SPATIO-TEMPORAL DISTRIBUTION OF FEVER-RELATED MALARIA AND NON-MALARIAL CASES AMONG CHILDREN AGED BELOW FIVE YEARS AND THEIR RELATIONSHIP WITH RAINFALL, IN SIAYA COUNTY, KENYA

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(Public Health)

JOMO KENYATTA UNIVERSITY

OF

AGRICULTURE AND TECHNOLOGY

2022

Spatio-Temporal Distribution of Fever-Related Malaria and Non-Malarial Cases among Children Aged Below Five Years and their Relationship with Rainfall, in Siaya County, Kenya

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A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Public Health of the Jomo Kenyatta University of Agriculture and Technology

2022

DECLARATION

This thesis is my original work and has not been presented for a degree at any other University.

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This thesis has been submitted for examination with our approval as the University Supervisors.

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DEDICATION

I dedicate this work to my family.

ACKNOWLEDGMENT

I’m grateful to the entire Millennium Villages Project, Sauri fraternity, for allowing me to undertake this work. To my supervisors, Dr. John Gachohi and Professor Mohammed Karama, who have always been generous and supportive during all phases of the research, Thank you. To the Jomo Kenyatta University of Agriculture and Technology, School of Public Health, and the Institute of Tropical Medicine and Infectious Diseases, thank you for giving me a platform to learn.

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ABBREVIATIONS AND ACRONYMS

ACT	Artemisinin-Combination Therapy
AIDS	Acquired Immune Deficiency Syndrome
CDC	Center for Disease Control and Prevention
CHW	Community Health Worker(s)
FUO	Fever of Unknown Origin
HIV	Human Immunodeficiency Virus
ICCM	Integrated Community Case Management
IMCI	Integrated Management of Childhood Illness
KDHS	Kenya Demographic and Health Survey
KEMRI	Kenya Medical Research Institute
KMIS	Kenya Malaria Indicator Survey
MDG	Millennium Development Goals
MOH	Ministry of Health
NHSSP	National Health Sector Strategic Plan
OPD	Out-Patient Department
RDT	Rapid Diagnostic Test
SSA	Sub-Saharan Africa
UNICEF	United Nations Children's Fund
WHO	World Health Organization

ABSTRACT

Children below five years of age account for about 80% of malaria deaths globally. As malaria continues to decline in many parts of sub-Saharan Africa and malaria rapid diagnostic tests become increasingly used, it is crucial to evaluate the critical outcomes from innovative strategies involving community health workers (CHWs) and local health facilities in fever management accounting for the spatial and temporal heterogeneity in infection risk. This study aimed to determine the proportion of fever cases due to malaria and non-malarial infections in space and time among children below five years of age and their relationship with rainfall in Siaya County in Kenya. A prospective longitudinal incidence study of all children tested for malaria by CHWs, and in health facilities were conducted between January 2013 and December 2015. The incidence proportion of malaria cases reported by CHWs increased with time, and the difference over the years was statistically significant ($P<0.001$). At health facilities, the incidence proportion of malaria cases decreased with time though the difference between the years was not statistically significant ($P=0.399$). For non-malarial cases reported by CHWs, the incidence proportion was lowest in 2014 and highest in 2013, and the difference over the years (2013-2015) was not statistically significant ($P>0.001$). At the health facilities, the incidence proportion of non-malarial cases was highest in 2014 and lowest in 2015, and the difference between the years (2013-2015) was not statistically different ($P>0.001$). None of the tested rainfall regimes (current, lagged, or cumulative) were associated with malaria and non-malarial cases ($P>0.1$). Five villages (Ramula, Marenyo, Uranga, Bongo, and Lihanda) had a significantly higher incidence proportion of malaria cases ($P<0.05$), while all villages except Nyawara, Marenyo, and Nyandiwa had a significantly higher incidence proportion of non-malarial cases ($P<0.05$). CHWs have the potential to play a role in the management of fever-related illnesses. The risk of diagnosing malaria seems predictable, while non-malarial cases occur throughout the year. These findings present opportunities for preparedness and policy actions to scale-up community health services.

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

Fever, the most well-recognized sign of an infection, is defined as an elevated axillary temperature (≥37.5°C) in a child or an adult (WHO, 2013). Approximately 28% of children between zero and four years with fever cases are likely to seek treatment in an African public sector clinic (Gething *et al.,* 2010). Moreover, the most well-recognized sign of malaria infection is a fever, which accounts for over 30-50% of all pediatric hospital visits and up to 50% of hospital admissions in sub-Saharan (UNICEF, 2004; Gething *et al.,* 2010). In Kenya, fever is the most common symptom exhibited by people seeking health care (Breiman *et al.,* 2011; Burton *et al.,* 2011), and malaria, a significant contributor to fever, is estimated to cause approximately 20% of all deaths of children under five years of age (Division of Malaria Control, 2011). Besides malaria, non-malaria febrile illnesses also contribute to significant morbidity and mortality. Studies have shown that 50 to 75% of fever episodes in children under five presenting at outpatient clinics are associated with acute respiratory infections (D'Acremont *et al.,* 2014). In hospitalized older children and adults, non-malaria febrile illnesses are due to HIV infection (Crump *et al.,* 2013).

As most healthcare workers in Africa associate fever with malaria, rapid diagnostic tests (RDTs) have been developed to improve the rational treatment of children with fever (WHO, 2012). When the result of a malaria test (rapid diagnostic test [RDT] or microscopy) is positive for a patient with a fever, the episode is considered to be malaria (WHO, 2013). When the result is negative, the fever is deemed not due to malaria and is sometimes referred to as a 'non-malarial febrile illness (WHO, 2013). This management has, over time, realized significant changes in recommendations to reduce associated morbidity and mortality from malaria and non-malarial febrile illnesses (WHO, 2015, WHO, 2018). One of the recommendations is the integration of community health workers (CHWs) into the primary health care systems (WHO, 2016).

Malaria is a complex disease, and many factors influence its transmission and prevalence. For example, precipitation, temperature, and humidity significantly determine mosquito reproduction and mortality (Bi *et al*., 2013; Reiner *et al*., 2015). Temperature and rainfall influence both the development of mosquitoes and subsequently increase their numbers (Imbahale *et al*., 2011). Thus, a pattern exists where periods of low and high risks can be characterized. Where CHWs complement health facilities, data from community-based surveillance can be utilized to describe spatial and temporal patterns of variation in infection or disease incidence (Hamainza *et al.,* 2014). Evidence was therefore needed to show whether CHWs could innovatively and effectively play a role in these strategies.

Increased utilization of CHWs in managing malaria and other childhood infections has been comprehensively reported (Seidenberg *et al.,* 2012, Kisia *et al.,* 2012, Sing and Sachs, 2013; Ashenafi *et al.,* 2014*;* Abbey *et al.,* 2015). These reports suggest that properly supervised CHWs can lead to improved management of uncomplicated childhood fever cases in areas with limited health facilities, thereby reducing child mortality. However, literature on the characterization of the space-time pattern of utilization and performance of CHWs in terms of diagnosis of malaria and non-malarial cases carried out longitudinally is scarce. The lack of longitudinal data on CHWs utilization and performance implies that governments and research partners cannot adequately evaluate the impact of CHWs on health outputs and outcomes. The presence of longitudinal data could also unravel existing and dynamic patterns of acceptability of CHWs by the communities they serve. Furthermore, without data that spans years, governments and research partners cannot assess the global trends and progress made over time. This study set out to address these concerns from an evidence-based perspective.

Malaria is the commonest cause of fever in western Kenya, with an entomological inoculation rate (EIR) of approximately 15.67 (PMI VectorLink Project, 2020). The "Millennium Villages Project" located in this region was an integrated rural development approach initiated in 2004 and ended in 2015 (Mitchel *et al*., 2018). Professionalized CHWs were one aspect of the "Millennium Villages Project" health system aimed at scaling up community health delivery (Sachs, 2018; Mitchell *et al.,*

2018). To address the aforementioned data needs and evidence-based health systems evaluation, this study aimed to determine trends (for three years) in the number of fever cases diagnosed as malaria and non-malarial in the "Millennium Villages Project" in Siaya County in Kenya. An attempt was made to determine the periods (months and years) with the highest proportions of fever-related malaria and non-malarial by the two institutions (CHWs and health facilities). The study also sought to assess the relationship between fever-related malaria and non-malarial cases and rainfall in the study area. Integrating climatic information enriched this study in determining the role of rainfall patterns in malaria and non-malarial infections over time and space and whether these dynamics were implicitly captured in cases diagnosed by the two institutions. Data was collected longitudinally between January 2013 and December 2015 from 158 CHWs in 10 villages and outpatient departments (OPD) of 10 health facilities in Gem Sub-County, Siaya County, Kenya. CHWs managed uncomplicated malaria cases with Artemisinin-based Combination Therapy (ACT) and referred non-malarial cases to clinics or hospitals. Attempts were made to determine the difference in spatial and temporal effects of the fever-related cases in this age group. The study findings would support policy actions toward scaling-up community health services and strengthening the management of malaria and non-malarial cases in resource-limited settings.

1.2 Statement of the problem

Fever is the common presenting symptom in children under-five years seeking health care in Africa, with Kenya no exception. According to the Kenya Demographic Health Survey of 2014, the national prevalence of fever was 24%, and Siaya County recorded one of the highest prevalences of 44.9%, almost double the national rate. Variations in climate have been described as a possible contributing factor (Kenya National Bureau of Statistics *et al.*, 2015). This region is classified as "malaria endemic," making it easy for malaria to spread. Incidence rates of malaria have been reported but not those of fever in general (Sewe *et al.,* 2015). To treat non-malarial febrile illness properly, the World Health Organization (WHO) called for investigations on non-malarial causes of fever as a priority due to the declining malaria incidence in most endemic settings (WHO, 2013). Thus, to determine the

causes of fever, this study aimed to assess the distribution of fever-related malaria and non-malarial cases, which vary by geography and season, in space and time in a local malaria-endemic epidemiological context where data was not available. The findings would provide the best evidence to inform clinical management, including diagnostics focused on point-of-care techniques, resource allocation in a limited setting, not only for malaria but also for non-malarial febrile illness, and future prediction modeling for fever occurrences.

1.3 Study Justification

Malaria and non-malarial febrile diseases have a negative impact on child survival in Siaya County and Kenya in general. Siaya County has the highest testing and treatment rate for malaria among children (Kenya National Bureau of Statistics *et al*., 2015). Though the Country has adopted an integrated approach to managing common childhood illnesses (MOH, 2020; MOH, 2021), malaria prevalence in Siaya County remains the second highest in the country (DNMP and ICF, 2021). Understanding trends of fever cases attributable to malaria and non-malarial febrile diseases would contribute to the knowledge of malaria and non-malarial patterns. This evidence would further strengthen the effective and efficient targeting of limited resources. Secondly, this would contribute to essential policy interventions for future planning, providing improved opportunities for taking preventative measures. Finally, this would give evidence that CHWs have the potential to be increasingly accepted and utilized by communities as part of a functional health care system.

1.4 Study Objectives

1.4.1 Broad objective

To determine the proportion of fever cases from malaria and non-malarial infections among children below five years of age and their relationship with rainfall in space and time in Gem Sub-County, Siaya County in Kenya.

1.4.2 Specific Objectives

1. To determine the proportion of fever-related malaria cases in space and time among children aged below five years in Siaya County in Kenya;
2. To determine the proportion of fever-related non-malarial cases in space and time among children aged below five years in Siaya County in Kenya;
3. To determine the relationship between rainfall and fever-related malaria and non-malarial cases among children aged below five years in Siaya County in Kenya;
4. To establish differences in space and time in the outcomes of fever-related malaria and non-malarial cases as diagnosed by community health workers and health facilities among children aged below five years in Siaya County in Kenya.

1.5 Hypotheses

Ho1: Fever-related malaria and non-malarial cases are uniformly distributed in space and time in the study area.

Ho2: Rainfall contributed to fever-related malaria and non-malarial cases in space and time in the study area.

H_{03}: Fever-related malaria and non-malarial cases showed different effects in space and time in community health workers and health facility diagnoses.

CHAPTER TWO

LITERATURE REVIEW

2.1 Fever

The fever syndrome is a common complaint among persons seeking health care in low-resource areas (Crump *et al*., 2013). Fever is defined as the abnormal elevation in body temperature, and many factors influence the temperature measurement results in humans (Mackowiak *et al*., 2021). There are several causes of febrile illness in African children and include malaria, bacterial infections, viral infections, fungal bloodstream infections, parasitic infections, urinary tract infections, enteric fever, and HIV infection, among others (Moyo *et al*., 2020; Crump *et al.,* 2013; D'Acremont *et al.,* 2014; Mahende *et al.,* 2014). These diseases contribute to morbidity and mortality among children under-five years in the sub-Saharan African region.

To appropriately manage fever cases, the causative agent must be identified (WHO, 2013). Furthermore, it is crucial to determine the distribution of diseases, which vary by season and geography, the immunity and age of the patient, and the level of care (D' Acremont *et al.,* 2014; WHO, 2013). For instance, *dengue*, a mosquito-borne disease, is an important cause of febrile illnesses in Asia and is less frequent in Africa (Mayxay *et al.,* 2013). *Chikungunya,* an emerging mosquito-borne disease that occurs as epidemics in certain African regions, has been documented for the first time in the United Republic of Tanzania in febrile patients during inter-epidemic periods (Crump *et al.,* 2013).

According to the Kenya Demographic and Health Survey of 2014 (Kenya National Bureau of Statistics *et al*., 2015), acute respiratory infection (ARI), malaria, and dehydration caused by severe diarrhea were the significant causes of child morbidity and mortality in Kenya. About six in every ten children with such symptoms who sought treatment had ARI (66%), fever (63%), and diarrhea (58%). Moreover, the multiple cluster indicator survey of 2011 (Kenya National Bureau of Statistics and ICF Macro, 2013) report for Siaya County in western Kenya showed that 29% of

children under five who sought treatment had a fever. In separate studies conducted in the region, fever, cough, and diarrhea were the key clinical complaints among children, with a substantial overlap between malaria and pneumonia (Burton *et al.*, 2011).

A better understanding of the burden of acute febrile illnesses in populations and individual patients is needed. In this situation, the aim would be treatment, improvement of health outcomes, reducing the prevalence of severe disease and death, and maintaining drug effectiveness (Gething *et al.*, 2010). Notably, most health care workers in Africa associate fever with malaria. Rapid diagnostic tests for malaria have been developed, and there have been calls to expand their use to improve the rational treatment of African children with fever (WHO, 2012). Before such an expansion, it is vital to determine the proportion of African children who develop fever each year and the proportion likely to have malaria. This understanding would lead to a new policy on diagnostics, which is expected to be more effective if spatial and temporal heterogeneity in infection risk and parasitemia in fevers is determined (Gething *et al.*, 2010).

Patients' options for fever treatment are evident. A trained medical health provider sees about 42% of febrile children in sub-Saharan Africa in the public sector compared with 10% in the formal private sector and 3% in the informal private sector (WHO, 2019). A high proportion (36%) of febrile children do not receive medical attention (WHO, 2019). Inadequate access to health care providers or lack of awareness of malaria symptoms among caregivers is among the contributing factors (WHO, 2019). Precise algorithms for managing acute fevers at the community level and peripheral health facilities have been developed by the WHO and UNICEF, which builds on Integrated Community Case Management, Integrated Management of Childhood Illness, and Integrated Management of Adolescent and Adult Illness (WHO, 2011). In these guidelines, diagnostic tests for malaria are performed at the first visit with a history of fever or a temperature ≥37.5 °C in areas of high malaria transmission (WHO, 2013). The African Region has had the most significant increase in levels of malaria diagnostic testing, from 38% of suspected malaria cases tested in 2010 to greater than 80% in 2018 (WHO, 2019). Once a malaria test has

been performed and confirmed positive, an antimalarial medicine should be prescribed. Patients with danger signs seen at health facilities with no inpatient service or the community level should be referred immediately after pre-referral treatment with an antimalarial agent without losing time by performing a malaria test (WHO, 2015, MOH, 2020, MOH, 2021). The integrated management of childhood illness policy guidelines recommends prescribing antimicrobial drugs only to children with a clinically documented disease and follow-up visits in case of persisting symptoms (WHO, 2013).

In adults, the integrated management of adult illnesses guidelines recommend that a malaria test be performed in high malaria transmission areas, and treatment with antimalarial agents be prescribed if the test is positive (WHO, 2011). In low malaria transmission areas, malaria testing is recommended only in the absence of other apparent causes of fever (dysentery, gastroenteritis, pneumonia, soft tissue or muscle infection, flu-like illness, bronchitis, severe or surgical abdominal conditions, pelvic inflammatory disease, sinusitis, tonsillitis, sore throat, kidney infection or dental abscess) (WHO, 2011). In adults, HIV can present as an acute febrile illness and, if not diagnosed, can lead to missed opportunities for prevention of transmission (Sanders *et al.,* 2011) and early initiation of antiretroviral treatment.

2.2 Malaria: a significant contributor to fever

Malaria is an acute mosquito-borne infectious febrile disease caused by the *Plasmodium* parasite and transmitted to humans through bites of female *Anopheles* mosquitoes. Five species of the *Plasmodium* parasite are recognized: *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale,* and *P. knowlesi.* Malaria due to *P. falciparum* is the most significant public health challenge and predominates in Africa (WHO, 2019). *P. vivax* has a wider distribution because it can develop in the Anopheles mosquito vector at lower temperatures and survive at higher altitudes and in cooler climates. It also has a dormant liver stage (known as a hypnozoite) that enables it to survive during periods when Anopheles mosquitoes are not present to continue transmission, such as during the winter months (WHO, 2015). Although *P. vivax* can occur throughout Africa, the risk of *P. vivax* infection is considerably reduced in the region

by the high frequency of the *Duffy* negativity trait among many African populations; in individuals without the *Duffy* antigen, red blood cells are resistant to infection with *P. vivax* (WHO, 2015).

In Kenya, nearly 70% of the population is at risk of malaria, with children under five years of age and pregnant women the most vulnerable (DNMP and ICF, 2021). Parasitological diagnosis of malaria accounts for 13%-15% of outpatient hospital visits in Kenya among children under five presenting with fever at health facilities, according to the Kenya Malaria Indicator Survey of 2020 (DNMP and ICF, 2021). In Siaya County, 31% of the deaths in parts of Siaya (Asembo, Gem, and Karemo) among the under-five population (excluding neonates) were due to malaria. Over 87% of pediatric admissions at Siaya district hospital (now County referral hospital) were due to malaria (Sewe *et al.,* 2015). In the 2005 Millennium Villages Project (MVP) baseline survey in the Sauri sub-location in Gem Sub-County, in Siaya County, 66% of male children and 60% of female children under five tested positive for malaria parasitemia (Mutuo *et al*., 2007). Recently in the KMIS of 2020, the prevalence of malaria among children aged six months to 14 years in Siaya County (based on microscopy) was 29% (DNMP and ICF, 2021), the second highest among the 47 counties in Kenya.

Malaria symptoms appear seven days (10–15 days) after an infective mosquito bite. The initial symptoms of malaria are fever, headache, chills, and vomiting. The clinical features in children include fever, failure to eat or drink, chills, rigors, sweating, and irritability, and in young children, febrile convulsion may complicate a sudden rise in temperature (WHO, 2015). These symptoms are initially nonspecific and may be challenging/difficult to recognize as malaria. If not managed within 24 hours, *P. falciparum* malaria can progress to severe illness (WHO, 2015, MOH 2020). The response to malaria infection depends on the infecting species, prior exposure, and subsequent level of immunity, with children under five years living in high malaria transmission areas unable to mount a robust immune response to malaria infection (White & Watson, 2018).

Strategies to control and eliminate malaria include vector control, which is achieved mainly through the use of insecticide-treated mosquito nets (ITNs) or indoor residual spraying (IRS); chemoprevention (which suppresses blood-stage infection in humans), and case management (which includes prompt diagnosis and treatment) (WHO, 2015). The use of insecticide-treated bed nets is an essential intervention in malaria control because high coverage is needed. The WHO recommends that populations at risk of malaria be targeted with bed nets to substantially reduce parasitemia and child mortality (WHO, 2019).

Indoor residual spraying (IRS) involves careful, controlled spraying of insecticides along the inside walls of a home or community building. Four classes of chemicals are currently recommended by the World Health Organization for use in IRS, including *organochlorines, carbamates, pyrethroids, and organophosphates* (WHO, 2015). The number of people protected globally by the IRS reduced from 180 million in 2010 to 97 million in 2019 (WHO, 2020). Reasons for the declining global IRS coverage may include the switch from pyrethroids to more expensive insecticides in response to increasing pyrethroid resistance or changes in operational strategies (e.g., decreasing at-risk populations in countries aiming to eliminate malaria) (WHO, 2015).

Chemoprevention in pregnancy, referred to as intermittent preventive treatment in pregnancy (IPTp), involves the administration of *sulfadoxine-pyrimethamine* (SP) during antenatal clinic visits in the second and third trimesters of pregnancy (WHO, 2015). It has been shown to reduce severe maternal anemia (Cibulskis *et al.*, 2011), low birth weight (Eisele *et al.*, 2012), and perinatal mortality (Bhatt *et al.*, 2015). Intermittent preventive treatment in infants (IPTi) with sulfadoxine-pyrimethamine (SP), delivered at routine childhood immunization clinics (at 2, 3, and 9 months of age), protects in the first year of life against clinical malaria and anemia; it reduces hospital admissions for infants with malaria and admissions for all causes (Aponte *et al*., 2009, WHO, 2015). Seasonal malaria chemoprevention (SMC) with amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP) for children aged 3–59 months has the potential to avert millions of cases and thousands of deaths in children living in areas

of highly seasonal malaria transmission areas in the Sahel sub-region (Liu *et al*., 2015).

In most malaria-endemic areas, less than half of patients with suspected malaria infections are infected with the malaria parasites. Therefore, parasitological confirmation by light microscopy or rapid diagnostic tests (RDTs) is recommended in all patients before antimalarial treatment starts. Artemisinin-based combination therapy (ACT) of uncomplicated *P. falciparum* malaria has been estimated to reduce malaria mortality in children aged 1–23 months by 99% and in children aged 24–59 months by 97% (Thwing *et al.,* 2011). The five ACTs currently recommended for use are *artemether* plus *lumefantrine, artesunate* plus *amodiaquine, artesunate* plus *mefloquine, artesunate* plus *sulfadoxine-pyrimethamine* (SP), *and dihydroartemisinin* plus *piperaquine* (WHO, 2015). The choice of ACT should is based on the therapeutic efficacy in the country or area of intended use (WHO, 2015).

2.3 Non-Malarial fever

Infectious diseases are the leading cause of morbidity and mortality among children in SSA (Liu *et al.,* 2012*;* Liu *et al.,* 2015). For a long time, fever in children of SSA was presumptively treated as malaria (Oladosu & Oyibo, 2013). However, in the recent decade, malaria has substantially declined in many endemic settings of SSA (WHO, 2015; Noor *et al., 2014*). Studies conducted have shown that most (50–75%) febrile episodes in children under five years of age presenting at outpatient clinics are associated with acute respiratory infections and invasive bacteria, including previously under-recognized animal-associated bacterial bloodstream infections (Crump *et al.,* 2013; D'Acremont *et al.,* 2014; Bisoffi & Buonfrate, 2013). For example, in Africa, where malaria is common, bacteremia is responsible for more deaths in hospitalized children than malaria (Moyo *et al*., 2020). In the prevalent malaria region of western Kenya, children with severe acute respiratory infections had respiratory syncytial virus and influenza virus as the most likely viral causes and pneumococcus as the most likely bacterial cause (Feikin *et al*., 2013). About a third of African children diagnosed with severe malaria have another cause of infection (probably bacterial infections) (White *et al*., 2022). Treatment should be instituted

with broad-spectrum antibiotics until bacterial causes are ruled out (White *et al*., 2022).

Streptococcus pneumonia (S. pneumonia), *nontyphoidal salmonella* (NTS), *Haemophilus influenzae* (H. influenza), and *Staphylococcus aureus* (S. Aureus) have consistently been reported as the most frequent bacterial causes of severe febrile illness among African children (von Mollendorf *et al*., 2022; Greenhill *et al*., 2015). The importance of these pathogens to childhood febrile illness depends on the local environment and the presence of risk factors such as malnutrition, HIV/AIDS, anemia, environmental hygiene, sanitation, and vaccination coverage (Brent *et al*., 2006, UNICEF, 2021). In the malaria-endemic region of Niger Delta in Nigeria, the prevalence of non-malarial febrile illnesses was 45%: Urinary tract infection was 8.42%, otitis media 7.89%, and pharyngitis 5.78% of the fevers (Pondei *et al.,* 2013). *S. aureus, E. coli, and S. pneumoniae* were the most common isolates from ear swabs, urine, and throat swab samples, respectively (Pondei *et al.,* 2013).

Epstein-Barr virus (EBV), an important etiologic agent of *infectious mononucleosis*, has also been noted as a common infection in Kenya in acute febrile illnesses in children under-five, with its incidence higher (35.7%) in regions considered holoendemic for malaria (L. Victoria basin and coast) compared to (22.9%) for hypoendemic regions (Highland of Kisii and semi-arid areas) (Masakhwe *et al.,* 2016). Viral hemorrhagic fever, a general term for a severe illness sometimes associated with bleeding, may be caused by several viruses. This term is usually applied to diseases caused by *Arenaviridae* (Lassa fever, Junin, and Machupo), *Bunyaviridae* (Crimean-Congo hemorrhagic fever, Rift Valley fever, Hantaan hemorrhagic fevers), *Filoviridae* (Ebola and Marburg) and *Flaviviridae* (yellow fever, dengue, Omsk hemorrhagic fever, Kyasanur Forest disease) (WHO, 2016). Hemorrhagic fevers can cause an outbreak of febrile illness 2 to 21 days later, associated with clinical manifestations that could include rash, hemorrhagic diathesis, and shock (Borio *et al.,* 2002, LaBeaud *et al.,* 2015).

In pregnant women, McGready *et al.* (2010) observed that febrile episodes occurred in 5.0% of pregnant women attending antenatal clinics. Arthropod-borne diseases,

e.g., malaria, rickettsial infections, dengue, and zoonotic disease, e.g., leptospirosis, contributed to almost half of all febrile illnesses, 47.3%. Co-infection was observed in 3.9% of women, mainly malaria and rickettsia. Pyelonephritis, 19.7%, was also a common cause of the fever. In the adult population (Non-pregnant), Nadjm *et al.* (2012) observed malaria in 20.2% and bacteremia in 13.1% of admissions. HIV was equally common among those with (43.2%) and without P. falciparum (36.2%) (Nadjm *et al.*, 2012).

Petersdorf and Beeson defined fever of unknown origin (FUO) as a temperature greater than 38.3°C (101°F) on several occasions, more than three weeks' duration of illness, and failure to reach a diagnosis despite one week of inpatient investigation (Haidar & Singh, 2022). Common causes include infectious diseases (34%), collagen-vascular diseases (23%), and neoplasms (19%) (Haidar & Singh, 2022). After investigations, most children with no diagnosis have a fever that resolves with no sequelae (Chow and Robinson, 2011). However, the need for invasive diagnostic techniques should be considered when laboratory tests or simple imaging procedures fail to discern the origin of FUO (Rigante & Esposito, 2013).

2.4 Relationship of malaria and non-malarial fever cases with climate

The transmission of many infectious diseases can be influenced by weather, especially for pathogens that spend part of their development outside the human body. This transmission of vector-borne diseases typically occurs within seasonal patterns, in which the role of temperature and rainfall are well documented (Polgreen, & Polgreen, 2018).

Malaria is a complex disease, and its transmission and prevalence are influenced by many factors, among which rainfall, temperature, and humidity play a significant role in determining mosquito reproduction and mortality (Reiner *et al.,* 2015; Bi *et al.,* 2013). Rainfall affects vector abundance by providing vector breeding sites and supporting vector development during the immature stages (Imbahale *et al*., 2011). This development is achieved through stagnant water pools, which are fertile breeding grounds for mosquitoes (Chaves *et al*., 2012). It is estimated that the mean temperature ideal for the development of mosquito vectors is between 25–27 °C,

while the development terminates at 10°C and 40°C when the vector survival rate is low.

Understanding the reasons for variation in factors associated with malaria transmission is complex but crucial to determining specific and vital indicators for epidemic prediction. For instance, in a study conducted in Ethiopia, rainfall was significantly associated with malaria and minimum temperature (Dabaro *et al.,* 2021). In Ghana, precipitation and maximum temperature at a lag of two months were used to successfully fit a biological transmission model to malaria (Oheneba-Dornyo *et al*., 2022), while in Senegal and the malaria epidemic-prone region of Baringo in Kenya, climate appeared to drive the interannual variation of malaria incidence (Fall *et al*., 2022, Kipruto *et al*., 2017). Contrary to these findings, there was a weak correlation between monthly rainfall and malaria incidence in studies conducted in Cameroon and Ethiopia (Nyasa *et al*., 2022; Sena *et al*., 2015). In Tanzania, it was found that malaria incidence was positively correlated with rainfall and the potential for a seasonal forecasting system in the development of a malaria early warning system (Jones *et al.,* 2007).

In malaria-endemic regions of Laos, Mayxay *et al.* (2013) aimed to determine the causes of non-malarial acute fever in patients. With the exclusion of influenza, the top five diagnoses when only one etiological agent per patient was identified were dengue (8%), scrub typhus (7%), Japanese encephalitis virus (6%), leptospirosis (6%), and bacteremia (2%). 32% of the patients tested influenza PCR-positive, of which *influenza B* was the most frequently detected strain (87%). This outcome was different from another region in Laos, roughly 770 km apart, where malaria transmission did not take place: typhoid, scrub typhus (*Orientia tsutsugamushi*), murine typhus (*Rickettsia typhi*), *Neorickettsia sennetsu, dengue, leptospirosis, Japanese encephalitis virus*, and *influenza* were commonly isolated (Phetsouvanh *et al.,* 2006; Phongmany *et al.,* 2006; Vallee *et al.,* 2010; Newton *et al.,* 2009; Blacksell *et al.,* 2007; Moore *et al.,* 2012; Vongphrachanh *et al.,* 2010). This heterogeneity of causes of fever due to environmental and human factors across the country would affect policies for treating fever (White *et al., 2*012).

Oluleye and Akinbobola (2010) observed that malaria attack was common in November, December, and January; these three months corresponded to the dry season when streams were stagnant, ponds stable, and waterways were able to retain pockets of stagnant water. These conditions allowed the breeding of mosquitoes and a burgeoning population; thus, the high correlation coefficients indicated the dependence of increased malaria attacks on insufficient rain or total rainless climatic conditions. On the other hand, a negative correlation or diminished malaria attack occurred during the wet season when the flowing of rivers and continual waterways and pond surface disturbance would not give enough time for breeding mosquitoes but wash away mosquito eggs at each fall of rain.

Kenya displays large spatiotemporal diversity in its climate and ecology, and malaria transmission reflects this environmental heterogeneity in space and time. The annual variability of malaria infection in the highlands of Kenya is greatly influenced by climate events such as El Nino, with epidemic outbreaks of malaria observed during such events (Githeko *et al.*, 2006). In a study in a coastal region, malaria and non-malarial fever cases showed a marked spatial heterogeneity with a high risk of malaria linked to age, community development level, and the presence of rice fields. At the same time, temporal patterns were described through prevalence peaks closer to rainy seasons (Bisanzio *et al.,* 2015, Newton *et al.,* 1997). Children under five in the western part of Kenya's highlands had the highest malaria parasite prevalence (Munyekenye *et al.,* 2005, Zhou *et al.,* 2015). The months with the highest parasite densities appeared to be 1-2 months behind rainfall peaks (Munyekenye *et al.,* 2005, Zhou *et al.,* 2015). In a separate study, Zhou *et al.* (2004) found that the mean *An. gambiae* abundance was 8.9 mosquitoes per house in the long rainy season of May, but 1.6–3.2 mosquitoes per house during the dry and short rainy seasons while in contrast, *An. funestus* abundance was 0.6 mosquitoes per house in May and peaked (2.1 mosquitoes per house) in August, right after the long rainy season. Minakawa *et al*. (2002) also observed this distribution of the Anopheles mosquito in the Yala River region, and more than 70% of the anopheline adults were *An. gambiae* during the rainy season, and the proportions of *An. arabiensis* and *An. funestus* were 15.1% and 10.8%, respectively. During the dry season, the proportion of *An. gambiae* was reduced to 51.8%, and that of *An. funestus* increased to 40.5%, and the species

composition between the rainy and dry seasons differed significantly. Two studies in the Lake Victoria region (Kisumu and Miwani) showed a 22% increase in malaria parasite prevalence after extensive rainfall (Imbahale *et al.,* 2010) and a significant association of rain during the previous week with the population of female *An. gambiae* (Koenraadt *et al.,* 2004), respectively.

Before a predictive model becomes acceptable to end-users and policymakers, various processes have to be undertaken, including a participatory involvement of stakeholders and policymakers in its validation. Demystifying the models' statistics and mathematics is also necessary, which often discourages health end-users (Githeko, 2012). As Bhutta *et al*. (2008) observed, the transmission of Dengue by *Aedes aegypti* and *Aedes Albopictus* varies in space and time, and the dynamics of the disease depend on seasonal changes in weather and immunity. Transmission is susceptible to rainfall, temperature, and humidity; thus, dengue is a climate-sensitive disease in Asia, and epidemics have been associated with the monsoon season. However, the development of early epidemic prediction models has been challenging. For example, the population of *Aedes aegypti* in Dhaka city, Bangladesh, does not increase until the rainfall threshold of 150 mm/month is exceeded. Yet, it has been established that dengue epidemics are associated with rainfall in the range of 205-446 mm/month (Ahmed *et al.,* 2007). Likewise, the development of *Aedes aegypti* does not occur below 17°C and may cease above 44°C.

In contrast, the development of *Aedes albopictus* immature stages ceases below 10.4°C (Delatte *et al.,* 2009). Using climate data to predict malaria epidemics in the Kenyan Highlands, Githeko and Ndegwa (2001) found an association between rainfall and high maximum temperatures and the number of inpatient malaria cases 3-4 months later. The maximum transmission risk was demonstrated to have occurred four months before the peak of malaria epidemics. The model’s only data inputs were mean monthly rainfall and monthly maximum temperature. He proposed that decision-makers to use the tool to determine in which areas malaria epidemics were likely to occur and the severity of the epidemic, reducing uncertainties in decision-making and leading to better resource and disease management.

Few studies have formally examined the relationship between meteorological factors and the incidence of other childhood fever cases in the tropics, for instance, pneumonia, even though most child pneumonia deaths occur there. In the Philippines, lack of sunshine was most strongly associated with pneumonia among young children (Paynter *et al.*, 2013) as in Nigeria, where Oluleye and Akinbobola (2010) showed that periods of frequent rain were associated with a high prevalence of pneumonia infection. Yet, the relationship between rainfall and pneumonia was weak, suggesting that the reduction in temperature must have been due to cloudiness during the rainy season that acted effectively as a shield blocking off the sun rays and thereby reducing the overall diurnal air temperature. In rural Kenya, holoendemic for malaria, pneumonia incidence peaked during the twice-yearly high malaria seasons, 1–2 months after peak rainfall (Tornheim *et al.*, 2007), confirming earlier argument of overlap between malaria and pneumonia. Heavy rain has also been associated with increased outbreaks of enteric pathogens, usually due to contamination of water supplies, as described in tropical regions where diarrheal diseases typically peak during the rainy season (Bhavnani *et al*., 2014).

2.5 Community health strategy and its role in the management of fever

Kenya's Ministry of Public Health and Sanitation, through its National Health Sector Strategic Plan II (NHSSP II 2005-2010) introduced in 2005, emphasized promoting individual and community health (MOH, 2005). The purpose of the NHSSP II was to strengthen health services through several strategies, one of which was the community health strategy adopted in 2007. This strategy was a community-based approach, through which households and communities would actively participate in health and health-related development issues. Its goal was to enhance community access to health care by providing healthcare services for all cohorts and socioeconomic groups at household and community levels; building the capacity of community health extension workers (CHEWs), and CHWs to provide community-level services (Wangalwa *et al*., 2012).

Despite the impressive improvements in most regions in reducing under-five mortality, improving child survival remains a matter of urgent concern. In 2020

alone, roughly 13,800 under-five deaths occurred every day, a high number of largely preventable child deaths (UNICEF, 2021). These deaths could be avoided through early, appropriate and affordable treatment of sick children in the home or community with antibiotics, antimalarial or oral rehydration therapy. Much effort should focus on building individual, family, and community capacities to ensure appropriate self-care, prevention, and care-seeking behavior (Kerber *et al.,* 2007). In limited-resource and rural settings, community-level interventions are potentially effective ways to address the problem at its roots, as decisions to seek and access health care are strongly influenced by the socio-cultural environment (Wangalwa *et al*., 2012). These challenges are also necessitated by the chronic shortage of health workers, particularly in SSA. Because of various reasons, not limited to migration, illness, or death of health care workers, many countries in SSA are unable to educate and sustain the health workforce that could improve people's chances of survival and well-being (WHO, 2006). Therefore, to bridge this gap, task-shifting through CHWs has been adopted in many settings (WHO, 2008; MOH, 2017).

Through Community case management, a strategy responding to international recommendations to deliver community-level treatment for common, serious childhood infections, relies on trained, supervised community members to provide interventions such as antibiotics, oral rehydration therapy, antimalarial, zinc, and vitamin A. CHW programs have been utilized globally as part of primary health care approaches for many decades (Singh & Sachs, 2013). In most developing countries, these primary health care approaches were strengthened in the late 1970s after the *Alma Ata* declaration of 1978 aimed at increasing access to health care through the call for 'health for all.' Patients with a fever might decide to see a CHW, visit a public or private clinic or hospital, go directly to a pharmacy or drug shop or stay at home with or without medication (WHO, 2011; WHO, 2013).

Several studies have described the impact of CHWs in the management of childhood fevers; for instance, in Ghana, utilization of CHWs for management of fever in under-fives was 59.4%, with caregivers who were exposed to the communication intervention four times more likely to use the services of the CHWs compared to those who were not exposed (Abbey *et al.,* 2015). In Ethiopia, incorporating

integrated management of childhood illnesses (acute respiratory infection, diarrhea, and fever) within the health extension program service significantly improved the appropriate care-seeking behaviors for childhood illnesses (Ashenafi *et al.,* 2014), while in Zambia, children presenting with fever sought more care from CHWs compared to formal health centers and subsequently suggested that integrated community case management (ICCM) influenced local care-care seeking practices while reducing workload at primary health centers (Seidenberg *et al.,* 2012). In rural Kenya, 90% of the children with fever, cough or difficulty breathing, or diarrhea, 26% consulted a CHW (Garg *et al.,* 2001), while in separate studies, it was concluded that home treatment enhanced the promptness of antimalarial treatment contributing to 61% (47-75%) of care-seeking behavior for children under-five compared to 30% (18-43%) of those seeking care at health facilities (Hamel *et al.,* 2001). This trend was also noted in Nigeria by Salako (2001), where the most common form of first-line treatment was drugs from a patent medicine vendor or drug hawker (49.6 percent). Therefore, community case management delivered by CHWs has the potential to address health system barriers through reduced costs of treatment, interaction with a fellow community member who understands the family's situation, availability of caregivers outside regular "business hours," and more frequent follow-up (Kisia *et al.,* 2012).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study area

The study was conducted within the "Millennium Villages Project" in the highlands of Western Kenya, in Yala Division, Gem sub-County, in Siaya County. The project comprised 11 villages with a total population of approximately 65,000. The site is located at 34.75° longitude east and 0.24° latitude north, 30 km north of Lake Victoria, and 1,400-1,500 m above sea level. The average temperature in this area is 24°C, ranging from 18-27°C, with an annual rainfall of 1,800 mm. The rainfall pattern is bimodal: the long rainy season occurs from March to June, and the short rainy season from September to December. Subsistence agriculture is the main livelihood in the area. *Anopheles funestus* and *Anopheles gambiae sensu stricto (s.s)* are the main anopheline species found in the study area (Mutuo *et al.*, 2007).

3.2 Study Design

This was a prospective longitudinal study to determine the incidence of fever-related malaria and non-malarial cases in children under five years and its relationship with rainfall in space and time, in Siaya County, from January 2013 to December 2015.

3.3 Population and Sample

This study was a census of all fever cases tested for malaria in children under five years. The total population of children under five in the ten villages was 7,442 in 2013, 6,839 in 2014, and 7,285 in 2015 (Table 3.1). One village, Sauri, was excluded from the analysis since indoor residual spraying (IRS) had been carried out in 2014 and 2015, which could have influenced malaria and non-malarial outcomes.

Table 3.1: The population of children under-five years in the study area

Village	Total Population (children under five years of age)		
	2013	**2014**	**2015**
Gongo	577	489	456
Anyiko	523	491	436
Nyandiwa	653	607	563
Jina	300	388	554
Nyamninia	983	883	943
Ramula	798	711	785
Uranga	739	735	685
Marenyo	1,045	882	850
Lihanda	820	743	952
Nyawara	448	383	389
TOTAL	**7,442**	**6,839**	**7,285**

Source: Millennium Villages Project, 2016

3.4 Inclusion criteria

The clinical and parasitological diagnosis of malaria had been based on WHO treatment guidelines for malaria (WHO, 2010). Malaria had been suspected clinically based on fever or a history of fever and confirmed using a parasitological test: light microscopy or rapid diagnostic tests (RDTs). A positive RDT or microscopic examination had been classified and reported as a malaria case. In contrast, a negative RDT or microscopic test had been classified and registered as a non-malarial case. Therefore, data were obtained for all fever cases tested for malaria (suspected malaria) with either malaria or non-malarial outcome.

3.5 Exclusion criteria

Children over five years of age and adults presenting with fever (suspected malaria) were excluded from the study.

3.6 Study Context

3.6.1 Policy context: Kenya National CHW program "Community Health Strategy."

Kenya's Community Health Strategy 2006 institutionalized CHWs into Level 1 of Kenya's primary health care delivery system by clearly providing constructs that operationalize service provision at the community level (MOH, 2005, Aridi *et al*., 2014). The operationalization includes establishing a Level 1 care unit to serve a local population of 5000 people by instituting a cadre of well-trained CHWs: each worker provides Level 1 service to 20 households; One Community Health Extension Worker (CHEW) supports 25 CHWs and ensures that the recruitment and management of CHWs are carried out by village and facility health committees (MOH 2005). Community health extension workers also support CHWs through supervision and coaching and meet with their CHWs monthly (Oliver *et al.,* 2015).

Parts of the Community Strategy were revised in 2010 following resolutions of the Ministry of Health, Health Sector Coordinating Committee (HSCC). Household coverage was adjusted to correspond with the population density, ranging from one CHW covering 500 people for areas with dense populations. The policy document also stipulated that the CHWs were entitled to a minimum payment of Kenya Shillings 2,000 (US$ 20) a month as a performance-based incentive (Director of Public Health and Sanitation, 2011).

The CHWs conjoin national health facilities and the community members with specific responsibilities such as health promotion, disease prevention, care-seeking and treatment of diseases such as uncomplicated malaria and diarrhea, compliance with treatment and advice, and household follow-up (MOH, 2005).

3.6.2 The Millennium Villages Project approach

The "Millennium Villages Project" (MVP) was a demonstration project of the Earth Institute at Columbia University and a non-governmental organization, Millennium Promise Alliance. The project hypothesized that an integrated approach to rural

development could be used to achieve the Millennium Development Goals (MDGs). MDG 8 (Combat HIV/AIDS, malaria, and other diseases) (Singh and Sachs, 2013).

The MVP's CHW program strategies are described elsewhere (Singh and Sachs, 2013, McCord *et al.*, 2012). In brief, the CHW program of the MVP utilized a workforce of CHWs, with each CHW serving at least 100-150 households and approximately 650 people. Senior CHWs supervised the CHWs in groups of six. The seniors were supervised by health facilitators in a ratio of roughly 8 to 20, depending on the setting. The CHWs provided preventative care through health education and limited curative services. They were provided with a CHW kit with essential drugs such as oral rehydration solution, zinc, paracetamol, RDTs for malaria parasite detection in reported fever cases, and Coartem® for the household-level treatment of positive RDT cases. Only children presenting with fever were tested for malaria. The CHWs were supported by Information and Communications Technology (ICT) systems facilitated through a mobile telephone system. The mobile health technology used information collected at the household level by CHWs to monitor the child and maternal health and compliance with treatment administered at the clinic level. Currently, within MVP, CHWs are County employed and are considered to be volunteers, although, at the time of the study, they were receiving an additional 4000 Kenyan Shillings per month (~US$40).

3.6.3 Diagnosis and management of Malaria at Health Facility

Case management at the ten government health facilities in the study site (Table 3.2) was based on WHO guidelines for treating malaria (WHO, 2010). Only confirmed malaria cases of uncomplicated malaria were initiated on treatment with ACT. Cases of severe/complicated malaria were given initial treatment and immediately transported in an ambulance to a referral hospital for parenteral treatment. All non-malarial cases were referred to health facilities for further management.

Table 3.2: Health facilities and their levels in the study area

Health Facility	Level
Mindhine	Dispensary
Onding'	Dispensary
Masogo	Dispensary
Marenyo	Health Center
Bar Sauri	Health Center
Ramula	Health Center
Nyawara	Health Center
Lihanda	Health Center
Gongo	Health Center
Yala	Sub-county Hospital

Source: Kenya Master Health Facility List

3.7 Data collection methods and tools

The millennium village's project adopted an integrated data collection tool for CHWs and health facility reporting. For this study, data were collected using a structured data abstraction form for all monthly fever entries (suspected malaria), malaria, and non-malarial counts presented by CHWs and ten health facilities among children under-five years of age from January 2013 to December 2015.

3.8 Precipitation data

Fever-related malaria and non-malarial cases are rainfall-sensitive. Therefore, attempts were made to utilize the available supply of satellite-based rainfall information to supplement the scantily available ground-based precipitation data. Monthly satellite rainfall data for the study area and period were obtained from the Tropical Rainfall Measurement Mission (TRMM) (Kummerow *et al.,* 2000). Satellite-based TRMM precipitation estimate has been used in predicting and simulating mosquito population dynamics and mosquito-borne disease risk (Adimi *et al.,* 2010). Different rainfall regimes were assessed for the association with fever,

malaria, and non-malaria counts: current study month estimate, one-month, two-month, and three-month lagged values, and two-month and three-month cumulative rainfall.

3.9 Data Management and Analysis

3.9.1 Descriptive Analysis

Data were descriptively analyzed as proportions of fever, malaria, and non-malarial cases out of the total population of children aged under-five years in a specific village in a given month. Results were presented in frequency tables and graphs of proportions or counts.

3.9.2 Inferential Analysis

Malaria and non-malaria data from CHW were presented in the form of counts by month, year, and village, whereas the ones from health facilities were presented in the form of counts by month and year alone. In both cases, the data was assumed to follow a Poisson distribution used to model counts of disease events in a group of individuals. Several forms are applicable – count of cases over some time with the amount of person-time at risk having to be considered, count of cases of disease with the size of the population at risk being taken into consideration, or a count of outcome that is measured over a geographical area. In this study, the count of cases of confirmed malaria and non-malaria with the size of the population at risk being taken into consideration was used.

The Poisson regression model was described as follows: $\boldsymbol{E(Y) = \mu = n\lambda}$ Where: $E(Y)$ = expected number of malaria or non-malaria cases, n adjusted for the different sizes of the population at risk. In this case, n was recorded on a log scale, i.e., the log (population at risk) is referred to as an offset. λ represented a function that defined the infection occurrence. One of the ways that λ could be related to the predictors (independent variables) - in this case, rainfall and month of the year, and village were: $\lambda = e^{\beta_0 + \beta_1 x}$ *Or* $\ln(\lambda) = \beta_0 + \beta_1 x$. Consequently, the Poisson model

was $E(Y) = ne^{\beta_0+\beta_1 x}$ *Or* $\ln E(Y) = \ln n + \beta_0 + \beta_1 x$ *Or*

$$\ln E(occurrence) = \ln \frac{E(occurrence)}{n} = \beta_0 + \beta_1 x$$ Where

$\ln E(occurrence)$ was the log of the expected value of the occurrence of malaria or non-malaria cases, which was modeled as a linear combination of predictors. This formed the univariable analysis (rainfall, month, year, and village separately for data from CHWs and month and year separately for data from health facilities).

The Poisson model assumes that the mean and the variance are equal (conditional upon the predictors in the model) - that is, the mean and the variance of counts are equal following consideration of the effects of the predictors in the model. However, the variance may be greater than the mean in the raw data (i.e., unadjusted estimates) and still meet this requirement. Nevertheless, if the unadjusted variance is greater than twice the unadjusted mean, then over-dispersion is highly suspected. Over-dispersion is said to occur when the variance is much larger than the mean. This is common with count data and arises when the data are clustered – persons within a village or with time. Thus, part of the variation between villages or unit time (months or years) was due to the variation between villages or times. Therefore, the model does not fit the data well. This study dealt with this problem by fitting a model that allowed the variance to be larger than the mean by assuming that the variance is a function of the mean as follows: $\text{var} = (1+\alpha\mu)\mu = \mu + \alpha\mu^2$ Where α was the over-dispersion parameter. This formulation gives rise to a negative binomial model. Note that if $\alpha = 0$, then the variance will equal μ, and the model is a simple Poisson model. The interpretation of a negative binomial distribution as a Poisson distribution with extra dispersion corresponds to a random-effects model where the distribution of Poisson means is subjected to additional variation with a gamma distribution. As with Poisson distribution, the usual form was similar to the expressions provided above for the Poisson model, except that $E(Y)$ had a negative binomial distribution. The negative binomial model was fit using an iterative maximum likelihood estimation procedure. The level of significance was set at

$P \leq 0.1$. The statistical significance of the contribution of the individual contributor (or group of predictors) to the model was tested using likelihood ratio tests ($P<0.05$). Over-dispersion was evaluated using a likelihood ratio test that compared the usual Poisson model to the negative binomial model by testing whether $\alpha = 0$ (level of significance set at $P \leq 0.05$).

3.10 Ethical Considerations

Ethical approval was obtained from the Kenya Medical Research Institute (Non-SSC protocol 030). Secondary data for analysis were collected while delivering healthcare from CHWs and clinical staff from the health facilities.

The following ethical guidelines were out in place during the research period:

1. Research data remained confidential throughout the study. Data had been de-identified. Therefore, there was no access to the patient identifiers in the medical records.
2. A waiver on consent documentation (i.e., patient authorization) had been granted.
3. Authorization had been obtained from the facilities where the study was conducted.

CHAPTER FOUR

RESULTS

4.1 The Proportions of malaria cases in space and time by CHWs

The incidence proportions of malaria cases diagnosed by CHWs increased with time from 4% in 2013 to 10% in 2015 (Fig. 1). The months of July, May, and June had the highest incidence proportions of malaria cases (10.2%, 8.7%, and 8.7%, respectively), while January, February, and October had the lowest incidence proportions of malaria cases (5.5% 6.4%, and 6.4% respectively) (Fig.2).

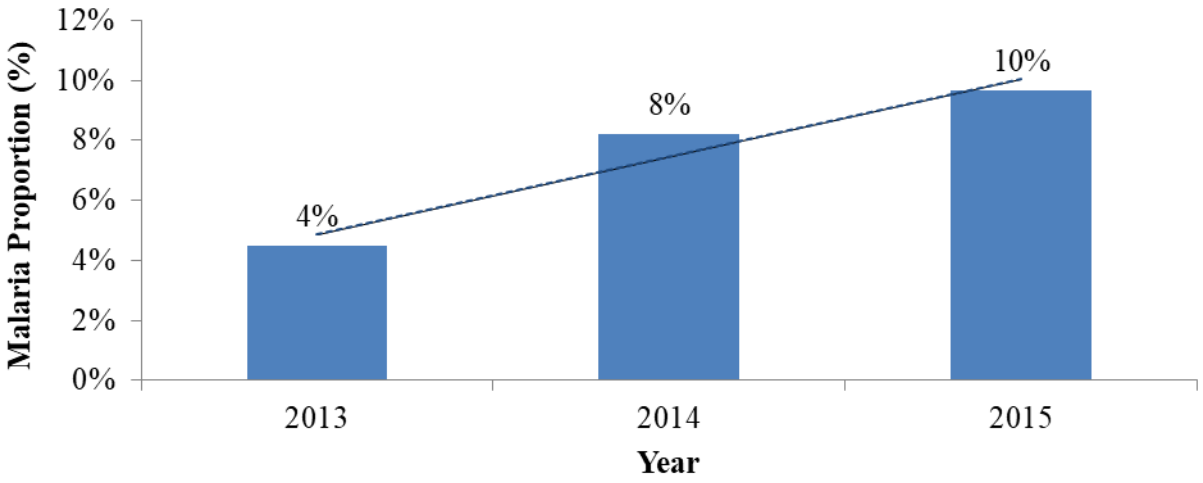

Figure 4.1: Incidence proportions of malaria cases diagnosed by CHWs by year 2013 to 2015 among children under-five years in Siaya County, Kenya

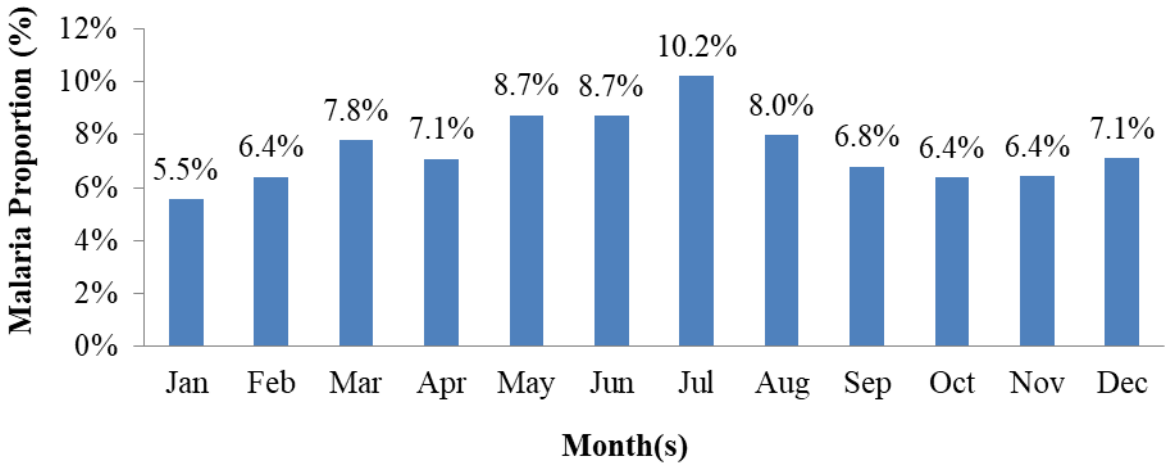

Figure 4.2: Monthly average incidence proportions of malaria cases diagnosed by CHWs by year 2013 to 2015 among children under-five years in Siaya County, Kenya

Five villages: Ramula, Gongo, Nyawara, Marenyo, and Jina in that order had the highest incidence proportions for malaria cases of 12%, 8.3%, 8%, 7.9%, and 7.7%, respectively, while Uranga, Anyiko, Lihanda, Nyandiwa, and Nyamninia recorded the lowest incidence proportions of 7.2%, 7.2%, 6.5%, 5.0% and 4.7% respectively (Table 4.1). The average incidence proportions of fever-related malaria cases in the ten villages between 2013 and 2015 were summarized in table 4.1.

Table 4.1: Mean (incidence) malaria proportions among children under-five years as reported by CHWs by village between the years 2013 and 2015 in Siaya County, Kenya

Village	Average Population median (IQR)[2]	Average fever counts mean (SD)[1]	Average Malaria counts mean (SD)[1]	Fever proportion (%) mean (SD)[1]	Malaria proportion (%) mean (SD)[1]
Anyiko, N = 36	491 (436, 523)	39.2 (14.9)	34.4 (13.3)	8.2 (3.5)	7.2 (3.1)
Gongo, N = 36	489 (456, 577)	51.3 (21.4)	41 (20.4)	10.4 (4.8)	8.3 (4.5)
Jina, N = 36	388 (300, 554)	38 (14)	29.9 (12.4)	9.6 (3.6)	7.4 (3)
Lihanda, N = 36	820 (743, 952)	63.9 (20.5)	54.7 (20.1)	7.6 (2.5)	6.5 (2.5)
Marenyo, N = 36	882 (850, 1,045)	76.4 (26.2)	69.4 (25.3)	8.4 (3.3)	7.7 (3.1)
Nyamninia, N = 36	943 (883, 983)	56.8 (28.2)	43.8 (24.4)	6 (3)	4.7 (2.6)
Nyandiwa, N = 36	607 (563, 653)	34.3 (24.9)	29.6 (22)	5.8 (4.3)	5 (3.8)
Nyawara, N = 36	389 (383, 448)	36.4 (22.7)	31.2 (20)	9.2 (6)	7.9 (5.3)
Ramula, N = 36	785 (711, 798)	102 (37.9)	92.1 (36.2)	13.2 (4.7)	12 (4.5)
Uranga, N = 36	735 (685, 739)	62.6 (26)	51.8 (24)	8.7 (3.9)	7.2 (3.5)
Overall, N = 360	669 (489, 820)	56.1 (31.6)	47.8 (29.5)	8.7 (4.5)	7.4 (4.1)

[1]Mean (SD); [2]Median (IQR)

4.2 The proportion of malaria cases in space and time in health facilities

The incidence proportions of malaria cases in health facilities decreased with time from 13% in 2013 to 11% in 2015 (Fig. 3). Similarly, the months of July, May, and June had the highest incidence proportion of malaria cases (20%, 19%, and 18% respectively), while December, October, and November had the lowest incidence proportions of malaria cases of 6%, 7%, and 8% respectively (Fig. 4).

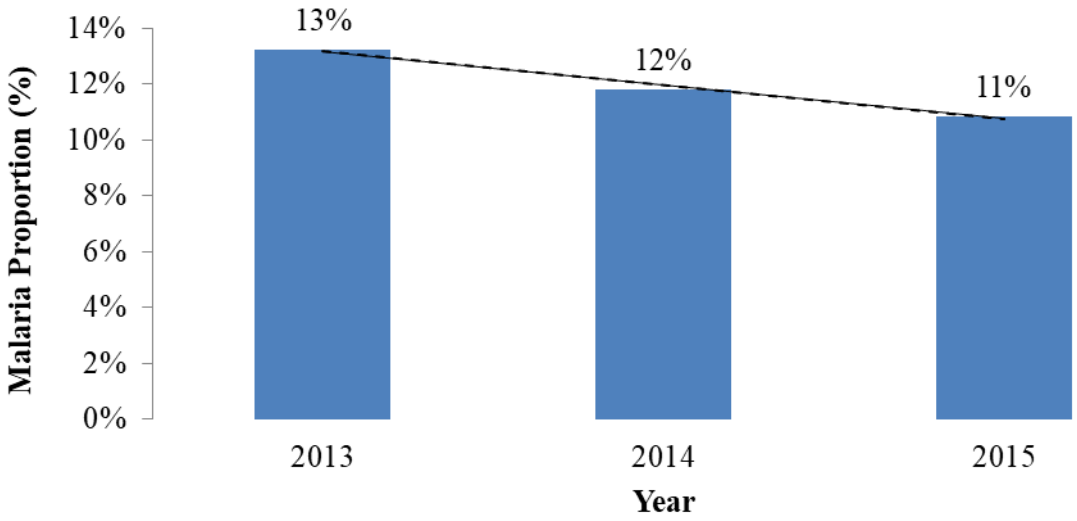

Figure 4.3: Average incidence proportions of malaria cases in health facilities in children under-five years between years 2013 to 2015 in Siaya County, Kenya

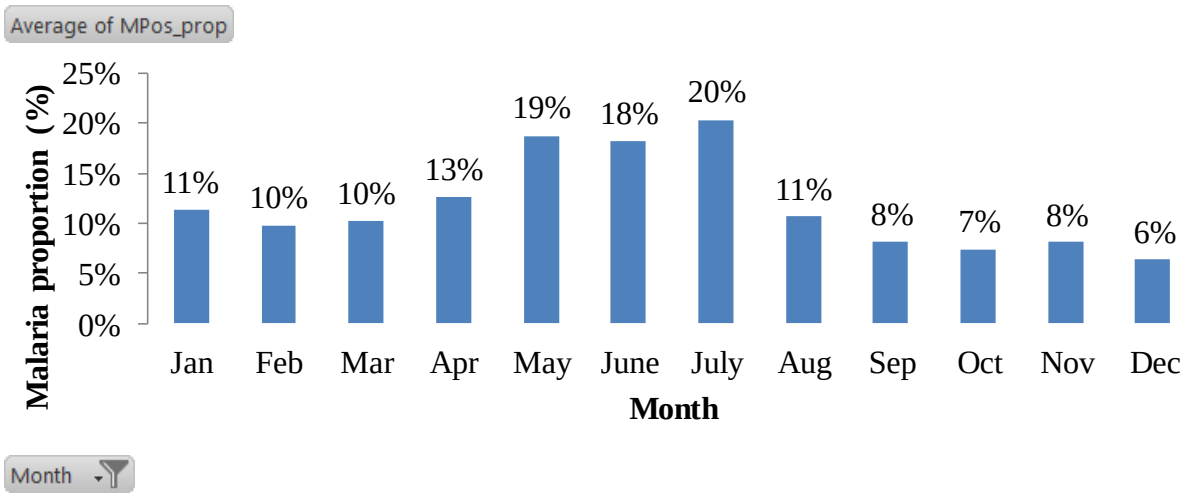

Figure 4.4: Monthly average incidence proportions of malaria cases in health facilities in children under-five years between the years 2013 to 2015 in Siaya County, Kenya

The average incidence proportions of fever-related malaria cases in the health facilities between 2013 and 2015 were summarized in table 4.2.

Table 4.2: Mean (incidence) malaria proportions among children under-five years as reported by health facilities between the years 2013 and 2015 in Siaya County, Kenya

Period	Average Population median (IQR)2	Average fever counts mean (SD)1	Average Malaria counts mean (SD)[1]	Fever proportion (%) mean (SD)[1]	Malaria proportion (%) mean (SD)[1]
2013, N = 12[1]	6886	1753.2 (651.4)	912.4 (377.4)	25.4 (9.4)	13.25 (5.48)
2014, N = 12[1]	6312	1563.5 (440.6)	745.6 (326.6)	24.7 (6.9)	11.81 (5.17)
2015, N = 12[1]	6613	1462.4 (527.4)	716.1 (350.8)	22.1 (7.9)	10.82 (5.3)
Overall, N = 36[1]	6613 (6312, 6886)	1593 (544.7)	791.4 (353)	24.1 (8)	11.96 (5.26)

[1]Mean (SD); [2]Median (IQR)

4.3 The proportion of non-malarial cases in space and time by CHWs

The incidence proportion of non-malaria cases by CHWs varied with time: lowest in 2014 at 1.3% and highest in 2013 at 1.4% (Fig. 5). The months of March, May, and July had the highest incidence proportions of non-malarial cases (1.8%, 1.43%, and 1.42% respectively in that order), while December, October, and September had the lowest incidence proportions of non-malarial cases of 1.02%, 1.08%, and 1.2% respectively in that order (Fig. 6).

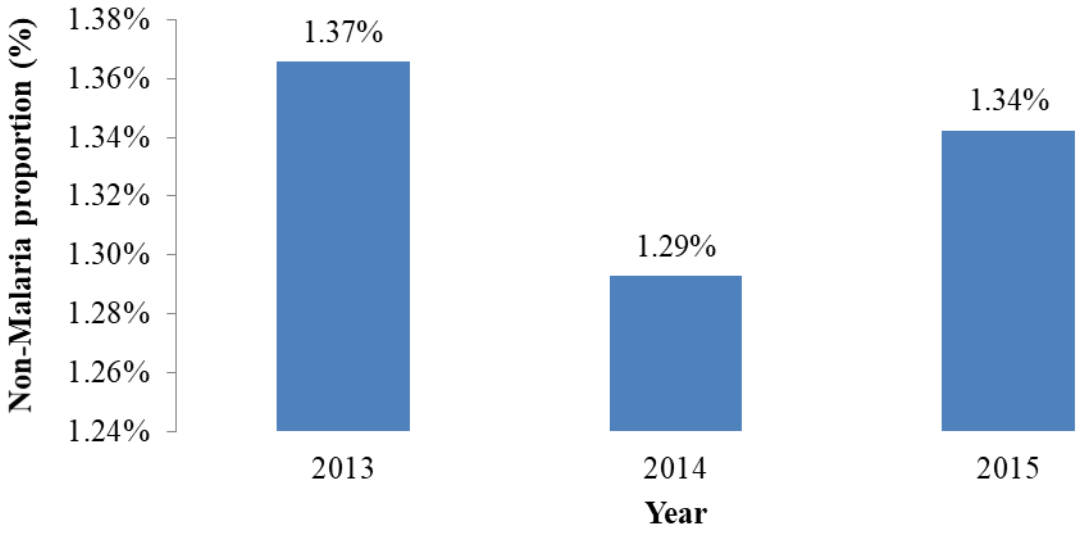

Figure 4.5: Average incidence proportion of non-malarial cases diagnosed by CHWs in children under-five years between years 2013 and 2015 in Siaya County, Kenya

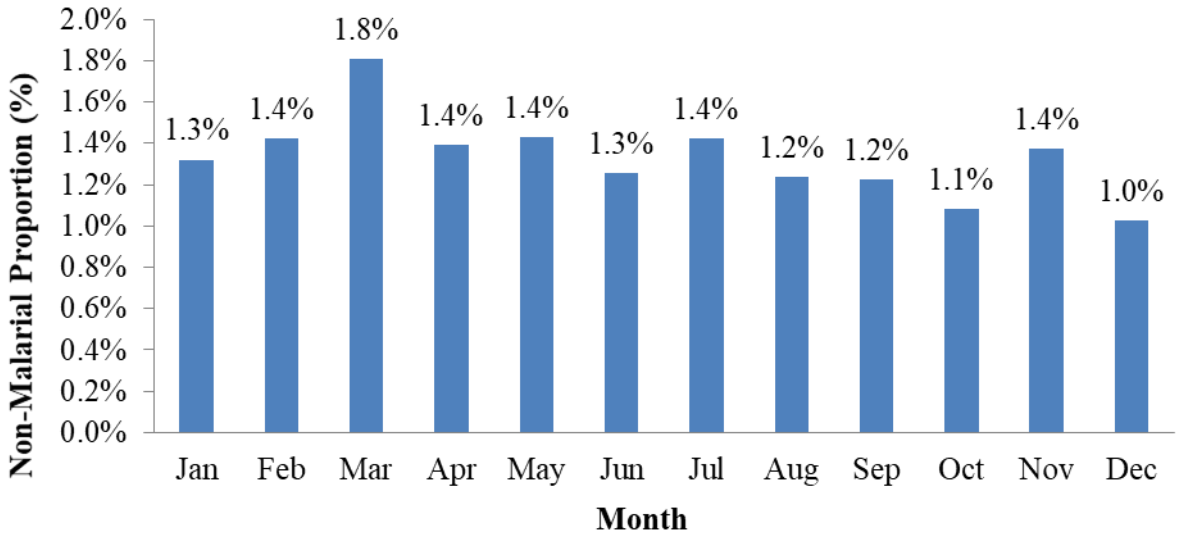

Figure 4.6: Average monthly incidence proportions of non-malarial cases diagnosed by CHWs among children under-five years between years 2013 and 2015 in Siaya County, Kenya

Jina village had the highest incidence proportion for non-malarial cases of 2.16%, while Nyandiwa and Marenyo recorded the lowest incidence proportions of 0.79%, as shown in Table 4.3.

Table 4.3: Mean (incidence) non-malarial proportions among children under-five years as reported by CHWs by village between the years 2013 and 2015 in Siaya County, Kenya

Village	Average Population median (IQR)2	Average fever counts mean (SD)1	Average Malaria negative counts mean (SD)1	Malaria negative proportion (%) mean (SD)1
Anyiko, N = 36	491 (436, 523)	39.2 (14.9)	4.8 (3.5)	1 (0.73)
Gongo, N = 36	489 (456, 577)	51.3 (21.4)	10.3 (4.6)	2.02 (0.9)
Jina, N = 36	388 (300, 554)	38 (14)	8 (3.7)	2.16 (1.25)
Lihanda, N = 36	820 (743, 952)	63.9 (20.5)	9.1 (5.1)	1.08 (0.58)
Marenyo, N = 36	882 (850, 1,045)	76.4 (26.2)	7 (3.5)	0.76 (0.39)
Nyamninia, N = 36	943 (883, 983)	56.8 (28.2)	12.9 (5.5)	1.38 (0.58)
Nyandiwa, N = 36	607 (563, 653)	34.3 (24.9)	4.7 (4)	0.79 (0.68)
Nyawara, N = 36	389 (383, 448)	36.4 (22.7)	5.2 (4.5)	1.32 (1.16)
Ramula, N = 36	785 (711, 798)	102 (37.9)	9.6 (4.7)	1.25 (0.59)
Uranga, N = 36	735 (685, 739)	62.6 (26)	10.6 (4.5)	1.49 (0.65)
Overall, N = 360	669 (489, 820)	56.1 (31.6)	8.2 (5.1)	1.32 (0.9)

1Mean (SD); 2Median (IQR)

4.4 The proportion of non-malarial cases in space and time in health facilities

The incidence proportion of non-malarial cases was highest in 2014 at 13% and lowest in 2015 at 11% (Figure 7).

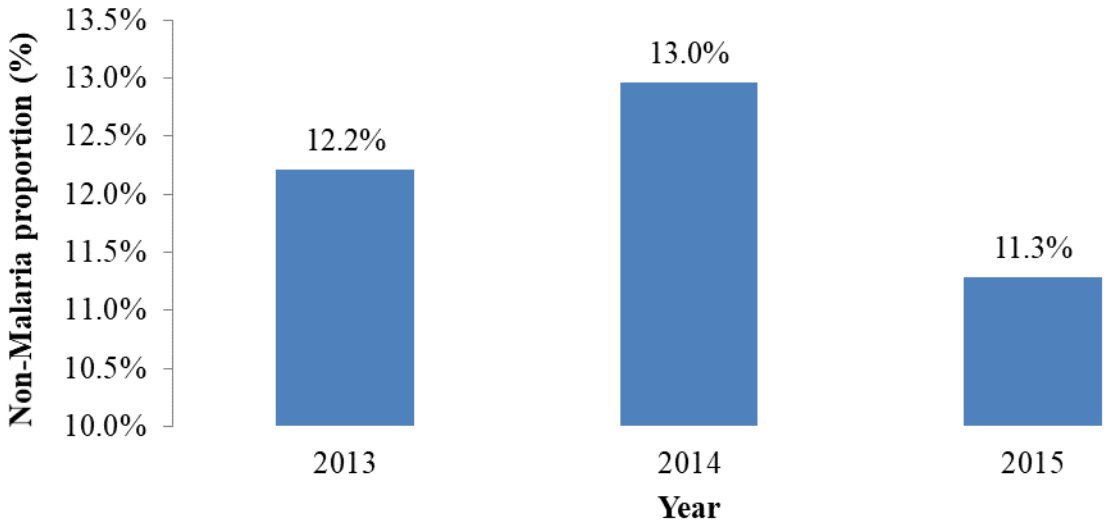

Figure 4.7: Average incidence proportion of non-malarial cases in health facilities among children under-five years between years 2013 and 2015 in Siaya County, Kenya

The months of July, May, and June had the highest incidence proportions of non-malarial cases (15.9%, 14.8%, and 14.5%, respectively, in that order), while December, November, and October had the lowest incidence proportions of non-malaria cases (8.7%, 9.2%, and 9.8% respectively in that order) (Fig. 8).

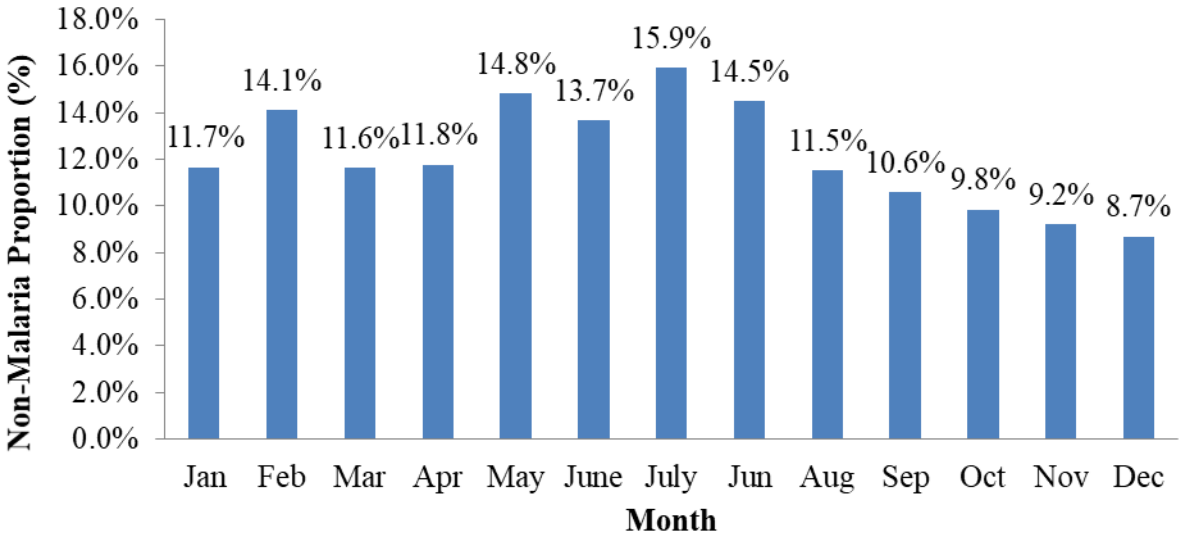

Figure 4.8: Monthly average incidence proportions of non-malarial cases in health facilities among children under-five years between years 2013 and 2015 in Siaya County, Kenya

The average incidence proportions of fever-related non-malarial cases in the health facilities between 2013 and 2015 were summarized in table 4.4.

Table 4.4: Mean (incidence) non-malarial proportions among children under-five years as reported by health facilities between the years 2013 and 2015 in Siaya County, Kenya

Period	Average Population median (IQR)2	Non-Malarial counts mean (SD)[1]	Non-Malarial proportion (%) mean (SD)[1]
2013, N = 12[1]	6886	840.8 (337.5)	12.21 (4.9)
2014, N = 12[1]	6312	817.8 (198.9)	12.95 (3.15)
2015, N = 12[1]	6613	746.2 (232.6)	11.28 (3.51)
Overall, N = 36[1]	6613 (6312, 6886)	801.63 (258.71)	12.15 (3.87)

[1]Mean (SD); [2]Median (IQR)

4.5 Relationship between rainfall and fever-related malaria and non-malarial cases

None of the tested rainfall regimes (current, lagged, or cumulative) were associated with malaria and non-malarial cases during the three years *(P*>0.1) (Tables 4.5 and 4.7).

Table 4.5: Association between malaria cases diagnosed by CHWs and independent variables in children under-5 years of age between January 2013 and December 2015 in Siaya County, Kenya

Variable	Variable category	Coefficient	95% Confidence interval	P>|z|	Likelihood ratio test P*	α	Likelihood-ratio test of α=0
Village	Marenyo	0.52	[0.30, 0.74]	0.000	0.000	0.21	0.000
	Nyawara	0.06	[-0.17, 0.28]	0.608			
	Nyandiwa	-0.21	[-0.44, 0.01]	0.064			
	Gongo	0.26	[0.04, 0.49]	0.021			
	Ramula	0.83	[0.61, 1.06]	0.000			
	Nyamninia	0.01	[-0.21, 0.24]	0.896			
	Jina	-0.13	[-0.36, 0.08]	0.234			
	Uranga	0.32	[0.10, 0.54]	0.005			
	Lihanda	0.23	[0.01, 0.46]	0.040			
Year	2014	0.52	[0.39, 0.64]	0.000	0.000	0.22	0.000
	2015	0.73	[0.61, 0.86]	0.000			
Month	February	0.15	[-0.13, 0.42]	0.301	0.001	0.28	0.000
	March	0.35	[0.07, 0.63]	0.012			
	April	0.26	[-0.01, 0.54]	0.063			
	May	0.45	[0.18, 0.73]	0.001			
	June	0.45	[0.18, 0.73]	0.001			
	July	0.59	[0.31, 0.87]	0.000			
	August	0.34	[0.06, 0.62]	0.015			
	September	0.18	[-0.09, 0.46]	0.193			
	October	0.12	[-0.15, 0.40]	0.374			
	November	0.15	[-0.12, 0.43]	0.284			
	December	0.24	[-0.03, 0.52]	0.088			
Rainfall	Current	0.00042	[-0.0006, 0.0015]	0.436	0.436	0.30	0.000
	1-month lag	-0.0004	[-0.0006, 0.0015]	0.410	0.411	0.30	0.000
	2-month lag	0.00014	[-0.002, 0.002]	0.896	0.896		
	2month cumulative	-0.00001	[-0.0006, 0.0006]	0.964	0.964	0.30	0.000
	3 month cumulative	0.00006	[-0.0004, 0.0006]	0.825	0.825	0.30	0.000
	4 month cumulative	-0.00005	[-0.0005, 0.0004]	0.847	0.847	0.30	0.000

*P is used to test the statistical significance ($P \leq 0.05$) of the contribution of the variable to the univariable model; ⩲ P is used to test the statistical significance of α (the overdispersion parameter). When the statistical significance of α is significant ($P \leq 0.05$), it suggests that the data's variance is higher than expected for a Poisson regression.

4.6 Differences in space and time in the fever-related malaria cases as diagnosed by CHWs

Five villages: Ramula (P=0.000), Marenyo (P=0.000), Uranga (P=0.005), Gongo (P=0.021), and Lihanda (P=0.040) in that order had a significantly higher incidence of malaria cases (P<0.05) (Table 4.5). In addition, the village variable was significantly associated (likelihood ratio test P<0.001) with malaria cases (Table 4.5). The incidence of malaria cases increased with time, and the difference between the years was statistically significant (likelihood ratio test P<0.001) (Table 4.5). All months had a higher incidence of malaria cases relative to January (P<0.05). The higher incidence of malaria cases was statistically different from January in March (P=0.012) and in the period May (P=0.001) to August (P=0.015). The long-term monthly sequence starting with the highest to the lowest incidence of malaria cases was July, May and June, March, August, April, September, November, February, October, and January.

4.7 Differences in space and time in the fever-related malaria cases as diagnosed in health facilities

In contrast with diagnoses by CHWs, the incidence of malaria cases diagnosed in facilities decreased with time though the difference among the years was not statistically significant (*P=0.399*) (Table 4.6). The months of May (P=0.003), June (P=0.001), and July (P=0.000) had a higher incidence of malaria cases relative to January (P<0.05). Again, in contrast with diagnoses by CHWs, seven months (February, March, August, September, October, November, and December) had a lower incidence of malaria cases relative to January. The lower incidence was statistically different from January for the period between September (P=0.044) and December (P=0.000) but not in February (P=0.403), March (P=0.536), and August

(*P*=0.698). The long-term monthly sequence starting with the highest incidence of malaria cases was July, June, May, April, January, August, March, February, September, November, October, and December. The likelihood ratio tests for all predictors were highly significant (P<0.001), implying that the data's variance was higher than expected for a Poisson regression model.

Table 4.6: Association between malaria cases diagnosed in health facilities and independent variables in children under five years of age between January 2013 and December 2015 in Siaya County, Kenya

Variable	Variable category	Coefficient	95% Confidence interval	P>|z|	Likelihood ratio test P*	α	Likelihood-ratio test of α=0
Year	2014	-0.16	[-0.49, 0.17]	0.337	0.399	0.17	0.000‡
	2015	-0.22	[-0.55, 0.11]	0.188			
Month	February	-0.13	[-0.46, 0.18]	0.403	0.000	0.04	0.000
	March	-0.10	[-0.42, 0.22]	0.536			
	April	0.11	[-0.21, 0.43]	0.505			
	May	0.50	[0.17, 0.82]	0.003			
	June	0.56	[0.23, 0.88]	0.001			
	July	0.59	[0.26, 0.91]	0.000			
	August	-0.06	[-0.39, 0.26]	0.698			
	September	-0.33	[-0.66, -0.01]	0.044			
	October	-0.42	[-0.75, -0.09]	0.012			
	November	-0.33	[-0.66, -0.01]	0.043			
	December	-0.58	[-0.91, -0.25]	0.000			

**P* is used to test the statistical significance (*P*≤0.05) of the contribution of the variable to the univariable model; ‡ *P* is used to test the statistical significance of α (the overdispersion parameter). When the statistical significance of α is significant (*P*≤0.05), it suggests that the data's variance is higher than expected for a Poisson regression.

4.8 Differences in space and time in the fever-related non-malarial cases as diagnosed by CHWs

All villages except Marenyo, Nyawara, and Nyandiwa had a significantly higher incidence proportion of non-malarial cases (Table 4.7). Nevertheless, the village variable was significantly associated (likelihood ratio test P=0.000) with non-malarial cases (Table 4.7). Temporally, the risk of reporting non-malarial cases in 2014 and 2015 was not significantly different from 2013 (Likelihood ratio test P>0.001) (Table 4.7). Long-term, the coefficient magnitude of all months did not differ substantially from January; indeed, only March was found to have a statistically higher risk of reporting non-malarial cases relative to January (P=0.030).

Table 4.7: Association between non-malarial cases diagnosed by CHWs and independent variables in children under-five years of age between January 2013 and December 2015 in Siaya County, Kenya

Variable	Variable category	Coefficient	95% Confidence interval	P>|z|	Likelihood ratio test P*	α	Likelihood-ratio test of α=0
Village	Marenyo	0.19	[-0.07, 0.47]	0.159	0.000	0.17	0.000 ⩢
	Nyawara	0.24	[-0.04, 0.52]	0.098			
	Nyandiwa	-0.08	[-0.36, 0.20]	0.577			
	Gongo	0.85	[0.59, 1.11]	0.000			
	Ramula	0.55	[0.28, 0.81]	0.000			
	Nyamninia	0.76	[0.50, 1.02]	0.000			
	Jina	0.53	[0.26, 0.80]	0.000			
	Uranga	0.71	[0.44, 0.97]	0.000			
	Lihanda	0.42	[0.15, 0.68]	0.002			
Year	2014	-0.11	[-0.27, 0.04]	0.157	0.268	0.27	0.000
	2015	0.00	[-0.16, 0.16]	0.999			
Month	February	0.07	[-0.23, 0.38]	0.636	0.06	0.25	0.000
	March	0.33	[0.03, 0.64]	0.030			
	April	0.07	[-0.23, 0.38]	0.643			
	May	0.09	[-0.21, 0.40]	0.553			
	June	0.01	[-0.29, 0.32]	0.921			
	July	0.08	[-0.23, 0.38]	0.619			
	August	-0.06	[-0.36, 0.26]	0.727			
	September	-0.09	[-0.40, 0.22]	0.582			
	October	-0.20	[-0.52, 0.12]	0.218			
	November	0.04	[-0.26, 0.35]	0.765			
	December	-0.22	[-0.54, 0.09]	0.163			
Rainfall	Current	-0.0002	[-0.001, 0.000]	0.675	0.675	0.27	0.000
	1-month lag	-0.0009	[-0.002, 0.000]	0.076	0.076	0.27	0.000
	2-month lag	0.001	[-0.001, 0.005]	0.372	0.372	0.27	0.000
	2month cumulative	-0.0005	[-0.001, 0.0002]	0.169	0.169	0.27	0.000
	3 month cumulative	-0.0003	[-0.0009, 0.0002]	0.180	0.180	0.27	0.000
	4 month cumulative	-0.0003	[-0.0009, 0.0002]	0.202	0.202	0.27	0.000

*P is used to test the statistical significance ($P \leq 0.05$) of the contribution of the variable to the univariable model; ⩢ P is used to test the statistical significance of α (the overdispersion parameter). When significant ($P \leq 0.05$), it suggests that the variance in the data is higher than would be expected for Poisson regression.

4.9 Differences in space and time in the fever-related non-malarial cases as diagnosed in health facilities

The Incidence of non-malarial cases in 2014 and 2015 was not statistically different from 2013 (Likelihood ratio test $P>0.001$) (Table 4.8). However, on a monthly average, July was the only month with a higher incidence of non-malarial cases relative to January ($P=0.031$).

Table 4. 8. Association between non-malarial cases diagnosed in health facilities and independent variables in children under 5 years of age between January 2013 and December 2015 in Siaya County, Kenya

Variable	Variable category	Coefficient	95% Confidence interval	P>|z|	Likelihood ratio test P*	α	Likelihood-ratio test of α=0
Year	2014	0.01	[-0.24, 0.26]	0.937	0.63	0.096	0.000
	2015	-0.10	[-0.35, 0.15]	0.424			
Month	February	0.19	[-0.19, 0.58]	0.338	0.057	0.058	0.000
	March	-0.005	[-0.39, 0.38]	0.977			
	April	0.009	[-0.37, 0.39]	0.962			
	May	0.24	[-0.14, 0.63]	0.221			
	June	0.20	[-0.18, 0.58]	0.314			
	July	0.43	[0.04, 0.81]	0.031			
	August	-0.005	[-0.39, 0.38]	0.979			
	September	-0.08	[-0.47, 0.30]	0.670			
	October	-0.16	[-0.55, 0.22]	0.401			
	November	-0.23	[-0.62, 0.15]	0.240			
	December	-0.30	[-0.68, 0.09]	0.091			
Rainfall	Current	-0.001	[-0.003, 0.0003]	0.122	0.130	0.09	0.000
	1month lag	-0.001	[-0.002, 0.0007]	0.240	0.246	0.09	0.000
	2 month cumulative	-0.0009	[-0.002, 0.0002]	0.098	0.104	0.09	0.000
	3 month cumulative	-0.0006	[-0.002, 0.0003]	0.196	0.200	0.09	0.000

*P is used to test the statistical significance ($P\leq0.05$) of the contribution of the variable to the univariable model; ⩵ P is used to test the statistical significance of α (the overdispersion parameter). When significant ($P\leq0.05$), it suggests that the variance in the data is higher than would be expected for Poisson regression.

CHAPTER FIVE

DISCUSSION

Whereas the incidence proportions of malaria cases using household-administered RDTs diagnosed by CHWs increased with time, the incidence proportions of malaria in health facilities decreased over time during the study period. This trend in diagnosis concurs with a reported increase in effective utilization of CHWs as a source of advice and case management for children with fevers at the household level, corresponding with a decline in visits to government facilities and other sources, including shops in coastal Kenya (Kisia *et al*., 2012). It reflects a gradual shift in the use of health facilities towards the use of CHWs for health care by the community. It also demonstrates an emerging health care delivery system where most simple malaria cases (uncomplicated) are detected and treated at the household level. In contrast, severe malaria and non-malarial cases are referred to health facilities for further management. Moreover, the study findings support that CHWs can complement facility-based health service delivery to communities in developing countries such as Kenya (Kisia *et al.*, 2012).

It is possible that CHWs' deep and extensive understanding of the community's context and values and their permanent residency within the community generates widespread acceptable client-service provider relationships relative to health facility staff (Tiono *et al*., 2008, Nsabagasani *et al*., 2007). This shift to diagnosis and treatment by CHW increases the proportion of children who receive appropriate treatment for febrile illness and receive it early, within 24 hours of the onset of symptoms (Gyapong and Garshong, 2007). Potential benefits of this shift include decreasing the burden of uncomplicated pediatric fever cases and, therefore, availing health facility staff (Tiono *et al*., 2008) for other cases, particularly non-malarial cases.

Emerging professionalized CHW programs have deliberately and progressively been supported in extending primary health care from facilities to communities in rural and low-income settings in diverse countries (Liu *et al*., 2011). By integrating CHW programs into the formal healthcare delivery systems with training, supervision,

reporting, and feedback mechanisms, communities may be starting to be sensitive to these program mechanisms. Given the broader range of services CHWs provide, by taking advantage of the new technologies in health, qualitative research is needed to understand the experiences and attitudes of communities towards CHW programs. This would provide evidence to support further scaling up and deeper integration of a formal CHW cadre into primary health care systems. Areas of health that would greatly benefit are surveillance to detect epidemics early, rapid diagnosis and case management, and implementing preventive measures for diseases that contribute to mortality in sub-Saharan Africa.

Nevertheless, these findings were realized in the context of a project that emphasized paid, supervised, smart phone-empowered, a trained cadre of CHWs for improved quality of services, retention, and accountability (Singh and Sachs, 2013). Whereas the approach and features of the project could have positively influenced the results presented in this paper, the findings are a pointer to the fact that if well supported and motivated, CHW activities can have a profound effect on improving public health in the communities. The cost of scaling up a CHW sub-system was computed to be US$6·56 per head per year for the rural population, including smartphone utilization (Earth Institute, 2011). This demonstrates how a high-impact system can be implemented at a low cost that national governments in sub-Saharan Africa can afford.

To further understand why there was an increase in fever-related malaria cases detected by CHWs over the study period, possible reasons are: (1) decreased availability or use of vector control programs and dilapidation of the healthcare infrastructure; and (2) climate variability. Malaria is a climate-sensitive disease with temperature influencing the development rates and longevity of malaria parasites and mosquito vectors (Craig *et al*., 1999). In addition, rainfall affects the availability of mosquito aquatic stage breeding sites and, thus, mosquito population dynamics (Craig *et al*., 1999). July, May, and June had the highest incidence proportions of malaria cases diagnosed by CHWs and at health facilities after the onset of extended rainfall. However, there is no evidence to support substantial climate variability as measured by the average annual variance in the temperature and precipitation during

the study period to result in the observed increases in detection. In addition, the period of study was too short for detailed analyses of the effects of climate variability. On the progressive temporal preference of CHWs, a previous study in Kenya reported diverse barriers to both the demand and delivery of prompt and effective treatment for malaria in children under five years of age at government health facilities (Chuma *et al*., 2010). Notably, the effects of extreme rainfall on local infrastructure, for instance, flood damage to roads and bridges, can affect community access and mobility to health facilities and shift the demand for health care to the closest available CHWs. This study has no evidence that these factors may have played a role in this context.

Moreover, the study period coincided with the commencement of the devolved health care service delivery in Kenya. Therefore, the dilapidation of the healthcare infrastructure can theoretically be ruled out due to initial enthusiasm about the new health delivery system. A separate study examined pediatric hospitalizations due to malaria over two 36-month periods: September 2003 to August 2006 and September 2006 to August 2009 (Okiro *et al*., 2010). These two periods represented significant shifts in intervention policy change and scaled intervention (pre- and post-, respectively). Whereas all sites showed a significant reduction in malaria cases between these two time periods, the situation was different in Siaya County, where malaria admission rates rose in the second period compared to the pre-scaled intervention period before September 2006 (Okiro *et al*., 2010). This suggests that malaria transmission risk is persistently high in Siaya County and requires attention.

Non-malarial cases occurred throughout the year with no significant variation across the years, though in lower proportions compared to malaria. Increasing access to parasitological diagnosis of malaria through microscopy and rapid diagnostic tests has raised awareness among health care workers and, indeed, in the communities that even in a malaria endemic setting, non-malarial fever cases contribute to significant morbidity and mortality. Malawi's prevalence of non-malarial febrile illness was higher in children under five (Kapito-Tembo *et al*., 2020). The most common clinical diagnoses among febrile patients with negative mRDTs were respiratory infections, gastroenteritis, and musculoskeletal pain (Kapito-Tembo *et al*., 2020). This

demonstrates the burden of non-malarial fever-related illnesses among children under-fives. In this study area, CHWs were trained to refer non-malarial fever cases, indicating that CHWs would experience difficulties evaluating and managing patients with fever when the mRDTs were negative. This calls for health care planning to prioritize training, point-of-care diagnostics, and treatment algorithms for CHWs to similarly reduce the burden of uncomplicated non-malarial fever cases seen at health facilities (Sinyangwe *et al*., 2016). In a study in Ghana, endemic for malaria, the incidence of non-malarial fevers was higher among infants with low birth weights, infants from households of poor socioeconomic status, and infants living furthest from a health facility (Asante *et al*., 2016). These dynamics could have played a role in this study. Similar to malaria cases, the months of March, May, and July had the highest incidence proportions of non-malarial cases after the onset of long rains. Few studies have examined the relationship between rainfall with the occurrence of non-malarial fever cases (Garcia-Vidal *et al*., 2013, Paynter *et al*., 2013). Lack of sunshine was strongly associated with pneumonia among young children in the Philippines (Paynter *et al*., 2013). In rural Kenya, pneumonia incidence peaked during the twice-yearly high malaria seasons, 1-2 months after peak rainfall (Tornheim *et al*., 2007). Heavy rain has also been associated with increased outbreaks of enteric pathogens, usually due to contamination of water supplies (Bhavnani *et al*., 2014). However, this study did not aim to determine specific causes of non-malarial fevers. Still, a pattern existed whereby, coinciding with the onset of long rains in March, the risk of diagnosing non-malaria fever cases was high at the community level. With this seasonal predictability of malaria transmission and non-malarial fever occurrences, these findings present an opportunity for temporally targeted refresher CHW and facility-based health care providers' training and improved capacity in terms of availing prevention strategies, diagnostic kits, and medications.

Studies have also reported an association between rainfall and malaria incidence three to four months after the commencement of rains (Van der Hoek *et al*., 1997, Githeko & Ndegwa, 2001, Hay *et al*., 2005, Chaves *et al*., 2012, Toure *et al*., 2016). In May 2002, exceptional rainfall in the western highlands of Kenya led to malaria epidemics in some districts in June and July (Brooker *et al*., 2004), and the months

with peak parasite densities appeared to be one to two months following rainfall peaks (Munyekenye *et al*., 2005, Zhou *et al*., 2015). Predictably, increased rainfall generates multiple breeding sites for mosquitoes and other vectors, thus increasing their numbers and influencing the vectorial capacity. However, in this study, none of the tested rainfall regimes (current, lagged, or cumulative) was associated with reporting malaria and non-malarial fever cases during the three years. A similar observation has been reported where other environmental parameters, i.e., vegetation index and surface temperature, demonstrated strong associations (Adimi *et al*., 2010). In Western Kenya (and Africa in general), weather stations are sparse, and data emanating from them are unreliable. For this lack of meteorological information, satellite-based methods were used to source the rainfall data. Previous reports have favorably validated satellite products derived from the TRMM sensor with ground-based weather stations (Dinku *et al*., 2008).

Moreover, the TRMM has been demonstrated to present a superior spatial and temporal estimate of precipitation in Africa (Dinku *et al*., 2008) relative to other satellite-based rainfall estimate products. Other reasons that could have influenced the observed lack of relationship in this study include topography, vegetation, and soil type differences, as well as shallow groundwater behavior, which have been reported to influence malaria transmission at micro-habitat levels (Bomblies *et al*., 2009). Similarly, there is good evidence of associations between non-malaria febrile illnesses and climate on several temporal and geographical scales, especially for vector-borne diseases, many enteric infections, and certain water-related diseases (Ogden, 2017, Hales, 2019). For instance, many enteric diseases show a seasonal pattern, suggesting climate sensitivity. In the tropics, diarrheal diseases typically peak during the rainy season (Bhavnani *et al*., 2014). Floods and droughts are each associated with an increased risk of diarrheal diseases, although much of the evidence is anecdotal. These suggestions are plausible, however, since heavy rainfall can wash contaminants into water supplies. At the same time, drought conditions can reduce freshwater availability, increasing hygiene-related diseases.

Significant village-scale spatial variations in malaria and non-malarial diagnosis were observed across villages with regard to community-based diagnosis in this

study. These findings could be due to two reasons and interaction between them. The variations may have occurred due to variations in the locations of the villages across the study site, as observed by Chanda *et al.* (2011) in Zambia. Spatial epidemiology describes how the temporal dynamics of a host, vector(s), and pathogen populations interact spatially within a permissive environment to enable transmission (Reisen, 2010). In the context of spatial epidemiology in this study, villages on the outer edges of the study area (Ramula, Gongo, Nyawara) had high malaria cases compared to villages in the center of the study area (Nyamninia, Nyandiwa, Lihanda). Inter-village heterogeneity in local hydrology can generate different micro-habitats of suitable breeding areas following rain, perhaps exhibiting different levels of malaria transmission. Village-scale spatial variability in hydrology may also be associated with either the presence/absence of vegetation that provides resting sites for adult mosquitoes or with topographic effects. In this manner, village-scale hydrological conditions may become important determinants of local malaria transmission (Bogh *et al*., 2007). The observation could further influence that the characteristic spatial scale of Anopheles mosquito population movement is approximately one to two kilometers (Costantini *et al*., 1996), roughly equivalent to the size of villages in Kenya. Indeed, studies have reported that breeding habitats with high transmission intensity frequently occur within tens to hundreds of meters of the nearest human habitation (Minakawa *et al*., 2002). Secondly, socio-economic and socio-cultural factors influencing health-seeking behavior could generate village-level spatial effects. One possible explanation for this is the distance to the CHW versus the distance to health centers. Families far from health centers are more likely to utilize CHWs than those close to health centers to manage uncomplicated fever-related malaria and non-malaria (Blanas *et al*., 2013).

In addition, individual factors in terms of the performance of CHWs and corresponding perception of effectiveness may have varied from one village to another. It is also possible that the level of support supervision by support managers was not objectively constant across the villages. This latter reason is supported by studies that evaluated CHW performance in 1998, 1999, and 2001 in Siaya, Kenya, which reported that critical reasons for the inadequacies in performance appeared to be guideline ambiguities and weak and subjective clinical supervision (Kelly *et al*.,

2001). In Ethiopia, socio-economic, geographic, and demographic factors were closely associated with the risk of malaria in different villages (Ayele *et al*., 2013), while in Nigeria, Ghana and Kenya, there were increased risks of non-malaria fever cases among the poor and among rural populations (Novignon and Nonvignon, 2012, Gayawan *et al*., 2014). High population density and inadequate water supply have also been associated with specific non-malaria febrile infections (Bemis *et al*., 2014, Nagi *et al*., 2014, von Mollendorf *et al*., 2015, Nakhapakorn and Tripathi, 2005). Therefore, this study hypothesizes that socio-economic and socio-cultural factors within community-malaria and non-malarial case management associated with CHWs may affect perceived spatial variations in malaria and non-malarial transmission risk and detection.

This study was not without limitations. A lack of control groups made it difficult to assess the internal validity of these findings. However, this study utilized the baseline report of 2005 (Mutuo *et al*., 2006, Sanchez *et al*., 2007) in the "Millennium Villages Project" to determine the initial burden of malaria in the study area that could have informed the differences in observed results. More so, the fact that this multi-year study hypothesizes improved trends of CHW and health facilities utilization is similar to many studies conducted in the same geographical context corresponding to a non-reported significant change in the favorable climatic conditions for malaria and non-malarial disease transmission. Secondly, one village, "Sauri," had undertaken IRS within the study period that could have influenced malaria and non-malarial outcomes. In the analysis, data from the village were excluded to limit the bias that could have been observed. Lastly, this study did not acquire data that would increase the understanding of factors associated with the utilization of CHWs relative to the utilization of health facilities. Further studies would be needed to answer whether increased utilization of CHWs and increased diagnosis of malaria and non-malarial fever are associated with improved access to prompt and effective fever management.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

1. The incidence proportions of malaria increased with time in the cases diagnosed and reported by CHWs and decreased with time in health facilities. The chance of a malaria case being diagnosed by CHWs versus being diagnosed in a health facility was similar in 1-3 months following the long rainfall period: March-June.
2. Non-malaria fever cases occurred throughout the year at lower proportions than malaria at the community level reported by CHWs and in the health facilities.
3. Rainfall, tested under different regimes (current, lagged, or cumulative), was not a predictor for diagnosing malaria and non-malarial cases by CHWs and in health facilities.
4. Significant village-scale spatial variations in the incidence proportions of malaria and non-malaria cases were across the ten villages.

6.2 Recommendations

The following recommendations were made from this study.

1. Strengthen and scale up CHW programs. The predictability of malaria cases presents opportunities for policy-targeted preparedness and control measures, including healthcare workers' training and supportive supervision, to realize overall case management of fever-related illnesses. This has the potential for improved management of malaria in Kenya, thereby reducing the burden on facility-based management.
2. Strengthen the management of non-malarial fever cases. A continuum of care is critical in managing non-malarial fevers, including building the capacity of health care providers in managing simple non-malarial fevers, for instance, pneumonia with antibiotics, diarrheal diseases with oral rehydration salts, etc.

This should be accompanied by sensitizing communities on non-malarial cases throughout the year in a malaria endemic setting.

3. Research predictors influencing disease transmission. This study did not have data on spatial hydrologic variability that is thought to influence local, village-scale mosquito abundance in water-limited, seasonal malaria transmission areas. Further research is needed on predictors of malaria and non-malarial fever occurrences.
4. Village-scale spatial variations in the incidence proportions of malaria and non-malaria cases provide opportunities for targeted stratification and planning of resource allocation.

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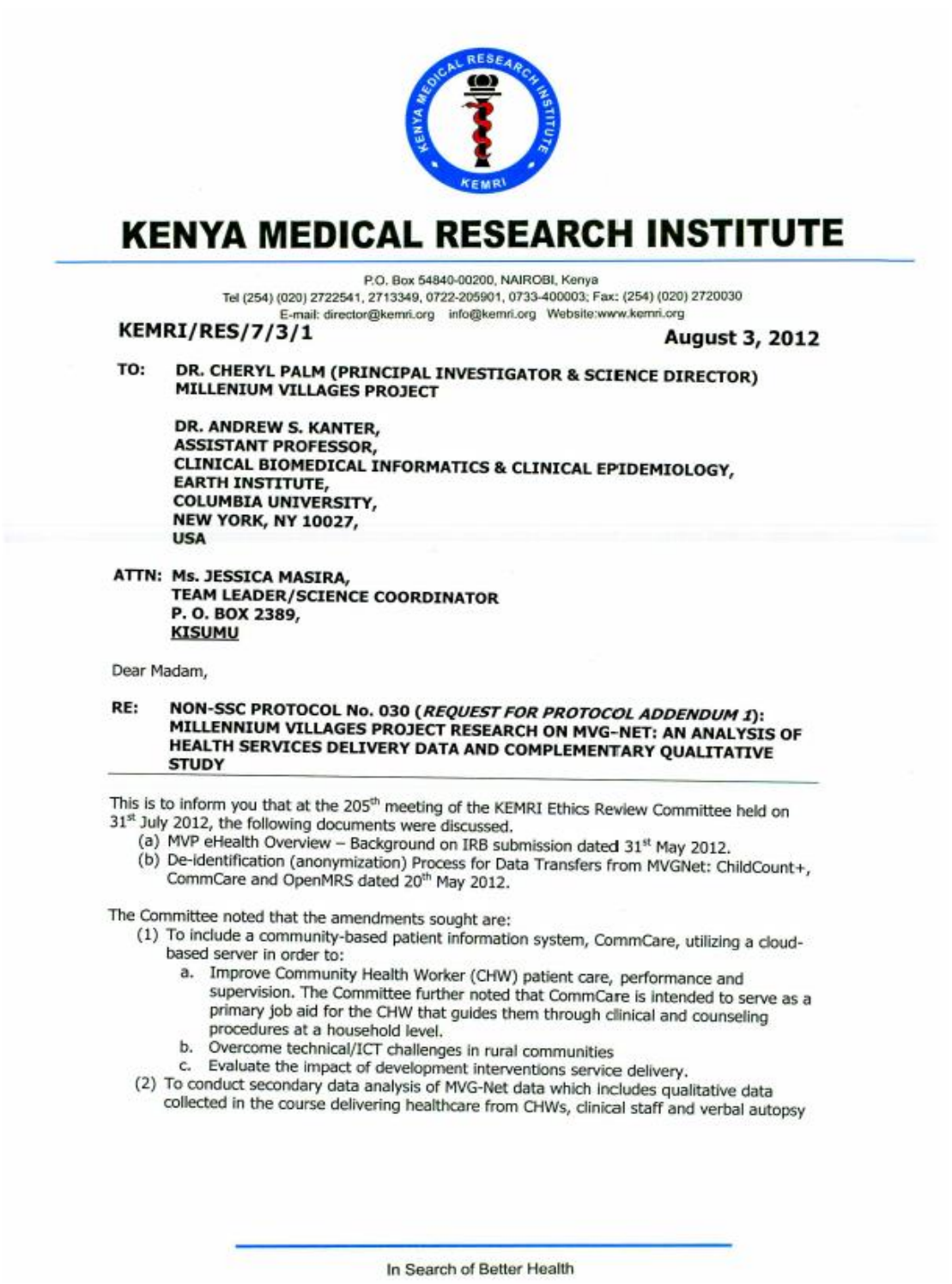
APPENDICES

Appendix I: Ethical Approval



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KEMRI/RES/7/3/1 **August 3, 2012**

TO: **DR. CHERYL PALM (PRINCIPAL INVESTIGATOR & SCIENCE DIRECTOR)**
MILLENIUM VILLAGES PROJECT

DR. ANDREW S. KANTER,
ASSISTANT PROFESSOR,
CLINICAL BIOMEDICAL INFORMATICS & CLINICAL EPIDEMIOLOGY,
EARTH INSTITUTE,
COLUMBIA UNIVERSITY,
NEW YORK, NY 10027,
USA

ATTN: **Ms. JESSICA MASIRA,**
TEAM LEADER/SCIENCE COORDINATOR
P. O. BOX 2389,
KISUMU

Dear Madam,

RE: **NON-SSC PROTOCOL No. 030 (*REQUEST FOR PROTOCOL ADDENDUM 1*): MILLENNIUM VILLAGES PROJECT RESEARCH ON MVG-NET: AN ANALYSIS OF HEALTH SERVICES DELIVERY DATA AND COMPLEMENTARY QUALITATIVE STUDY**

This is to inform you that at the 205th meeting of the KEMRI Ethics Review Committee held on 31st July 2012, the following documents were discussed.

(a) MVP eHealth Overview – Background on IRB submission dated 31st May 2012.
(b) De-identification (anonymization) Process for Data Transfers from MVGNet: ChildCount+, CommCare and OpenMRS dated 20th May 2012.

The Committee noted that the amendments sought are:

(1) To include a community-based patient information system, CommCare, utilizing a cloud-based server in order to:
   a. Improve Community Health Worker (CHW) patient care, performance and supervision. The Committee further noted that CommCare is intended to serve as a primary job aid for the CHW that guides them through clinical and counseling procedures at a household level.
   b. Overcome technical/ICT challenges in rural communities
   c. Evaluate the impact of development interventions service delivery.
(2) To conduct secondary data analysis of MVG-Net data which includes qualitative data collected in the course delivering healthcare from CHWs, clinical staff and verbal autopsy

In Search of Better Health

specialists. The data will be de-identified therefore the study team will not have access to the patient identifiers or the code for/link to the identified patient data in the electronic medical records.

The request for waiver of documentation of consent (i.e. patient authorization) is granted. However, please obtain written authorization from the facility administration in which you intend to conduct this aspect of the study prior to its execution.

The Committee concluded that the Addendum 1 be approved for implementation. You are required to submit any proposed changes to the study to the ERC for review and the changes should not be initiated until written approval from the ERC is received.

Please note that any unanticipated problems resulting from the conduct of the study should be brought to the attention of the ERC and you should advise the ERC when the study is completed or discontinued.

Sincerely,

DR. CHRISTINE WASUNNA,
ACTING SECRETARY,
KEMRI ETHICS REVIEW COMMITTEE

Appendix II: Data abstraction form

Spatio-temporal distribution of fever-related malaria and non-malarial cases among children aged below five years and their relationship with rainfall, in Siaya County, Kenya

Data Abstraction Form

PARASITOLOGY (Health Facility) **Month: .....Year: .....** **Name of health facility.....MFL Code: .....**			
Malaria Test	**Total Fever cases tested for Malaria**	**Total Number Positive**	**Total Number Negative**
Malaria blood slide (Under five years)			
Malaria Rapid Diagnostic Tests (Under five years)			
TOTAL			

PARASITOLOGY (Community, CHWs)

Month: .....Year: .....

Name of community health unit (CHU): .....

Malaria Test	**Total Fever Cases Tested for Malaria**	**Total Number Positive**	**Total Number Negative**
Malaria Rapid Diagnostic Tests (Under five years)			
TOTAL			

Appendix III: Research Publication

Apat, D.O., Gachohi, J.M., Karama., Kiplimo, J.R and Sachs, S.E. (2017). Temporal variation in confirmed diagnosis of fever-related malarial cases among children under-5 years by community health workers and in health facilities between years 2013 and 2015 in Siaya County, Kenya. Malaria Journal, **16**: 454. https://doi.org/10.1186/s12936-017-2100-9