initiate treatment at home, especially for perceived mild cases of malaria. What is unknown from these results is whether caretakers store drugs in preparation for future malaria cases or if they are left over from previous episodes. If they are leftover drugs, it is possible that the increased ACT-use rates have resulted in increased rates of ACTs stored at home. If this is the case, however, it is possible that patients with malaria are not completing the recommended doses and storing partial doses.

It is unclear as to why children of Christian and Protestant caretakers were more likely to get an ACT as compared to Muslim caretakers. More research is needed to understand differences in health-seeking behaviors among various religions. This finding suggests that health education campaigns should focus on areas with high Muslim populations to encourage appropriate treatment-seeking behaviors and to possibly work with local religious leaders to identify specific barriers to treatment.

Knowledge of malaria transmission and perceived efficacy of malaria tests were both associated with ACT-use. Children of caretakers who could correctly identify mosquitoes as the correct, and only cause, of malaria were more likely to receive an ACT. There was no difference between caretakers who could not correctly identify the cause of malaria and those who identified both correct and incorrect causes. Caretakers with both low and no malaria transmission knowledge erroneously believe that something other than mosquitos can transmit malaria. People who rely on local illness concepts and beliefs about disease transmission and causes to guides their treatment practices may be

more likely to continue using the same antimalarials that they are accustomed to.

Children whose caretakers had stronger beliefs about malaria test accuracy were more likely to receive the recommended antimalarial drug. It may be likely that caretakers with high levels of malaria knowledge and perceived efficacy towards malaria-related services may be more likely to be aware of nationally-recommended treatment guidelines and to follow them. These results suggest that improved educational campaigns are needed.

Surprisingly, children who were blood-tested were less likely to receive an ACT. Almost 92% of the children who were blood-tested had positive results for malaria, and 44% of positive tests received a non-ACT antimalarial. These results suggest that caretakers may be more likely to use malaria tests when they are certain that their child has malaria, as very few of the tests were negative. If the caretakers paid for the blood test, it is possible that even though the test indicated malaria, they opted for cheaper drugs to reduce the overall cost.

The findings that children whose parents perceive their child to have more severe illness and younger children were more likely to receive a non-ACT antimalarial is concerning. It is possible that respondents answered the question about severity in a manner different than was initially intended, raising questions about the validity of the responses. At the beginning of each illness roster, caretakers were asked about the severity of their child's illness. This question could have been understood to ask about the illness severity overall, from the first symptom through illness resolution. If this was the case, caretakers who gave their children an ACT may have experienced a faster reduction in fever and other malarial symptoms, and therefore perceiving the illness as a whole to not have been as severe. Caretakers who gave their child non-ACT antimalarials

may have waited a longer period of time to see a reduction in symptoms or may have had to seek additional care.

The finding that children over the age of five were more likely to get an ACT contradict the results from a pilot study conducted in drug shops in Uganda that found children under five years of age were more likely to receive the recommended treatment compared to older children (e.g., Talisuna et al., 2012). However, national survey results indicate that among young children, those between the ages of three and four were more likely to receive an ACT as compared to children under three years of age (UBOS, 2012).

When considering the various findings together, the children most at risk, the children with more severe illness, and the children with confirmed malaria are all more likely to take a non-ACT antimalarial. Although these results are surprising, they are consistent. It may be possible that when caretakers are more certain about the presence of malaria, whether it is through a confirmed blood test or a severe illness, they are less likely to use a drug that they are not as familiar with. Rutebemberwa, et al., (2009) found that caretakers in Uganda continued to perceive Chloroquine and sulfadoxine-pyrimethamine (SP) as effective drugs after they had stopped being recommended as first-line drugs for malaria treatment. Previous studies from Uganda suggest that caretakers do not understand the nationally-recommended treatment guidelines, and cannot name the first-line drug (Littrell, 2013; Rutebemberwa, et al.,). Drug retailers in Tanzania indicated that their customers based their preferences partially on their past experiences with the drug, indicating that it takes time to accept new drugs on the market (Ringsted et al., 2011). Several other studies indicate that previous experiences in the healthcare sector influence where caretakers seek treatment during the next suspected

malaria episode. Positive experiences encourage caretakers to engage in the same treatment behaviors, while negative actions may deter caretakers from returning (Chibwana et al., 2009; Idowu et al., 2008; Iwelunmor et al., 2010). Previous experiences with antimalarials influence which drugs caretakers choose for subsequent cases. If caretakers have high levels of perceived efficacy in non-ACT antimalarials based on previous experiences, they may be wary to try a new drug for the first time, especially on young children, when the illness is severe, or when they have confirmed the presence of malaria parasites.

Strengths and Limitations

There exist several limitations to this research. The first is the attrition rate over the 12 months of the study. Since the baseline enrollment, 270 households (10%) were lost to follow-up. The people who either moved out of the study area or chose to end their participation in the study may be different than the rest of the population sample.

Another limitation is reporting bias due to survey fatigue. Participating caregivers were interviewed up to ten different times over the period of twelve months. The interview format was the same each visit, and respondents could have omitted some illnesses in order to shorten the interview times. In order to mediate potential fatigue, enumerators worked with the same households each month in order to develop a relationship with the respondents, and to encourage participant willingness for dedicate an hour of their time each month. Small gifts of typical household items were provided to respondents to show appreciation for their time.

A third limitation is that ACT-use was self-reported. Subsidized ACTs were introduced and heavily promoted halfway through the study, and before the collection of the data used in this analysis. Due to promotional campaigns emphasizing ACTs, it is possible that the word ‘ACT’ was viewed as an equivalent for ‘antimalarial.’ In order to reduce ACT reporting bias, enumerators never asked if their child received an ACT directly; respondents openly listed the drugs their child received. In their responses, many caretakers stated the most common brand name, ‘Coartem,’ which indicates a greater likelihood of accuracy as compared to caretakers who listed, ‘ACT.’

Finally, the malaria transmission variable was taken from an earlier survey round in the study. It is assumed that malaria knowledge had not changed significantly over time. Local illness concepts greatly affect how people perceive the causes and levels of malaria. While more people may have understood that mosquitoes transmit malaria, it is unlikely that many people stopped believing local perceptions of transmission.

Despite these limitations, the results of this study contribute to a growing body of literature on antimalarial treatment use. Previous studies focus predominantly on socio-demographic and access factors such as SES, cost, caregiver education, child’s age, and place of treatment. This study has considered several knowledge and attitude factors that assist in understanding antimalarial treatment outcomes, and has identified key determinants of appropriate antimalarial utilization.

The results from this analysis present an encouraging picture of ACT uptake that encourages the subsidization and expanded distribution of ACTs. This research has provided valuable insights into understanding the caretakers who continue to rely on non-ACT antimalarials. The finding that the most severe illness and most at risk populations

may be some of the last people to prefer ACTs over previously-recommended drugs is critical in designing policies and interventions that encourage appropriate treatment outcomes.

While this research was conducted on a sample of the population in the eastern region of Uganda, the findings may be generalizable to other regions in the country. Furthermore, the results may be transferable to other countries and situations. These findings may be useful in understanding antimalarial utilization in other malaria-endemic countries in Africa as well. The way in which people develop preferences for health products, services, and medical drugs are similar across many cultures. Caretaker hesitation to try a new drug on her young child may not only apply to malaria, but other childhood illnesses as well. It may be further applied to understanding how caretakers perceive the efficacy of malaria testing and uptake testing behavior. This information may be useful in understanding the uptake of various types of health services or products.

Policy Implications, Recommendations, and Future Research

The uptake of ACT-use for children with suspected malaria has been promising after the introduction of subsidized ACT drugs through the AMFm. It appears that the increase in access, especially in local areas, coupled with the reduction in price has had a significant effect on the overall use of ACTs, as made apparent by the high rates of reported ACT use at home and in drug shops. However, a third of children continue to receive non-ACT antimalarials as the first treatment for malaria. Most alarming is that younger children, those with more severe illness, and those with confirmed malaria appear to rely on non-ACT antimalarials.

If caretakers in Uganda are still learning to accept ACTs as the most effective drug available for their children, then it would follow that until they become more commonplace, and they view non-ACT antimalarials as ineffective, that changing their behavior for small children, the most at risk, would be slower to occur. Studies focusing on RDT-use in Uganda and Tanzania found that children under five with negative test results were more likely to receive an antimalarial as compared to older children although international and national guidelines advise against this behavior (Ishengoma, et al., 2011; Kyabayinze et al., 2010; Mubi et al., 2011). These results provide further evidence that caretakers are less likely to make changes in their treatment-seeking behaviors for their young children, and will continue engaging in the same behaviors until new behaviors or drugs become the norm.

National drug administration bodies may consider limiting the availability of monotherapies and non-artemisinin based therapies that are available in local drug shops. Previous research indicated that oral artemisinin monotherapies (AMT) were stocked by 76% of all wholesalers, and non-ACT drugs were stocked by 89% of wholesalers (ACTwatch Group & PACE/Uganda, 2013). As structural barriers appear to have limited the use of appropriate treatment in the past, it would follow that limiting access to non-ACT antimalarials would decrease their use.

Furthermore, high rates of non-ACT antimalarial use occur at formal healthcare facilities. The provision of these drugs may create confusion about which drugs are recommended and are more effective. Patient-provider interactions are an ideal opportunity to educate caretakers about recommended treatment. Health workers should be trained in how to discuss the various treatment options, explain the risk of using non-

ACT drugs, and to encourage their patients to seek recommended ACTs for every case of malaria.

Intense health education campaigns are recommended to increase awareness, confidence, and utilization of national treatment guidelines and government recommended ACTs. Campaigns must focus on risks of using non-ACT antimalarials. Caretakers may be exposed to campaigns promoting ACTs, but are not aware that they should replace the use of previously-recommended antimalarials. Campaigns should focus specifically on encouraging caretakers with young children and with severe illness to immediately seek appropriate treatment. Finally, health education campaigns need to highlight the importance of finishing the recommended ACT doses. The high rates of reported ACT-use at home may indicate that household members are not completing the entire recommended dose, and are storing them for future use.

Future research is recommended to explore how much caretakers understand about testing and treatment guidelines, how they decide to try new treatments that become available, and how they perceive the effectiveness of ACTs, especially as they compare to non-ACT that they had relied on for many years. What is particularly important to explore is how caretakers process the information of not using drugs that had been promoted through healthcare facilities, national guidelines, and campaigns for many years.

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Figure 5.1

Sample Selection Process

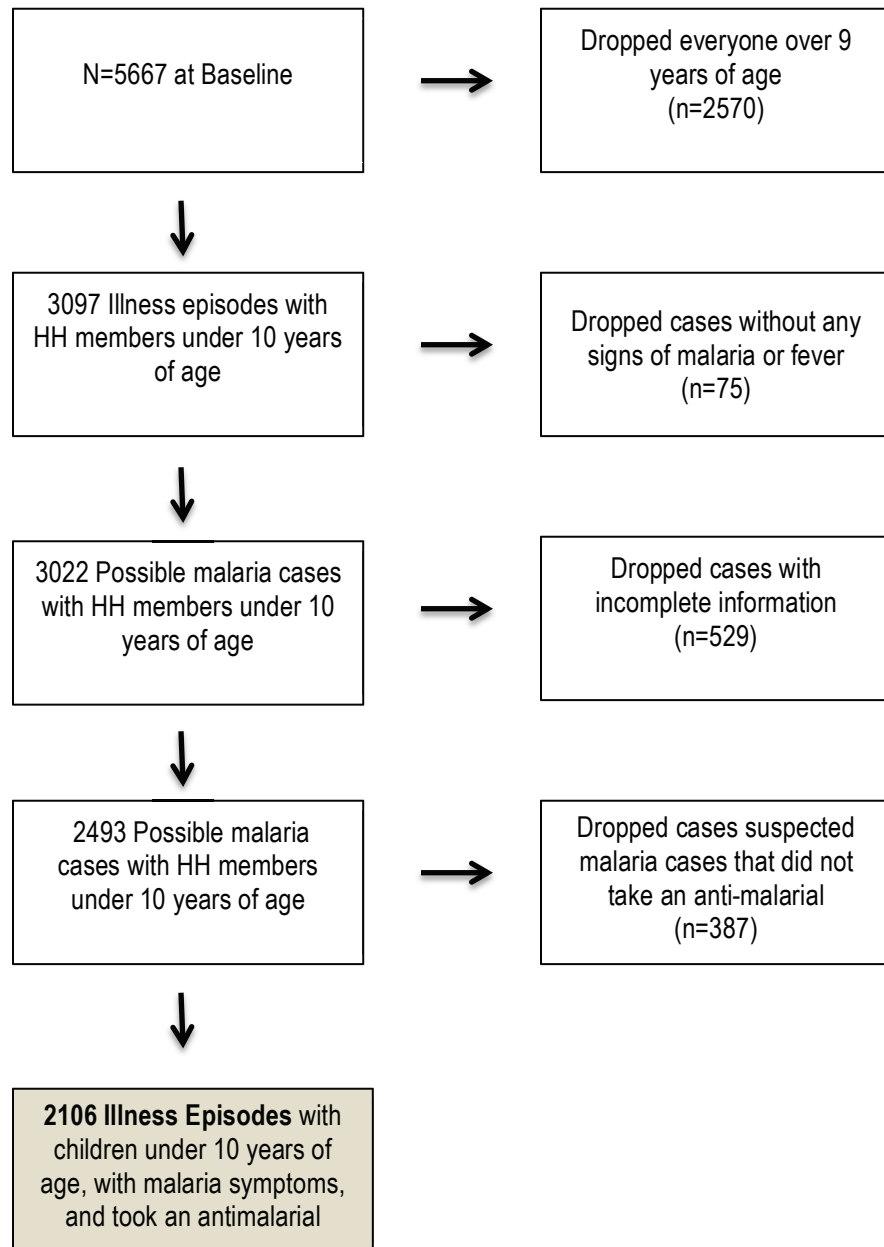


Table 5.1

<i>Sample Characteristics (n=2106)</i>		
	N	%
Child's Gender		
Male	1,038	50.7
Female	1,068	49.3
Age of Child		
Under Five Years	1473	69.9
Five and Older	633	30.1
Marriage		
Monogamous	1359	64.5
Polygamous	462	21.9
Other	285	13.5
Education		
No education	289	13.7
Primary	1421	67.5
Secondary or Higher	396	18.8
Religion		
Catholic	636	30.2
Protestant	1233	58.6
Muslim, Other	237	11.3
Urban		
Rural	1703	80.9
Urban	403	19.1
Tested for Malaria		
Not Tested	1525	72.4
Tested	581	27.6
Malaria Test Attitude		
Disagree	472	22.4
Agree	1634	77.6
Self-treatment Attitude		
Agrees	1633	77.5
Disagrees	473	22.5
Test Adherence Attitude		
Agrees	1404	66.8
Disagrees	698	33.2
Malaria Knowledge		
No Knowledge	682	32.4
Low Knowledge	999	47.4
High Knowledge	425	20.2
Fever Knowledge		
Low Knowledge	802	38.2
High Knowledge	1300	61.9

Sample Characteristics - continued

	N	%
Place Treatment Initiated		
Self-treatment	688	31.3
Drug Shop/Pharmacy	758	36.0
Formal Facility	660	32.7
Type of Antimalarial		
Non-ACT	723	34.3
ACT	1383	65.7

Table 5.1A

Sample Characteristics - Continuous Variables

	Median	Q1	Q3	SD	Range
Respondent's Age (years)	31	25	38	10.08	18-80
SES	3	2	5	2.09	0-10
Antimalarial Knowledge	2	2	3	1.17	0-7
Perceived Malaria Prevalence	5.3	3	7.7	2.86	0-10
Perceived Severity	7	5	9	2.31	0-10

Table 5.2

Bivariate Associations between Categorical Predictor Variables and Treatment Outcome

	Substandard Antimalarial	ACT	P-value
	N (%)	N (%)	
Child's Gender			0.808
Male	359 (34.59%)	679 (65.41%)	
Female	364 (34.08%)	704 (65.92%)	
Marriage			.964
Monogamous	465 (34.22%)	894 (65.78%)	
Polygamous	161 (34.85%)	301 (65.15%)	
Other	97 (34.04%)	188 (65.96%)	
Education			.269
No Education	103 (35.64%)	186 (64.36%)	
Primary and Less	472 (33.22%)	949 (66.28%)	
Secondary or Higher	148 (37.37%)	248 (62.63%)	
Religion			<.001
Catholic	217 (34.12%)	419 (65.88%)	
Protestant	395 (32.04%)	838 (67.96%)	
Muslim	111 (46.84%)	126 (53.16%)	
Child's Age			.033
Less than Five Years	527 (35.78%)	946 (64.22%)	
More than Five Years	196 (30.96%)	437 (69.04%)	
Urban			0.174
Rural	573 (33.65%)	1130 (66.35%)	
Urban	150 (37.22%)	253 (62.78%)	
Self-treat Attitude			.859
Agrees	559 (34.23%)	1074 (65.77%)	
Disagrees	164 (34.67%)	309 (65.33%)	
Test Adherence Attitude			.813
Agrees	484 (34.47%)	920 (65.53%)	
Disagrees	237 (33.95%)	461 (66.05%)	
Malaria Test Attitude			.028
Disagrees	182 (38.56%)	290 (61.44%)	
Agrees	541 (33.11%)	1093 (66.89%)	
Malaria Knowledge			0.003
No Knowledge	261 (38.27%)	421 (61.73%)	
Low Knowledge	342 (34.23%)	657 (65.77%)	
High Knowledge	120 (28.24%)	305 (71.76%)	
Fever Knowledge			.203
Low Knowledge	262 (32.67%)	540 (67.33%)	
High Knowledge	460 (35.38%)	840 (64.62%)	
Blood Tested for Malaria			<.001
Not Tested	473 (31.02%)	1052 (68.98%)	
Tested	250 (43.03%)	331 (56.97%)	
Place Treatment Initiated			<.001
Home	144 (20.93%)	544 (79.07%)	
Drug Shop/Pharm	354 (46.70%)	404 (53.30%)	
Formal Facility	225 (34.09%)	435 (65.91%)	

Table 5.2A

Bivariate Associations between Continuous Predictor Variables and Treatment Outcome

	Non-ACT Antimalarial	ACT	P-value
	Mean (SD)	Mean (SD)	
Respondent's Age	32.35 (9.64)	33.31 (10.29)	.037
SES	4.01 (2.14)	3.80 (2.06)	.024
Perceived Malaria Prevalence	5.16 (2.85)	5.38 (2.86)	.102
Antimalarial Knowledge	2.50 (1.18)	2.36 (1.16)	.012
Perceived Illness Severity	6.97 (2.18)	6.33 (2.35)	<.001

Table 5.3

Unadjusted Odds Ratios between Demographic Characteristics, Attitudes, Knowledge, and Behavior and Treatment Outcome

Variable	Unadjusted Odds Ratio	95% CI
Religion		
Catholic	1.00	
Protestant	1.10	(.90 – 1.35)
Muslim, Other	.59***	(.43 - .80)
SES	.95*	(.91 – .99)
Age (Child)		
Under Five Years	1.00	
Five Years or More	1.24*	(1.02 – 1.52)
Perceived Malaria Prevalence	1.02	(.99 – 1.06)
Urban		
Rural	1.00	
Urban	.86	(.68 – 1.07)
Malaria Test Attitude		
Disagrees	1.00	
Agrees	1.27*	(1.03 – 1.57)
Blood Test for Malaria		
Not Tested	1.00	
Tested	.60***	(.49 - .72)
Malaria Knowledge		
No Knowledge	1.00	
Low Knowledge	1.19 [†]	(.97 – 1.46)
High Knowledge	1.58***	(1.21 – 2.05)
Fever Knowledge		
Low Knowledge	1.00	
High Knowledge	.89	(.74 – 1.07)
AM Knowledge	.91*	(.84 – .98)
Severity	.88***	(.85 - .92)
Place Treatment Initiated		
Home	1.00	
Drug Shop/Pharmacy	.30***	(.24 - .38)
Formal Facility	.51***	(.40 - .65)

Note. * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$; [†] $p \leq .10$

Table 5.4

Parameter Coefficients for the Multilevel Model for Various Indicators of Antimalarial use

	Antimalarial Use
Random Effects	
<i>Variance</i>	
Household-level	1.63 (.16)***
Village-level	.69 (.12)***
<i>Intraclass Correlation</i>	
Household-level ICC	.49 (.05)
Village-level ICC	.07 (.02)
Log-likelihood	-1275.54
AIC	2557.07

Note. * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Table 5.5

Multilevel Logistic Model of Individual, Household, and Village-level Predictors of Antimalarial Use

Independent Variables	n	ACT vs non-ACT Adj OR (95% CI)
<i>Fixed Effects</i>		
<i>Individual-Level Factors</i>		
Severity	2106	.89 (.84-.95)**
Child Age		
Under Five	1473	1.00
Five or Older	633	1.37 (1.01-1.85)*
Tested		
Not tested	1525	1.00
Tested	581	.46 (.32-.66)***
<i>Household-Level Factors</i>		
Religion		
Catholic	626	1.00
Protestant	1233	1.16 (.80-1.67)
Muslim, Other	237	.53 (.30-.94)*
SES	2106	.95 (.87-1.03)
<i>Village-Level Factors</i>		
Malaria Knowledge		
No Knowledge	682	1.00
Low Knowledge	999	1.41 (.98-2.02)
High Knowledge	425	1.78 (1.11-2.86)*
Malaria Test Attitude		
Disagree	472	1.00
Agrees	1634	1.51 (1.02-2.24)*
Antimalarial Knowledge	2106	.89 (.78-1.03)
Place Treatment Initiated		
Home	668	1.00
Drug Shop/Pharmacy	758	.19 (.13-.27)***
Formal Facility	660	.60 (.40-.90)*
<i>Random Effects</i>		
Household-level variance		.157 (.16)***
Village-level variance		.65 (.12)***
Residual intra-class correlation		.07 (.023)
Log-likelihood		-1187.03
AIC		2404.06

Note. * $p \leq .05$; ** $p \leq .01$; *** $p \leq .001$

Chapter 6: Overall Conclusions

Overview

Significant progress in malaria control has been made, and progress towards MDGs has been achieved. This is due in large part to IRS and ITN prevention programs. However, no single intervention is sufficient to reduce the malaria burden alone. These programs need to continue in order to prevent malaria transmission, while diagnostic capabilities and appropriate, timely treatment are made more accessible. Of immediate concern is to ensure that all children with malaria receive appropriate treatment. Increasing testing behavior has become an integral component to malaria strategies and treatment recommendations in order to preserve resources, limit exposure to unnecessary side effects, increase diagnosis of the true illness, and curb artemisinin resistance. Testing rates have increased dramatically in recent years, but presumptive treatment continues to be the preferred treatment method for suspected malaria.

Although trends are difficult to assess due to insufficient and inconsistent data, it appears that malaria incidence is decreasing in Uganda. There have been significant efforts to increase access to recommended treatments in terms of availability by increasing the distribution to drug shops and subsidizing high costs. It well known that access and cost are significant barriers to appropriate treatment, and that eliminating these barriers can result in a significant uptake in ACT-use. However, it appears that at least a third of children under five in Uganda continue to use non-ACT antimalarials.

Summary of Findings

The overall goal of this dissertation research was to explore how to increase appropriate treatment-seeking behaviors and treatment outcomes for children under ten years of age with suspected malaria in Uganda. In order to achieve this, three study aims were presented and addressed.

In the first manuscript, a literature review was conducted to critically review the current scientific understanding of treatment-seeking patterns and determinants of behavior for suspected malaria in children in Africa. Describing patterns of treatment-seeking behaviors has been well documented through previous work. Caretakers of young children prefer to treat mild illness at home, and rely on the formal facilities for more severe illness. Children who seek care at formal facilities are more likely to receive nationally-recommended treatments, and children who rely of self-treatment often receive non-ACT antimalarials or a non-antimalarial.

The main challenge is to understand how to encourage caretakers to seek immediate treatment in the formal sector, and to forego basic trial-and-error treatments at home. The majority of the research that addressed this topic focused on the determinants of seeking care in the formal sector versus the informal sector. Illness severity and access emerged as two of the most significant factors that affect seeking treatment in the formal sector. Other determinants include SES, the child's gender, mother's education, the child's age, local illness concepts, and perceptions about the quality of healthcare service. Many caretakers have a poor understanding of how malaria is transmitted, and these beliefs affect how they view the severity of the illness, and ultimately where they seek care.

The knowledge gleaned from these studies is useful in understanding the basic barriers and facilitators to seeking appropriate care. However, the majority of the research has neglected to assess the complex web of factors that influence decision-making about health care and understanding how patterns are formed for recurring illnesses. Very few studies assessed determinants at more than two levels of the healthcare system. Most of the previous research focused on a handful of determinants, which typically included mainly socio-economic factors and illness severity. While many studies discussed levels of malaria knowledge, namely how people understand malaria based on local illness concepts, most did not assess how they affect behavior. Similarly, attitudes were largely ignored in the reviewed studies. Many qualitative studies explained how caretakers develop opinions and beliefs about the quality and efficacy of services provided at different places, and how personal experiences influence future illness episodes. However, no study measured attitudes and included them in their analyses. It is clear that issues of cost and distance are difficult to surmount when illness are viewed as non-serious and caretakers believe they are easily managed at home. However, more research is needed to identify attitudes and knowledge that affect treatment-seeking decisions.

The second manuscript utilized quantitative data to address the gaps identified in the literature review. The specific aim was to identify facilitators and barriers to seeking treatment for febrile children under ten years of age at various levels of the health care system in Uganda. The outcome in this multinomial analysis included place of initial treatment seeking for suspected malaria. Outcomes included engaging in care at home, purchasing medicine from a local drug shop, and going to a formal healthcare facility. The results supported the findings seen in many other studies as described in the literature

review: children with more severe illness, living in an urban area, whose mothers have higher levels of education were more likely to seek care in a formal facility. In addition, caretakers who work outside of the house are more likely to rely on informal or home-treatment.

Various types of knowledge and attitude measures were assessed in this analysis. In general, attitudes about modern treatment were very high; very few caretakers believed in the efficacy of herbal treatments for the treatment of malaria. Attitudes and knowledge appear to play a more significant role in encouraging caretakers to seek any care outside of the house. None of the attitude and knowledge variables were significant when comparing treatment seeking at formal healthcare facilities to drug shops. Caretakers with higher levels of perceived efficacy in formal healthcare facilities and who had higher levels of antimalarial knowledge were more likely to initiate care outside of the house. Knowledge that fever is a symptom of illnesses other than malaria was associated with an increased likelihood of initiating care at home instead of a drug shop.

Attitudes and knowledge appear to influence treatment-seeking outside of the house while illness severity and access affect caretakers' decisions about which type of facility they utilize. Different types of predictors are at work at various level of the healthcare system. These results present a more complicated picture of treatment seeking than is seen in the current literature. This information may be used to target specific behavior change campaigns to specific segments of the population.

Finally, the third manuscript addresses the issue of the continued reliance on presumptive treatment, which leads to the overutilization of ACTs. The specific study aim was to identify determinants of appropriate treatment outcomes for suspected malaria

in children under 10 years of age. Overall, ACT-use was common for the treatment of uncomplicated malaria in children among this sample. Caretakers frequently provide ACTs that are stored at home and purchased from local drug shops. Children who were blood tested for malaria, were five years of age or older, and experience less severe illness were more likely to receive a non-ACT antimalarial. Children of caretakers who were non-Muslim, had high levels of knowledge about malaria transmission, and had higher levels of perceived efficacy in malaria-related services were more likely to receive an ACT.

Strengths and Limitations

This research has several limitations that are discussed here. The biggest limitation in the literature review was the variability in health sector definitions and treatment-seeking outcome. Studies compared different definitions of the healthcare system including informal versus formal sectors, private versus public sectors, and traditional versus modern treatment. Most studies focused on determinants of seeking care in the formal sector, while a few focused on seeking any care, and a handful considered more than two levels of the healthcare system. These differences made clear comparisons a challenge. Furthermore, there was a significant amount of variability in the range and types of predictors used in the analyses. Some studies considered one or two predictors, while others included several types of predictors. Despite these differences, clear patterns emerged, and the most salient determinants studied to date were identified.

The second limitation is the attrition rate among participants. Respondents moved out of the study area or chose to end their participation in the study during each round of

interviews. By the last round used in this dissertation, just over 10% of the original sample had been lost to follow-up. The respondents who were lost to follow up may have been different than the respondents who remained in the study.

A third limitation is respondent bias. Caregivers were interviewed up to ten different times over the period of twelve months, which may have resulted in survey fatigue. As the data collection team utilized the same illness roster during each follow-up round, respondents may have been able to anticipate how to answer the questions in order to shorten the interview time. In order to mediate potential fatigue, enumerators worked with the same households each month in order to develop a relationship in hopes that the respondents would continue to welcome someone they knew and trusted. Occasional small remunerations such as laundry soap and cooking oil were provided to participants to show appreciation for their time.

The reliance on self-reporting throughout the study is another type of respondent bias. Caregivers provided detailed information about all household illnesses, and recall bias may have resulted in omitted or erroneous information. It was decided to visit households once a month to limit the time period to recall information, and to space out visits long enough to not increase survey fatigue. In addition, the intense promotion of ACTs for malaria treatment may have presented confusion. Many respondents may have equated ‘ACT’ with ‘antimalarial,’ resulting in high rates of reported ACT-use. In order to mediate this bias, enumerators never asked if their child received an ACT, but rather requested respondents to openly list the drugs their child received. In their responses, many caretakers stated the most common brand name, ‘Coartem,’ which indicates a greater likelihood of accuracy as compared to caretakers who listed, ‘ACT.’

Finally, a fourth limitation is measurement. This research focused on knowledge and attitudes as salient explanatory variables. For most of these variables, respondents identified their attitudes and beliefs on a four-point scale of agreement. It was determined during the univariate analyses that many of the attitude variables were so highly skewed that it was not possible to include them in the final analyses. Social desirability may have influenced the general direction of one's opinion, but a larger scale (e.g. from 0-10) may have resulted in more variation among the sample. In this case, stronger beliefs and attitudes could be compared to weaker ones. In addition, specific local illness concepts were not measured. Various perceptions of cause and categorization of malaria may have had a more significant effect on where caretakers initiate care.

Despite these limitations, the results of this study contribute to a growing body of literature on treatment-seeking behaviors and antimalarial treatment use. This study has identified additional predictors of health-seeking behavior and treatment outcomes. Previous studies focused predominantly on illness severity, socio-demographic factors and access. However, this study found that various knowledge and attitude concepts also influence treatment seeking. Furthermore, this research has provided valuable insights into understanding the caretakers who continue to rely on non-ACT antimalarials.

Another strength of this study is the generalizability of the results. These results may assist in understanding treatment-seeking behaviors in other malaria-endemic African countries and may inform the development of behavior change campaigns. These results may be utilized as well in the development of campaigns to increase treatment-seeking behaviors for other recurring illness in Uganda. Regardless of the illness,

caretakers who are more informed about the disease and have higher levels of perceived efficacy in the healthcare services offered will seek out appropriate treatment.

As malaria incidence continues to decrease, Uganda will transition from being classified as having on-going malaria to being in the pre-elimination phase. At that time, the early identification and treatment of all malaria cases will be essential to reaching elimination. The results from this study will assist in understanding treatment-seeking behavior and the central role the consumer plays in the malaria control process.

Policy Implications, Recommendations, and Future Research

Historically, access has been a significant barrier to healthcare utilization practices. Recent efforts and study evaluations have indicated that attempts to minimize this barrier have been successful in increasing appropriate treatment use. Policies should continue to be supported that maintain the widespread distribution of subsidized ACTs, especially in rural areas. However, the same strategy planning should be applied to malaria diagnostic tests. Policies, laws, and treatment guidelines should focus on increasing diagnostic utilization in all levels of the healthcare system. Free diagnostic services should be promoted within the formal healthcare facilities. Increasing RDT availability at lower levels of the formal healthcare system that may not typically have microscopes should be made a priority. Laws that permit and encourage community-based facilities to sell and use RDTs will increase the accessibility of testing. Furthermore, a policy that requires a blood confirmation before selling an ACT may greatly reduce presumptive treatment in local drug shops.

National drug administration bodies may consider limiting the availability of monotherapies and non-artemisinin based therapies that are available in local drug shops. High stocking rates of non-artemisinin and monotherapy drugs will lead to their overuse. Additional support at the district level is required to increase supervision of the types of drugs stocked and sold in local drug shops.

Health worker training to increase positive experiences between patients and providers need to be prioritized and made part of all routine health-related events such as medical school, specific trainings, workshops, and seminars. Trainings should target all healthcare workers that deal with diagnosing and/or treating malaria including doctors, nurses, CHWs, and drug shop owners. Patients and caretakers develop an increased sense of perceived efficacy of malaria-related services based on their experiences and interactions, which encourages them to return for similar illness episodes. Finally, changes should be made to alleviate long waits and stock outs that deter patients from returning to public health centers.

This research has presented a number of areas that require more research and should become the central focus of future health education campaigns. More research is needed to understand how caretakers perceive and try new drugs, and how they decide to stop using an older drug. The rationale behind the changes in nationally-recommended treatment for malaria may not be well-understood by consumers. More research is needed to understand consumer beliefs and attitudes about non-ACT antimalarials in order to support the development of appropriate campaigns to encourage ACT-use now. This additional research may be used in the promotion of any future recommendation changes as well.

Future research may also include improving attitude measurement, and assessing how additional attitude variables affect treatment-seeking behaviors at drugs shops and formal healthcare facilities. Finally, it would be beneficial to explore local illness concepts in detail and assess how they affect treatment-seeking decisions.

Intense education-based campaigns are recommended that target caretakers of young children, and focuses specifically on the dangers of ignoring mild illness. Campaigns should focus improving malaria knowledge in general, and promoting the nationally-recommended treatment guidelines. Components of campaigns to increase malaria knowledge should include increasing accurate understanding about how malaria is transmitted, dispelling local myths about transmission, explaining other common causes of childhood fever, and explaining that mild illness that is not treated appropriately may develop into severe illness. Efforts to increase consumer understanding of treatment guidelines should focus on explaining the difference between ACT and non-ACT drugs as well describing the dangers of using non-recommended treatments. Campaigns should also target health workers that diagnose and treat malaria. The focus should be to increase the quality of patient-provider relationships, and to capitalize on one-on-one interactions to explain national guidelines, other sources of fever, and the effectiveness of diagnostic confirmation.

Katrina A. Berg

Personal Data

Date of Birth: February 3rd 1977

Place of Birth: Springfield, Massachusetts, USA

Education

2008-2014 **Johns Hopkins School of Public Health;** Baltimore, MD
Doctor of Philosophy in Social and Behavioral Sciences
Department of Health, Behavior and Society
Defense: July 2014

2007 **Josef Korbel School of International Studies;** Denver, CO
M.A. International Development
Concentration in Global Health Affairs

2000 **Eckerd College;** St. Petersburg, FL
B.A. Anthropology and Spanish
Minor in Religious Studies

Research Experience

2012-Present **Qualitative Researcher: Johns Hopkins School of Medicine**
Evaluation of East African Diploma in Tropical Medicine and Hygiene
Developed focus group guide and trained local moderator in evaluation purpose and appropriate interviewing techniques. Conducted and supervised 6 focus group discussions in Tanzania and Uganda to ascertain student academic, cultural, and professional experiences in the course. Analyzed focus group data and presented results and recommendations as part of the evaluation team.

2010-2011 **Study Coordinator: Clinton Health Access Initiative**
Study Title: Evaluating the Feasibility of Introducing Malaria Diagnosis in the Private Sector in Eastern Uganda.
Supervised field components of a randomized controlled trial focused on introducing malaria diagnostics into the private sector in Uganda. Conducted four-month pilot study to finalize survey tools, sampling plan, intervention training, and program roll out. Assisted in developing qualitative questionnaire for focus groups with heads of household about current beliefs in malaria treatments and practices. Managed data collection activities including household census of 92 villages, interviews

with 2760 participants at baseline and monthly follow-ups, and data entry of over 10,000 surveys. Developed and oversaw data collection quality control assurance measures.

- 2010 **Research Assistant: Center for Communication Programs**
Integrated HIV Serological and Behavioral Surveillance among Persons Attending Alcohol Consumption Venues in Gaborone, Botswana
Engaged in formative research stages of study to explore links between drinking alcohol, sexual behavior, and HIV infection among people at the places where alcohol is sold and drank. Developed time location sampling (TLS) documents to be implemented in first stage of study. Prepared training material on TLS methodologies for local study team.
- 2009-2010 **Research Assistant: Center for Communication Programs**
Research to Prevention: Zambia
Conducted background review on current state of knowledge regarding street youth in Lusaka, Zambia. Completed a review of capture-recapture methodologies used in similar populations in order to initiate study design.
- 2009 **Research Assistant: Center for Communication Programs**
Strategic Radio Communication for Development Project, Tanzania
Traveled to Tanzania to monitor the initial formative research stages for a qualitative assessment of knowledge, attitudes, and practices of multiple concurrent partnerships. Carried out a mapping activity of HIV prevention programs in Tanzania with USAID partners and local NGOs.
- 2007 **Survey Coordinator: Centura Health**
International Medical Missions Survey Project
Managed data collection in four rural Amazonian villages and data analysis. Coordinated project logistics including budget management, river transportation as well as survey development, implementation, and evaluation. Recruited and trained a team of 5 volunteers and translators to conduct over 120 personal interviews in Spanish.

Teaching Experience

- 2012-2013 **Teaching Assistant**
Department of Health, Behavior and Society
Johns Hopkins School of Public Health
Health Communication Programs (two term class)
- 2011 **Teaching Assistant**
Department of Health, Behavior and Society
Johns Hopkins School of Public Health
Health Communication Programs (Online Class)

Publications

Berg, K., Sun, C. J., & Babalola, S. (2012). Predictors of parent-child communication among a nationally representative sample in Nigeria. *SAHARA J: Journal of Social Aspects of HIV/AIDS Research Alliance / SAHARA, Human Sciences Research Council*, 9(2), 95-103.

Cohen, J., Fink, G., **Berg, K.,** Aber, F., Jordan, M., Maloney, K., et al. (2012). Feasibility of distributing rapid diagnostic tests for malaria in the retail sector: Evidence from an implementation study in Uganda. *PloS One*, 7(11), e48296.

Cohen, J., Fink, G., Maloney, K., **Berg, K.,** Jordan, M., Aber, F., Dickens, W. (2013) “Effect on Malaria Testing and Treatment in Uganda of Introducing Malaria Rapid Diagnostic Tests in Drug Shops: An Impact Evaluation” (Under Review)

Hynes, N. & **Berg, K.** (2013). “Understanding Feedback Response Rates: An Evaluation of an Academic Multicultural Setting” (Working Paper)

Presentations

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| 2014 | Consortium of Universities for Global Health
Washington, DC
Poster Title: Lessons learned in training Global North and Global South physicians in the tropics: learning objective quality correlates with student perceived learning |
| 2013 | World Conference on Learning, Teaching and Educational Leadership
Barcelona, Spain
Presentation Title: Predictors of participation in faculty evaluation in a multicultural setting |
| 2009 | Social Aspects of HIV/AIDS Research Alliance Conference
Midrand, South Africa
Presentation Title: Parent-child communication about sexual issues in Nigeria |
| 2008 | George Washington University
Washington, DC
Presentation Title: Rural interviewing techniques |
| 2007 | Centura Health, Board of Trustees
Denver, CO
Presentation Title: Healthcare access in the Peruvian amazon: project recommendations |

Honors and Awards

- 2008-Present **Sommer Scholar, Johns Hopkins School of Public Health**
Full tuition and stipend awarded to students with the aim of developing leadership skills for their future careers.
- 2009 **Doctoral Special Project Funding, Johns Hopkins School of Public Health**
Department of Health, Behavior and Society
Special Project Funding awarded to departmental doctoral students on a competitive basis.
- 2009 **Social Aspects of HIV/AIDS Research Alliance**
Full scholarship awarded to attend conference in South Africa
- 2007 **Global Health Summer Achievement Award**
Korbel School of International Studies

Skills

Computers: STATA, ATLAS.ti, Epi Info, Microsoft Office Products

Languages: Proficient in Spanish, Conversational in Bemba