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2017
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UNIVERSITY OF WITWATERSRAND

FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

TITLE

Factors influencing malaria morbidity in Rwanda 2010: a cross-sectional survey study using generalised structural equation modelling

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MASTER OF SCIENCE IN EPIDEMIOLOGY AND BIOSTATISTICS

Date: 19-January-2017

Declaration

I Muhammad Abu Bakar bearing Student No: 1139039, a bonafide student of Department of Epidemiology and Biostatistics, Wits School of Public Health, would like to declare that the project title **"Factors influencing malaria morbidity in Rwanda 2010: a cross-sectional survey study using generalised structural equation modeling"**. A partial fulfilment of **Masters of Sciences in Epidemiology and Biostatistics Degree** done at the University of the Witwatersrand Johannesburg South Africa is my original work in the year of 2016 under the guidance and supervision of Dr Eustasius Musenge, Senior Lecturer in the Department of Epidemiology and Biostatistics.

It has not been submitted previously for any degree or examination at this or any other University.

……

Muhammad Abu Bakar

19-January-2017

Dedication

My first sincere gratitude goes to the Almighty God who gave me life and strength during my stay in South Africa. Thank you, ALLAH!

- I would like to express my sincere gratitude to my father, ***Gulzar Ahmad***, to my mother, ***Shamsha Gulzar***, and to my elder brother, ***M.M Abdullah***, sister in law ***Dr Nimra Mehroze*** my Sisters ***Sumbal Usman and Iqra Gulzar.*** I am very thankful for their kind love, prayers and support from my childhood, and during this research project. At last my loving younger brother Taimoor Ahmad for his courage and support.

Abstract

Background

Malaria is one of the primary public health concerns in the world and an important cause of morbidity and mortality in sub-Saharan Africa. Malaria morbidity is associated with poverty and vulnerability as it is not easy for the poor people to access preventive treatment and protective measures. In Rwanda, malaria prevention has become a major problem against the double-barrelled burden of an overstretched health system and strained financial resources.

Methods

This research was a cross-sectional survey study design based on data from Rwanda collected in 2010 through the Malaria Indicator Survey as part of the Demographic and Health Survey. The primary outcome variable was an ordinal variable with these three categories; no malaria, probable malaria, and confirmed malaria cases. The outcome variable was formulated by combining rapid malaria test and confirmatory blood smear laboratory test. Statistical analysis was done using survey ordinal logistic regression modelling adjusting for random effects for direct effects and generalised structural equation modelling (G-SEM) to obtain total (direct and indirect) effects of malaria morbidity.

Results

The 11,865 participants had a mean age of 22 years, and two-thirds of the participants were females (67%). Household related variables (socio-economic status, health insurance, age in years) showed a significant total effect on malaria infection. Socioeconomic status had the

greatest total effect which was a sum of the direct and indirect effects influenced indirectly by education, health insurance and the number of rooms for sleeping.

Conclusion

Poverty is still the core issue to the morbidity patterns driving the malaria epidemic in Rwanda. Access to health insurance has a high positive impact on decreasing disease as such a special focus on some regions can be an effective intervention strategy. A better understanding of the drivers of morbidity directly and/or indirectly can better target interventions to be more efficient in those affected areas.

Keywords

Generalised structural equation modelling (G-SEM), Malaria morbidity, Malaria Indicator Survey (MIS), Demographic and Health Survey (DHS)

Preface

This research report covers an important aspect of infectious diseases in sub-Saharan Africa. Malaria is a serious public health challenge in the developing world especially sub-Saharan Africa. Poverty, lack of education and suitable environment for the propagation of the vectors make sub-Saharan Africa vulnerable to malaria infection. Children under five, pregnant women as well as older people are the most affected by malaria. The lack of resources both at national and household level makes fighting this disease difficult. This research report adopts a method that analyses the direct and indirect determinants of malaria in Rwanda in 2010 in children and adults to help improve interventions for malaria prevention. This information will be useful for policy makers as well as public health practitioners in coming up with informed interventions in malaria control.

Acknowledgement

I would like to express my sincere gratitude to the people who helped me in some ways or another during this research process. My heartfelt thanks to you all;

- To my supervisor **Dr Eustasius Musenge** for his guidance and supports throughout my research report. His professional experiences and useful comments; critiques and advice inspired me to complete this research.
- An unforgettable thank you to my uncle **Dr Salman Aslam Minhas** for his guidance and support.
- To my friends, university fellow and classmates with whom we shared good and hard moments of school life.

- At last but not least, School of Public Health, Faculty of Health Sciences at the University of the Witwatersrand Johannesburg, South Africa.

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Abbreviations

G-SEM	Generalised structural equation modelling
MIS	Malaria indicator survey
DHS	Demographic and health survey
SES	Socio-economic status
ALMA	African Leaders Malaria Alliance
LLINs	Long-lasting insecticidal nets
ACT	Artemisia combination therapy
NISR	National Indicator Survey of Rwanda
WHO	World Health Organization
FA	Factor Analysis
GDP	Gross Domestic Product
UN	United Nations
WHA	World Health Assembly
CDC	Centre for Disease Control
NISR	National Institute of Statistics of Rwanda
USAID	United States Agency for International Development

UNICEF	United Nations Children's Fund
MOH	Ministry of Health
GAP	Global AIDS Program
UNFPA	United Nations Population Fund

Chapter 1 Introduction

1.1 Introduction

Malaria is a mosquito-borne infectious disease causing and alarming number of deaths in most tropical countries mainly in Sub-Saharan Africa. This chapter gives a brief background of malaria transmission and some epidemiological concepts. It will also describe the motivation of the research, objectives, problem statement and justification of this study. Figure 1 is the map of continental Africa showing the countries (in red colour) where malaria is endemic. Rwanda is in the intermediate risk range with disease incidence higher than 5% but less than 40% [1].



Figure 1: Map of Africa showing the distribution of Plasmodium falciparum malaria in Africa. (Courtesy "The Malaria Atlas Project, 2010") [2].

1.2. Background information

Malaria is a major public health issue in the world [2]. It is a preventable and treatable infectious disease transmitted by mosquitoes, yet it kills more than one million people every year in sub-Saharan Africa [2]. In sub-Saharan Africa, malaria is the leading cause of death in children less than five years of age and accounts for about 91% of deaths occurring in children less than five years of age and older people over sixty [2]. Furthermore, in many developing countries, malaria is a common cause of morbidity and mortality [2].

In 1998, the World Health Organization (WHO) launched the Roll Back Malaria (RBM) initiative under the leadership of Dr Gro Harlem [3]. The aim of the RBM initiative was to reduce the global burden of malaria from 2010 to 2015 through the implementation of eight essential elements as a strategy [3] which are mentioned hereunder;

1. Eradicate extreme hunger and poverty
2. Achieve primary education
3. Promote gender equality,
4. Combat malaria, AIDS/HIV and other infectious diseases
5. Reduce child mortality
6. Improve mental health
7. Ensure environmental sustainability
8. Develop global partnership

In relation to the MDG's target to lessen the burden of disease, six out of eight goals were achieved by 2015 [4]. As a result, fifty-five countries are on the right track since they have

achieved at least 75% reduction of the malaria burden according to the guidelines of the World Health Assembly's (WHA) target for 2015 [5].

The African Leaders Malaria Alliance (ALMA), in collaboration with the nine countries (Angola, Cameroon, Chad, Congo, Gabon, Equatorial Guinea, Central African Republic, Democratic Republic of Congo and Sao Tomé-et-Principe) developed an African Roadmap to eliminate malaria by 2030 [2]. According to the World Health Organization (WHO) country-specific statistics, 2.2 million inhabitants out of 11.5 million people are at risk of malaria in Rwanda [6].

Malaria is mesoendemic (area in which a disease incidence is sufficiently high) in the low-lands and hypoendemic (area in which a disease incidence is sufficiently low) in highlands of Rwanda [7]. As is the case in other sub-Saharan countries, in Rwanda the use of Long-Lasting Insecticidal Nets (LLIN), Indoor Residual Spraying (IRS) and treating malaria cases with Artemisinin-based combination therapy (ACT) had reduced malaria infection up to 50% [8,9]. In response to the RBM initiative in Africa, heads of nine affected countries (as mentioned above) held a conference in Nigeria (Abuja) on the 25th of April 2000 which later resulted as in Abuja declaration [10]. Officials then present, committed themselves to afford rigorous efforts to reduce the burden of malaria in Africa from 2010 to 2015. One of the targets of Abuja declaration was that 50% of all persons suffering from the disease should have access to cost-effective treatment within 24 hours of the onset of symptoms [10].

Globally, in endemic areas where transmission occurred in long regular seasons, infection rates were highest among children less than five years of age who had not yet established immunity to the disease, contrary to epidemic areas where malaria transmission took place in short

seasons; malaria infections in all age categories [11] was high. Furthermore, a study conducted in Ruhuha region of Rwanda concluded that there was also a high risk of malaria in older age above sixty during long regular malaria season [12]. The reason may be that older people did not sleep under treated bed nets as compared to young ones. Another reason might be because older people stayed out longer than younger ones who made them more likely to be bitten by mosquitoes [13,14].

1.3. Statement of problem

Many studies on determinants of malaria morbidity reveal that the prevalence of malaria is not uniform amongst the regions and different socio-demographic groups. Various measures for malaria control like ITN, IRS and anti-malarial drugs are known to be effective and relatively efficient. To make these controls measure more effective and efficient, it involves knowledge of malaria infection factors. It is, therefore, important to identify the direct and indirect determinants and study malaria morbidity related factors to inform efficient control measures [15].

1.4. Justification for the study

Sub-Saharan Africa carries the highest burden of malaria disease since 86% all global malaria cases were reported in sub-Saharan Africa in 2008 [16]. Almost 2.2 million people were at risk of contracting the malaria infection in Rwanda [17]. The nationals of Rwanda are among the poorest in Africa with a total gross domestic product (GDP) of 526 US dollars compared to Kenya's 978 US dollars in 2010 [1,18]. In Rwanda, 84% of the total population lives in the rural areas and out of these 74% live below the poverty datum line [7]. Furthermore, in Rwanda children under five and older people above sixty are at the highest risk of malaria infection [19].

Globally in 2010, it was estimated that there were 660,000 deaths due to malaria (of which a large proportion over 86%) were in children and older people above sixty [19]. It puts extra pressure on the management of health-care resources as the GDP is not adequate to effectively cover health problems. Understanding the determinants of malaria is essential in reducing disease morbidity [7].

There is a need to identify the determinants of malaria to overcome the pressure the disease puts on the health care system on a weak economic system. To combat the endemic, there is a need for decisive information about malaria for effective health care policies. A suitable system is required to control malaria burden in developing countries. The system should be affordable, easy to implement and need for funding should be clearly defined.

Studies have previously shown that the ecological, behavioural, household and individual factors are important drivers of malaria infections [20,21]. Therefore, this study focuses on determining the behavioural determinants of malaria episodes in poorer households and at an individual level in Rwanda in 2010 using malaria indicator survey (MIS) data that was accessible from the Demographic and Health Survey (DHS) website.

1.5. Research Question

What are the direct and indirect determinants of malaria morbidity in Rwanda in 2010?

1.6. Aim

The aim of the study is to identify direct and indirect determinants of malaria morbidity and their associated influence in Rwanda in 2010 using generalised structural equation models.

1.7. Study specific objectives

1. To describe the prevalence of malaria morbidity in Rwanda in 2010 with no covariates.
2. To identify at household individual level direct and indirect factors associated with malaria morbidity in Rwanda in 2010 using generalised structural equation model

1.8. Literature review

Previous work in the field of malaria infection was studied to understand the approach of the previous researchers and to benchmark the results of this study.

1.8.1. Life cycle of malaria

The biology of the disease involves two types of hosts: humans and mosquitoes (female Anopheles). The mosquito life cycle is divided into three phases as shown in Figure 2. These stages of the malaria are given hereunder;

1- **Human liver stage**

2- **Human blood stage**

3- **Mosquito stage**

1: Human liver stage

Malaria parasite sporozoites injected when a female Anopheles bites a person. These sporozoites are transformed into merozoites (daughter parasites) and travelled to the liver where they reproduce asexually. This is called ***Human Liver Stage*** as shown in Figure 2 [22]. Thereafter they start entering into new red blood cells.

2: Human blood stage

Merozoites are the type of parasites which target red blood cells. They replicate (multiply) inside of red blood cells, rupture and disseminate into other healthy cells. This process spreads

to billions of red blood cells in the bloodstream and leads to malarial disease. The infected red blood cells with merozoites in the bloodstream develop into gametocytes (the precursor cells of sperm and egg). Step 2 is called as the ***Human Blood Stage*** as shown in Figure 2.

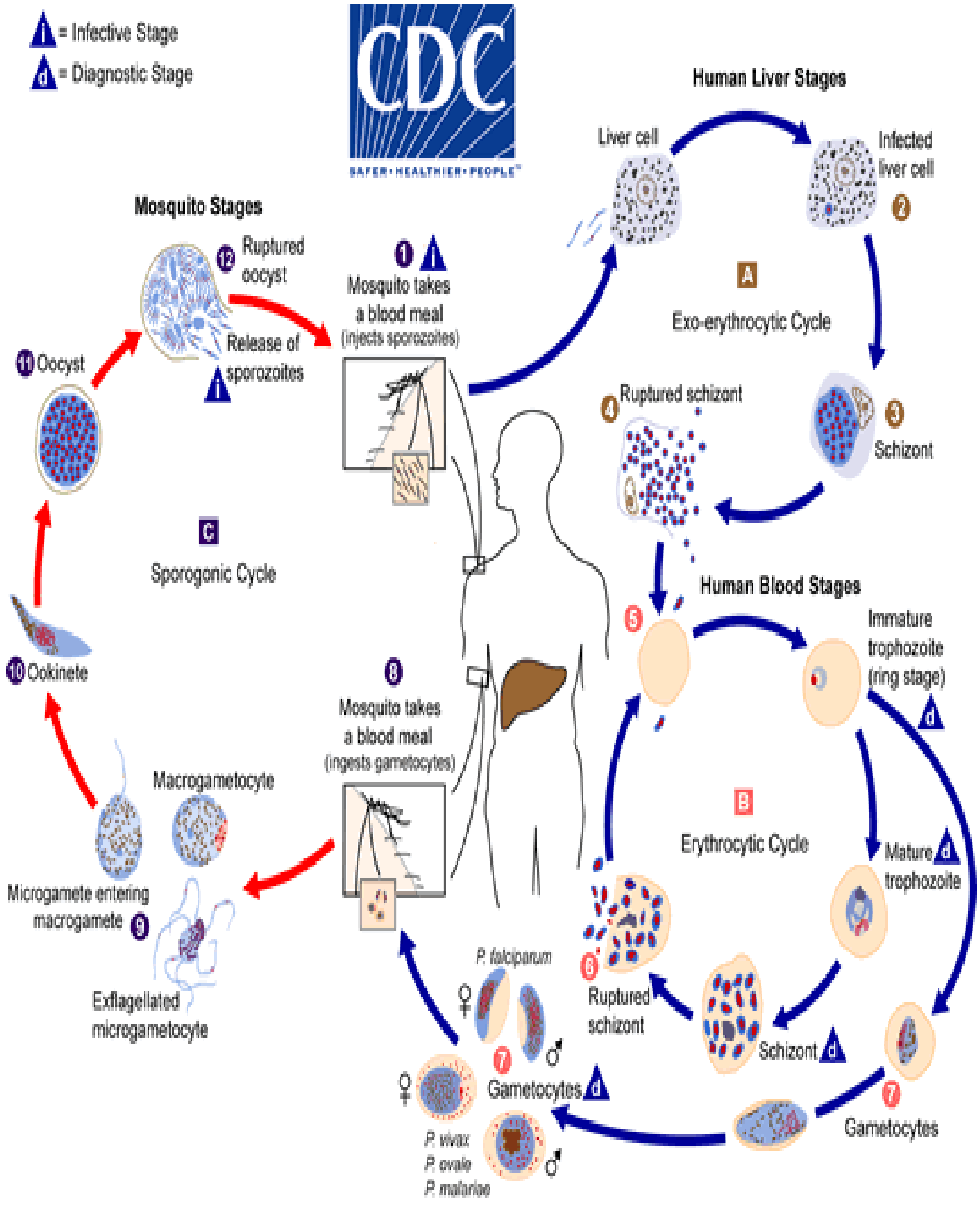


Figure 2: Malaria transmission and life cycle [18]

3: Mosquito stage

The parasites from human blood stage (3rd stage) cause the malarial symptoms. When the mosquito bites; it ingests the gametocytes (infected red blood cells with merozoites) from the bloodstream, which get ruptured into an insect's gut. These gametocytes develop into gametes. The male and female gametes are matched to form a zygote. A moving ookinete develops from a zygote and attaches to the mosquito's gut wall. The ookinete develops into an oocyte, which contains numerous infected sporozoites. After a period of about 10 to 18 days, the oocytes rupture and release their sporozoites which proceed to mosquito's salivary glands. At this point, a regenerated malaria life cycle (a human infection process) continues. Steps 3 to 7 are completed inside the mosquito's body as shown in Figure 2. Thus, the mosquito acts as a "vector" by carrying the disease from one person to another [22].

1.8.2. Transmission of malaria

Only 30 species out of 400 of Anopheles mosquito species are responsible for malaria transmission. The mode of malaria transmission depends on upon three factors [23];

1- **The vector**
2- **The human host**
3- **The environment**

Malaria transmission is common in places where mosquito longevity is higher (which means that parasites have sufficient time to complete their cycle inside a mosquito) and where a large number of people (hosts) are available. Increases in mosquito longevity and high human density are the primary reason why Africa carries nearly 90% of the malaria cases globally each year [23].

Human resistance is another major factor in the malaria transmission. Individuals with weak immunity are more vulnerable to the diseases. Due to the Plasmodium transmission by vectors, the environment is a determinant of malaria.

Geo-climatic factors (temperature, moisture and water quality) determine the presence of Anopheles breeding sites, the vector densities, the adult mosquito longevity and the vector capacity. Several studies have shown the association between environmental factors and malaria infection in the population populations [24,25].

1.8.3. Global and African malaria burden

Malaria is the most dangerous vector-borne disease in the world and especially prevalent in Africa [26]. Globally, an estimated 3.3 billion people were at risk of malaria in 2006 and 1.2 billion of those were living in Sub-Saharan Africa [27]. During the same year, an estimated 881,000 malaria deaths were reported, of which 91% were in Africa, and 85% of the reported deaths were in children less than five years of age [27]. In endemic African countries, malaria accounts for 25% to 35% of all outpatient visits, 25% to 45% of hospital admissions and 15% to 35% of hospital deaths [3] putting a huge pressure on health systems.

Malaria transmission is higher in areas where the lifespan of the mosquito is long [28], which enables the lifecycle of the parasite to be completed. This suggests that mosquitos have a long lifespan in the African region, with high human blood meal prevalence. Anopheles species particularly the Anopheles Arabiensis is responsible for more than 90% of the World's malaria deaths which occur in Africa [28]. Furthermore, the higher malaria risk in rural areas of developing countries can be attributed to poverty and poor lifestyle [29]. Factors which play the major role in disease risk includes proximity to the vector breeding sites, moderate use of

control measures, low income, illiteracy, land use near pools, and open houses [26,30]. A recent global report shows that due to good political commitment and better utilisation of funding, a 54% of the above reduction has been experienced in African (WHO regions) [5].

Historically, it is believed that the most deadly malaria specie P. falciparum is prevalent in sub-Saharan Africa [31]. Therefore, it has a significant influence on the health and socioeconomic well-being of people.

Malaria is a common disease of the tropical regions. Hence, it is particularly prevalent in sub-Saharan Africa [31]. It is believed that there is a malarial death reported every minute and an overall 86% of malaria deaths in children less than five years of age and older people over sixty are in Africa [32]. Malaria is hard to control in Africa due to the effectiveness of vector species and the predominance of most severe species P. falciparum [33].

Rwanda national routine data advocates for a different malaria distribution, since the whole population is at risk of malaria with the exclusion of those living at a very high altitude zones [8,15]. Various measures are used for disease control like Long-lasting insecticidal nets (LLIN), IRS and antimalarial drugs have been proven to be effective [8]. However recent studies have shown that these measures are hampered by drug resistance challenges as well as behavioural factors [26].

1.8.4. Factors associated with malaria morbidity

Malaria transmission was controlled by environmental and behavioural factors which affect the intensity of malaria distribution and transmission [34]. Malaria morbidity flourishes in

circumstances that stimulate the growth of the vector. Studies have shown that environment can result in increased malaria transmission [35].

Other factors are age, the level of education, place of residence, non-availability of insecticide-treated mosquito nets; rainfall levels, pools of still water that are good breeding grounds for the mosquitoes [35,36]. Studies carried out in Gabon and Tanzania showed that children less the age of five were most at risk of the transmission of malaria [13,37] living in the condition as mentioned above. Another study was done in Kenya revealed that parasitaemia decreased with age within children in the age group of a 1-4 year's having the highest prevalence of 83%, dropping to 60% in the 10-14 year age group and 70% of older people above 60 years [38]. Studies also reveal that malaria morbidity is affected by the level of education, by age and knowledge about disease transmission [35,36].

Agriculture methods of irrigation, as well as the building of dams, also promote the breeding of mosquitoes. Therefore, these factors can lead to malaria transmission [35,36]. Furthermore, a study found that temperature, rainfall and humidity cannot be viewed in isolation and that in addition we need to investigate human behaviour [39]. Human behaviour seems to play a role in creating ideal conditions for mosquitos to breed. Therefore, there is a need to control or change human behaviour to ensure that malaria illness is adequately monitored and controlled.

Socio-economic status (SES), immunisation, knowledge about disease transmission, and nutrition also play a role in malaria morbidity and mortality [40]. Nutritional status is linked with economic status. A well-nourished body is protected against malaria infection as compared to an immune vulnerable undernourished body [40]. Health status and sanitary facilities also linked with socio-economic status [39,24,40]. In addition, malaria is climate

sensitive [41]. Altitude is another factor that has been found to be important in malaria transmission, with a study finding that low altitude areas are more at risk compared to higher altitude areas [42].

1.8.5. Malaria control measures in Rwanda

In Rwanda, malaria prevention has become a major area of concern for the government of Rwanda and global health governing body like the World Health Organization (WHO) [43]. Three key interventions have been introduced namely ITNs, IRS and the use of anti-malarial drugs, to control the burden of malaria in Rwanda. For these preventive measures, political of Rwanda and World Health Organization (WHO) have invested billions of dollars in combating the malaria burden [43].

Moreover, these three control measures have also shown a significant reduction in malaria deaths in children and adults from 2005 to 2010 [8]. These preventive strategies contributed to the success of the disease control in the country. Nevertheless, a long-term cohort study shows that children below five years of age are still at high risk of malaria in Rwanda [8].

Despite improvements in control of malaria, the disease remains a leading cause of infection in children and adults in Africa [44]. Accurate diagnosis of malaria is part of case management. To target artemisinin-based combination therapy (ACT) to malaria-positive cases, the World Health Organization (WHO) recommends confirmatory blood smear lab testing to confirm malaria before commencing treatment [45]. Prompt diagnosis and treatment are essential to prevent fatal malaria, to reduce the numbers of patients who can transmit malaria, and to identify patients with other causes of illness rapidly.

Malaria confirmatory blood smear test remains the reference method for malaria parasite diagnosis, but its value is often undermined because it needs equipment and skilled laboratory technologists and cannot therefore be done quickly, at the point of care. Antigen-based malaria rapid diagnostic tests (RDTs), introduced in the 1990s, have increased from a few products to >250 tests, which are submitted annually for evaluation and inclusion in procurement lists used by countries [46].

The DHS survey also revealed the infection data of the households. The infection was tested and confirmed by using; [22]. Details of these two tests are provided in chapter 2.

1. Rapid malaria test
2. Confirmatory blood smear laboratory test (CBSLT)

1.8.6 Objective of this work

The primary objective of this study is to investigate the influence of direct and indirect factors of malaria morbidity in Rwanda using the Malaria Indicator Survey (MIS) data collected in 2010. Identification of direct and indirect factors influencing the spread of disease in developing countries are crucial in the preparation and implementation of policies and programs aimed at controlling the burden of malaria effectively and efficiently [47]. In addition, the health systems should be affordable and easy to implement in low-income countries [11]. However, the development of the policies requires suitable and sufficient information. The purpose of this work is to provide necessary information regarding the indirect factors to malaria infection.

1.9. Conceptual framework

Reiter P. in 2008 studied the effects of temperature on Malaria transmission. His study proposed that temperature, rainfall and humidity cannot be considered in exclusion without taking into account the behaviour of the human.

Additional factors that influence the malaria infection directly and/or indirectly;

1- **Household-related variables** (SES, age, education and health insurance)

1- **Behavioural variables** (Clean water facility for drinking and sleep under bed-net)

2- **Ecological variables** (Regions (north, east, west and south), cluster altitude in meters)

This study is considering all the direct and indirect factors with the inclusion of human behaviour as suggested by Reiter P. in 2008 [38]. This work not only considered human behaviour but related direct and indirect factors (mentioned above) which have not been considered in previous or historical studies.

Conceptual modelling technique and variables are divided into three main categories; ecological, household and/or individual level, and behavioural variables in the analysis with the purpose that these determinative factors run through the standard set of either 'proximate direct or indirect variables that have an influence on malaria morbidity [48,49]. Variables are either endogenous (dependent variable) or exogenous (explanatory variable) or both, which can be modelled by using generalised structural equation models. Details of these models provided in Figure 11 and Figure 12.

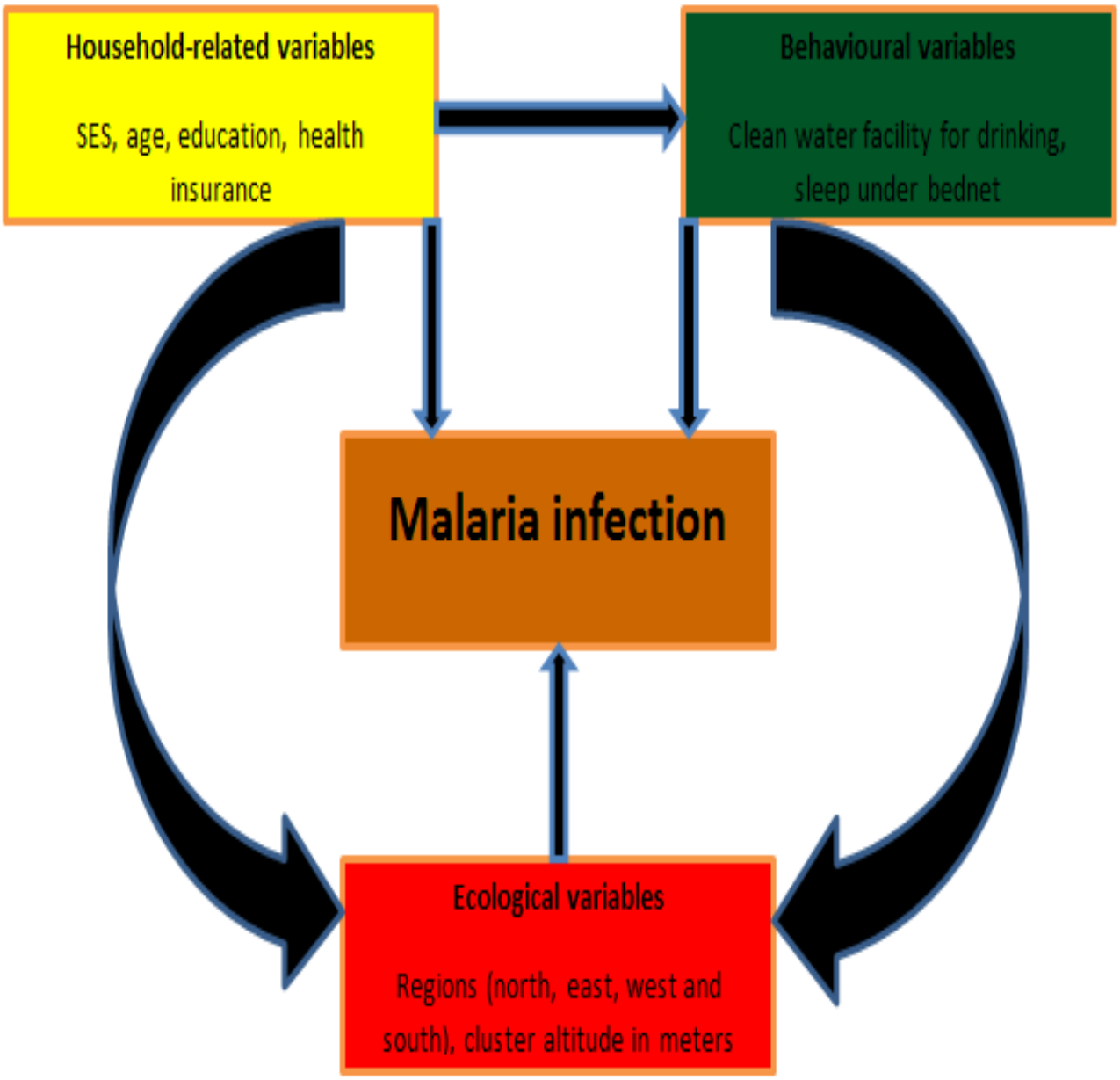


Figure 3: Conceptual frameworks for modelling malaria morbidity. The black arrows reflect a direct and indirect effect on malaria morbidity

Monitored variables were household related variables shown in yellow box, ecological variables shown in red box and behavioural variables shown in green box as illustrated in Figure 3. Pathways (direct and indirect) were modelled using generalised structural equation model to identify direct and indirect factors of malaria infection in Rwanda during 2010 as shown in Figure 11 and Figure 12.

In Figure 3, computation of the direct effect pathways, as shown by the black arrows, started from all the predictor variables, namely household related, behavioural and ecological variables and led to the dependent variable, malaria morbidity.

The significant predictor variables (exogenous variables) as an outcome (endogenous variables), the indirect effects (showing with black colour) were determined within and between the categories to identify the factors affecting malaria morbidity.

1.9.1 Structure of the Report

Chapter-1 covers the information about global malaria burden, malaria burden in Rwanda, malaria life cycle and transmission; gaps in existing knowledge for the treatment of malaria, research problem statement, research question, research justification, aim and objective of this study have been described. The conceptual model of malaria morbidity has been briefly discussed and the detail model will be explained in chapter-3. The control measures curtail the malaria infection in Rwanda is also discussed.

Chapter-2 covers the overall methodology. Study design, study area, Rwanda Malaria Indicator Survey (MIS) is also described. The methods of choosing dependent and independent variables are explained. The chapter deals with the data analysis through the proposed model.

Chapter-3 includes the results obtained from the mathematical model discussed in chapter-2. The results are presented in tabular and pictorial formats for further analysis.

Chapter-4 the discussion of the Results obtained from the model of chapter 3 is presented. This chapter also is a concluding chapter where recommendations are made for future research.

Chapter 2 Methodology

2.1. Introduction

This section covers the methodological approach of this research project, and how statistical and epidemiological methods were used to test internal and external validity. This part also explains the statistical methods used to control for confounding and other factors. It also describes the Generalised Structural Equation Modelling (G-SEM) method and its implementation in this study.

2.2. Description of Original Study

Over the years, demographic and health surveys have become a useful source of data enriched with various indicators for health planning and health development systems. Data on household health status collected through questionnaires and blood testing (confirmatory blood smear lab and rapid malaria test) was done for malaria diagnosis of the eligible individuals including (male, female and children). These two tests are described below;

1- Rapid malaria test

For the RDT for malaria, a drop of blood was obtained by a prick at the end of the finger. First Response test kits were used according to manufacturer recommendations. The results of the malaria RDT were recorded in the household questionnaire, which allows linking with the characteristics of the respondents. Results from the RDTs were used to diagnosis malaria and guide treatment of parasitemic children during the survey [22].

1. Confirmatory blood smear laboratory test (CBSLT)

For the (CBSLT), blood was collected from participants who agreed to malaria testing. Blood slides were stained with Giemsa stain prepared by the laboratory in advance of the fieldwork [22].

The results of these tests were either negative (no malaria infection) or positive (malaria infection). According to Center for Disease Control (CDC, 2014), the confirmatory blood smear lab test (CBSLT) results is more reliable in diagnosing the malaria infection infections [50].

The questionnaire collected identical information from men and women, but men's questionnaire excluded the information regarding reproductive health. The Rwanda's "Demographic and Health Survey (RDHS) 2010" was conducted nationwide and was first of its kind. A representative sample of 12,792 households including (men, women and children) selected from 492 clusters including visitors or permanent resident [22,51].

All of 492 clusters were chosen for the sample surveyed for the 2010 RDHS. There were approximately 26 houses per cluster of which 50% (13 houses) leading to the total number of houses was 5657 had experienced malaria morbidity. Although a total of 12,792 individuals were selected, only 11,865 individuals were identified and finally used at the time of the survey. From these 11,865 there were 2,465 males and 9,400 females. The number of children less than five years of age was 4,028 and above five was 7,837 [22,51].

The study was conducted at a cross-sectional survey design, and the primary objective was to collect up to date guideline for policy makers, researchers and program managers to be used in planning, monitoring and evaluation of population and health programmes.

The survey was carried out by National Institute of Statistics of Rwanda (NISR) and Ministry of Health (MOH) of Rwanda. This study was financed by the Government of Rwanda, United States Agency for International Development (USAID), the United Nations Children's Fund (UNICEF), and the Centers for Disease Control and Prevention/Global AIDS Program (CDC/GAP), the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United Nations Population Fund (UNFPA) and World Vision [22].

2.3. Study design

This study was conducted as a cross-sectional survey design. The dataset used is known as the Malaria Indicator Survey (MIS) dataset of Rwanda which was part of the Demographic and Health Surveys (DHS) 2010.

2.4. Inclusion Criteria

This study includes both males and females aged from 0-95 those who had a sample taken for malaria diagnoses were included in the study.

2.5. Study area

This study was conducted in Rwanda, a Central African country located South of the equator between latitude 1°4' and 2°51' South and longitude 28°63' and 30°54' East as shown in Figure 4. It has a surface area of 26,338 square kilometres and is bordered by Uganda to the North, Tanzania to the East, the Democratic Republic of the Congo to the West and Burundi to the South. Landlocked, Rwanda lies 1,200 kilometres from the Indian Ocean and 2,000 kilometres

from the Atlantic Ocean [52]. Rwanda is divided into five geographically-based provinces—North, South, East, West and the City of Kigali, with the provinces, further subdivided into 30 districts, 416 sectors, 2,148 cells, and 14,837 villages [52].

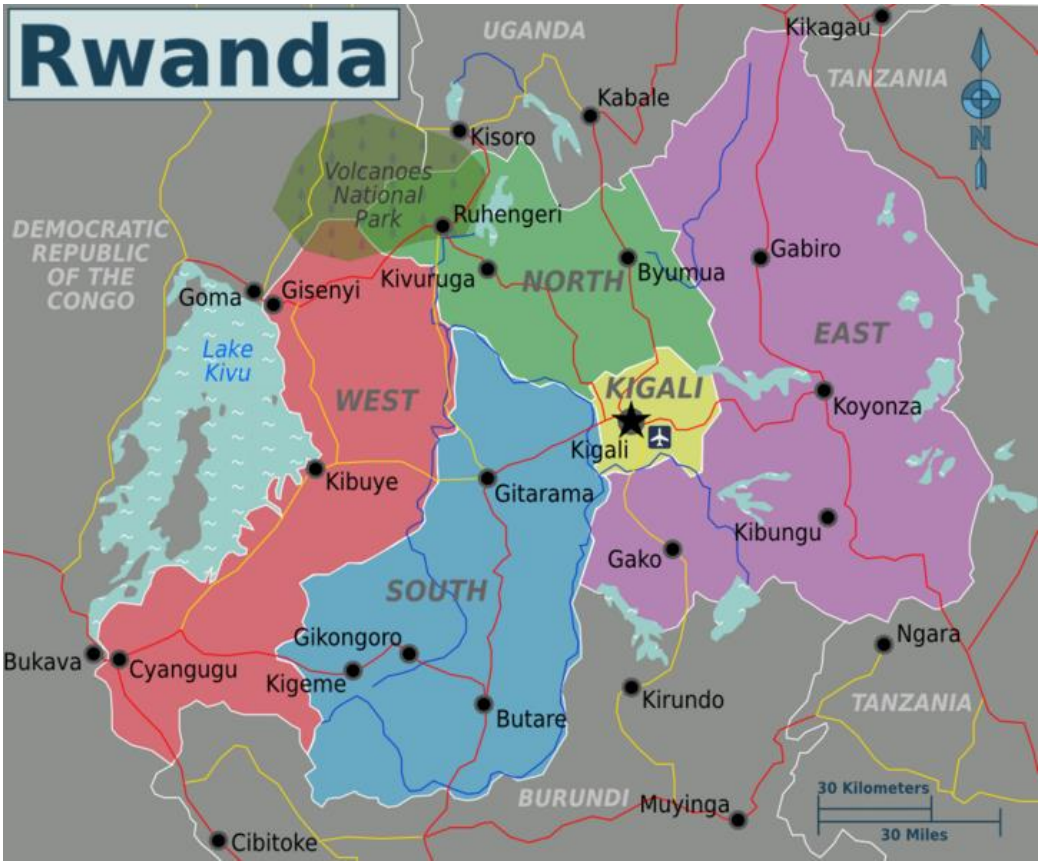


Figure 4: Map of Rwanda [56]

2.6. Demographic Health Survey Sampling Procedure

2.6.1. Two-stage sampling of Rwanda malaria indicator survey (MIS)

The data used for the analysis was obtained from the 2010 Malaria Indicator Survey (MIS) conducted by Rwanda Demographic and Health Survey (RDHS) program. The previous study collected the data elements on basic demographic and health indicators, malaria prevention, treatment and morbidity.

Sampling in the previous survey was done in two stages. In the first stage, 492 villages which formed the clusters were selected with probability proportional to the village size. The village population size also indicates the number of households in the village. The mapping and listing of all households in the selected villages were done. The resulting list served as the sampling frame for the second stage of sample selection. All of the 492 clusters were selected for the modelling as surveyed for the 2010 RDHS. The selected data contained 11,865 households consented to participate in the study and completed the individual's questionnaires. Data for children less than five years of age was collected from their mothers [52,53].

2.7. Data Analysis

The survey ordinal regression model is the proposed model for this study and is explained in this section. The model is capable of performing survey regression analysis on the dataset both for single and multiple variables. The detail of the model is given in the following sections.

2.7.1 Explanatory variables

Explanatory variables were grouped into following four categories and discussed below;

1. **Individuals variables**

- **Age:** Age is a continuous individual level variable in the analysis ranging from (0-95) years including (males, females and children).
- **Education:** Education is also an individual level continuous variable in the analysis. It explains the years of education acquired by the individuals.
- **Health Insurance:** Whether (coded as 1) or not (coded as 0) the individual had health insurance.
- **Socio-economic status:** Previous study recorded the individual level assets. To generate socio-economic status factor analysis was done using household's assets.

2. Household related variables

- **No of rooms for sleeping:** This variable explains the number of rooms of sleeping for each household. It is also a continuous variable ranging from (1-6).

3. Behavioural variables

- **Clean water facility for drinking:** This variable explains the health-related behaviour of individuals. This variable has recoded as "Yes" "No" means that household had clean drinking water.
- **Sleep under treated bed nets*:*** This variable describes the health seeking behaviour of the individuals. The household who used treated bed nets for sleeping was recoded "Yes" and those who did not be recoded as "No".

4. Ecological variables

- **Region:** This variable describes the geographical position of the household. It has four categories as (east, west, north and south and Kigali city).
- **Cluster altitude in meters:** This variable explains the cluster altitude of the household in meters above sea level since the malaria infections occurrence is low at higher altitudes.

2.7.2 Factor analysis for socio-economic status

Socio-economic status was the main factor in determining the malaria infection in this study. The following shows the factor analysis was used to determine the SES of the individuals. Factor analysis is a useful tool for investigating variables relationships for complex concepts such as socioeconomic status [54]. It allows researchers to investigate concepts that are not easily measured directly by collapsing a large number of factors into a few interpretable underlying factors. The following is the list of household assets;

1- Source of water

2- Type of toilet facility

3- Has a radio

4- Has a bicycle

5- Has a motorcycle

6- Has a car

7- Has a telephone

8- Share toilet

9- Has a mobile phone

10- Has cattle/s

11- Has goats

12- Has sheep

13- Has chickens

14- Has bulls

15- Has pigs

16- Has rabbits

17- Has bank account

18- Main floor material

19- Main roof material

20- Main wall material

21- Type of cooking oil use for cooking

22- Ownership of land

23- Has watch

Figure 5 shows the statistical process (mathematical model) to determine socio-economic of the individuals.

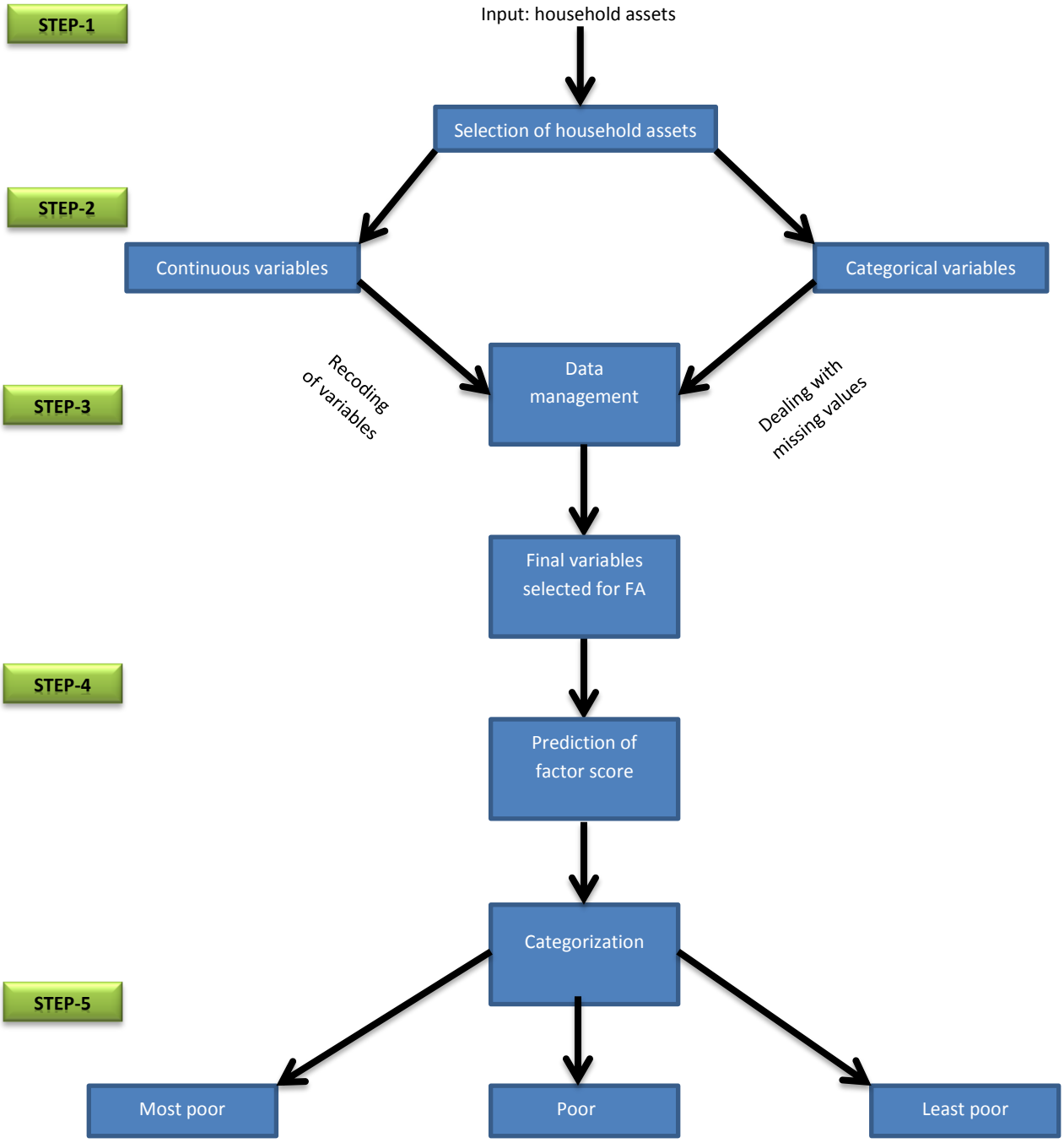


Figure 5: Flowchart to determine SES using factor analysis technique

Household assets are the basic data used as input to the model. The household assets have many factors which were used to determine the overall SES of the individuals. Figure 5 explains the statistical process step by step.

Step 1- Input household assets, that all coefficients are positive so that the index does indeed give an overall measure of SES. Any variable with a negative coefficient as well as variables with a large number of missing values should be omitted.

Step 2- This step investigates the property of input variable could be continuous or categorical.

Step 3- Data management, recoding of variables and checked for missing value. Variables were excluded with more than 10% missing values. In additional, variable is also recoding in a binary format.

Step 4- Selections of final variables and factorization were done. The highest Eigenvalue was used in the computation of the score. The first factor had an Eigenvalue of "2.48" and explained "64%" of the variability. Prediction of factor score was done in step 4.

Step 5- Categories of SES were formed by using the factor score obtained in step 5. From the histogram, as shown (Appendix A1.1), cutoff points were decided and formed three categories of SES. The first category was "Most Poor" with cutoff point " (min/-0.333878=1)". The second category was "Poor" with cutoff value "(-0.333879/0.3148308=2)". The third category was "Least Poor" and the cutoff point (0.3148308/max=3).

These categories are further used in the study to determine the influence of SES on malaria infection.

2.7.3. Outcome variable

The prevalence of malaria was 1.86 percent by rapid malaria test and 0.99 percent by confirmatory blood smear test in all age groups adopted from the Rwanda Malaria Indicator Survey [22]. The higher prevalence observed in the RDT results compared with blood smear test is expected since an RDT detects the presence of circulating antigens up to several weeks after malaria parasites have been cleared from the body. In contrast, microscopy detects the actual parasite. In addition, rapid diagnostic test (RDT) may not be able to detect some infections with lower numbers of malaria parasites circulating in the patient's blood [55].

The malaria outcome variable for this study was defined according to the Center for Disease Control (CDC) and World Health Organization case definition criteria. The CDC and WHO definition indicates that there are three possible states of malaria infection [50,56]. There was no question in DHS dataset regarding recently treated malaria cases.

1. No malaria
2. Probable or (symptomatic or asymptomatic) malaria infection
3. Confirmed malaria infection

Two types of tests were conducted on surveyed population (rapid malaria test and confirmatory blood smear laboratory test). Participants who showed a negative result in both the tests (rapid malaria test and confirmatory blood smear laboratory test) were put in the category of "No Malaria Cases". The participants who were not tested for confirmatory blood smear laboratory or either showed negative test but showed positive in the rapid malaria test were considered as "Probable or symptomatic or asymptomatic Malaria Cases". Those who have positive confirmatory blood smear laboratory test regardless of their results from rapid

malaria test either positive or negative were considered as confirmed malaria cases as shown in Figure 6. Sensitivity analysis was done using ordinal malaria variable, binary RDT variable and binary blood smear test variable. Results are reported in (Appendix 1.1, Table 4 and Table 5).

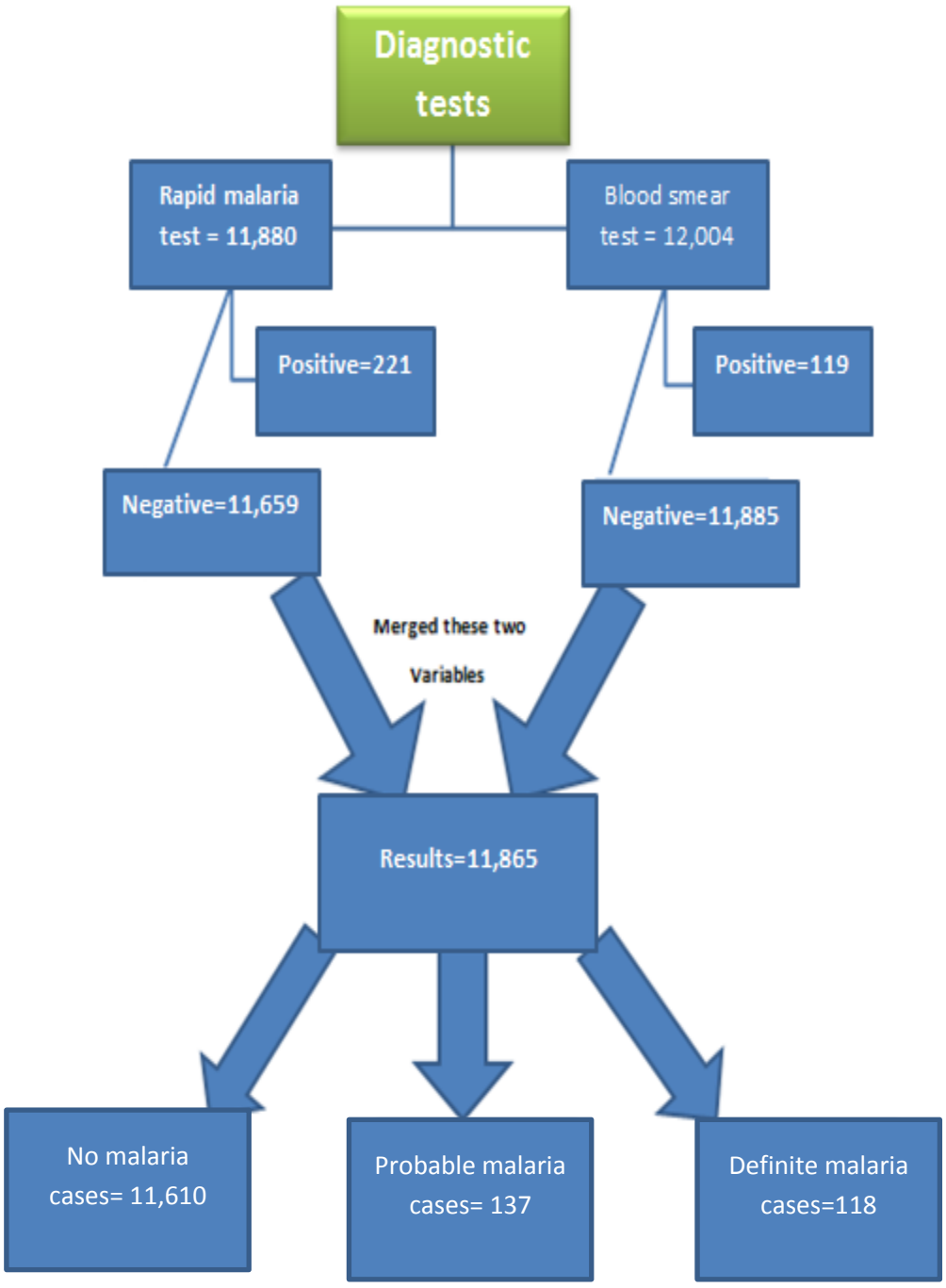


Figure 6: Flowchart of Rwanda's measure DHS malaria diagnosis outcome variable

2.8. Data Management

The data from Rwanda received in STATA format from "Measure DHS International". Variables were renamed for ease of handling with the help of the codebook. Missing data was excluded from the analysis. Data was analysed using STATA version 13 from STATA corporation. [1]

2.9. Statistical analysis methods

2.9.1. Power computation

There was no need for sampling for this study; instead, power computation was done using a STATA ado-file. [57] A sample prevalence of 2.1% comprised of 1.4% children and 0.7% adults adopted from the Rwanda Malaria Indicator Survey [22] and assuming a 3% population prevalence at an alpha level of 0.05. A design effect of 9 and intercluster correlation (ICC) of 0.071 with a total of 492 clusters and average households per cluster of 115. I obtained an 89% power as shown in (Appendix A2.1).

2.9.2. Survey setting Rwanda DHS data

Demographic and Health Survey (DHS) data as it takes into account the differences in sample sizes through the use of sample weights. Survey setting was done by using, region (Kigali, East, South, North and West) and place of residence (urban or rural). Each region (Kigali, East, South, North and West) has included both urban and rural area so design effect is 10 for this work. The sample weight is calculated by multiplying household sample weight (hv005) with 212 and divided by 100, 0000. The primary sampling unit is generated and is equal to the cluster number. The commands that are used to create survey setting below in green box;

```
egen strata = group(hv024 hv025)

gen sampwt = hv005*212/1000000

gen psu=hv001

svyset psu [pw = sampwt],
```

2.9.3. Inter-cluster Cluster Correlation

Demographic and Health Survey (DHS) data follow a hierarchical structure. Individuals are nested within the clusters, and clusters are nested in regions. The participants who lived in the same cluster or region may not be independent of one another. However, the regular individual-level regression analysis assumes that all individuals are independent. The multilevel modelling approach takes into account that people live in the same area may have some characteristics in common. It should be noted that individuals residing in the same household are not independent.

An important feature of the random-effects model is that it gives the information on the proportion of total variation explained by the cluster-level, individual level and household level. Random-effects models typically include a random intercept or random slopes. This analysis allows for random intercepts across clusters and household and assumes fixed effects of covariates across clusters and household. The model was built with cluster number and household number as random effects to analyse inter-class cluster correlations between individuals from the same cluster and household. The model includes several covariates; education in years, socio-economic status, age in years, and cluster altitude in meters, a number of rooms for sleeping, sleep under treated bed nets, clean water facility for drinking, region and health insurance.

The mathematical model for Rwanda adjusted for random effect is given in (Appendix-3). Inter-class cluster correlation calculation was done by using the formula;

$$\textbf{Inter-class cluster correlation} = \frac{sd(hv002)^2 + sd(_cons)^2}{sd(hv002)^2 + sd(_cons)^2 + sd(residual)^2}$$

2.9.4. Descriptive and bivariate analysis

Descriptive analysis was done using survey adjusted summary measures for categorical variables and well as continuous variables. For categorical variables weighted percentages (proportion) were used. For continuous variables mean and standard errors are reported as shown in Table 1.

Bivariate analysis was done using survey chi-square test adjusting for cluster effect to establish the relationship between two categorical variables (such as malaria morbidity and gender). This inferential statistics done using the adjusted Chi-square test (Rao-Scott adjustment) resulted in the F-statistic as later reported in Table 1. For the continuous explanatory variables such as age, survey univariate analysis was done.

2.9.5. Univariate and multivariable analysis

Statistical analysis was done using step-wise regression method by survey ordinal logistic regression adjusting for random effects. Univariable analysis was done using survey ordinal logistic regression model. During univariable analyses, the association of one explanatory variable at a time with the outcome was tested. The odds ratio, confidence interval and p-value were calculated for each variable and reported in Table 2 column 1.

In the multivariable analysis, statistical analysis was done using step-wise regression method by survey ordinal logistic regression adjusting for random effects. All factors with $p<0.05$ were

considered significant independent risk factor affecting malaria infection. The odds ratio, confidence interval and p value were calculated for each variable to determine the strength of the association between the explanatory variable and the outcome measure, using other variables as references for comparison. Results of the multivariable analysis are reported in Table 2 column 2.

The results were similar by using both sampling weights (svyset) and the robust method and comparable to the traditional ordinal regression method. The final results are reported in Chapter 3 Table 2.

2.9.6. Suest test for goodness of fit

Model goodness of fit to the final model was done systematically, by incrementally adding variables and utilising the seemingly unrelated estimation (suest) procedures. This test was used handle two forms of hypotheses testing.

Firstly, suest test was used to check the estimates and (co)variance of the coefficients of two models simultaneously. The null hypothesis was that the two sets of coefficients of interest are simultaneously equal to zero. If the test failed to reject the null hypothesis, this suggested that I remove the additional variable from the model.

Secondly, overall model fit to test if the model was a good fit with a null hypothesis of the model was overall a good model. If the test failed to reject the null hypothesis, this suggested that the model is a good fit to the data [68]. Details of suest STATA commands have been provided in Appendix 2.3.

2.9.7. Generalised Structural Equation Modelling

Generalised Structural Equation modelling (G-SEM) was used to model direct and indirect effects on the malaria outcome. The conceptual framework is a useful graphical display of the relationship that exists between an explanatory and dependent variable to quantify the associations used for generalised structural equation modelling (G-SEM). G-SEM is a systematic way of evaluating hypothesis involving pathways analysis against multivariable data [58]. Therefore, it is used for testing and estimating causal relationships (direct and indirect effect) through statistical data and qualitative causal assumptions.

Direct pathway defines as an effect of exposure which is not affected by a given set of potential mediators. In Figure 7, SES has shown direct pathway on malaria infection. Direct pathway gives direct effect.

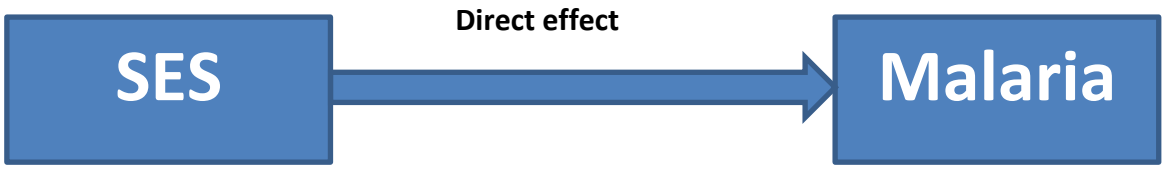


Figure 7: Describes direct pathway.

Indirect pathway defines as exposure effect which is affected by a given set of potential mediators. In Figure 8, the level of education has shown the indirect effect on malaria infection through SES. Indirect pathway gives indirect effect. Indirect pathway has explained as shown below;

Level of education ➔ SES ➔ Malaria infection

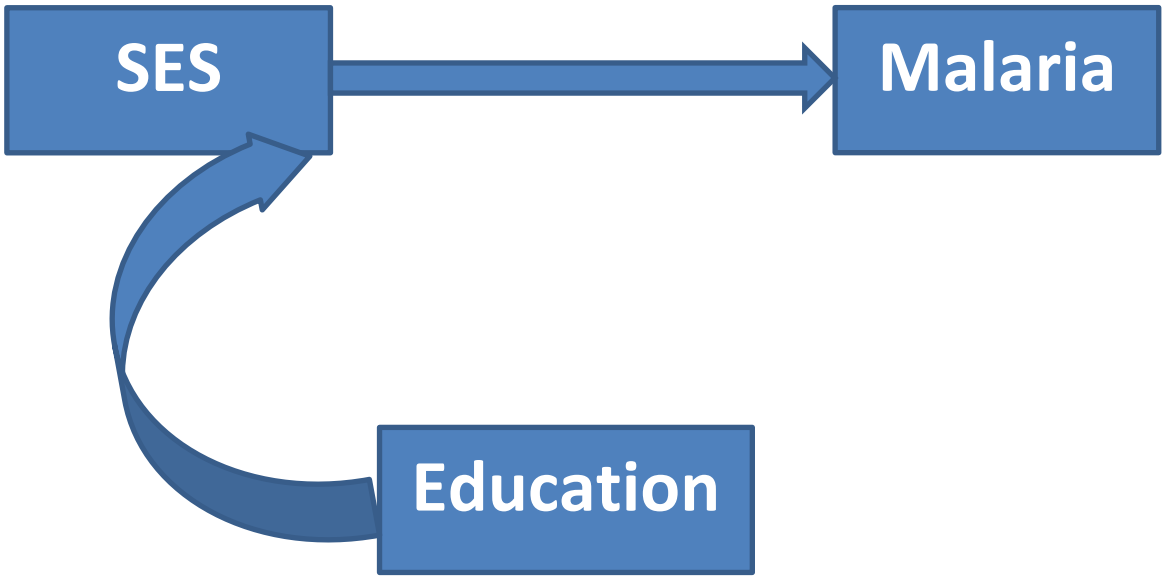


Figure 8: Describes indirect pathway.

Modelling in the G-SEM based on variables that were significant in the regression analysis to quantify the relationship of the relevant pathways. The fewer variables that are important being a factor of malaria infections have also used in G-SEM if they are shown no significant in the regression model. From the final survey ordinal regression model adjusted for random effect, variables like individual level, household related variables, ecological variables and behavioural variables were selected as underlying determinants for G-SEM modelling.

The G-SEM has advantages of being able to adjust for multiple factors and at the same time take into account various outcomes. Furthermore, it gives a refined estimation of positive and negative effect compared to those from multiple variable analyses. Mathematically direct, indirect and total effect presented in (Appendix 3.1).

The selection was based on variables that were most significant in the final survey ordinal regression model. The model fit was assessed using the root mean square error of approximation (RMSEA) due to its sensitivity to the number of estimated model parameters and ability to handle large samples [59]. Studies show that an RMSEA below 0.8 shows evidence of good fit, [59] hence the RMSEA of 0.03 from our G-SEM model was a good fit. All statistical analyses were carried out using Stata®13.1 (Copyright 1985–2013, StataCorp LP).

2.10. Ethics approval

The primary studies received ethical clearance from the Ministry of Health Research Ethics Committee in Rwanda, and informed consent was obtained from the individuals before data collection and malaria testing. The study's protocol was approved by the Faculty of Health Sciences, the University of the Witwatersrand as shown in (Appendix 6). The study protocol of secondary analysis was also presented to the University of Witwatersrand Human Research Ethics CommitteeFor Ethical permission which was granted before data analysis. The clearance certificate number is M151040 and a copy of ethical approval is attached in (Appendix 6). During data analysis, no personal identifiers were used, and linking results to individuals were not possible.

Chapter 3 Results

This chapter summarises the results of the survey. Results are presented in tabular and graphical format. Graphical results were obtained from mathematical and G-SEM modelling. The model is capable of assessing direct and indirect effects on malaria infection.

3.1. Descriptive statistics

The survey data contains 11,865 individuals with a mean age and standard error of 22, (0.089) years. These were the number of individuals who were tested for malaria using malaria blood smear test and rapid malaria test. The results of the malaria tests showed that 11,610 (97.67%) individuals had no malaria, 137 (1.26%) had probable malaria and 118 (1.07%) had definite malaria cases. Female individuals have approximately had the prevalence of 0.87% and male individuals were 1.74% as shown in Figure 9. The Eastern region had the prevalence of 2.56%, the Southern region had 1.0023%, the Western region had 0.0033%, the Northern had 0.0025% and the Kigali had the prevalence of 0.0029% as shown in Figure 10The mean of level of education with standard error was 2.76 (0.039) and the mean of cluster altitude was 1740 (10.43) meters.

Table 1 shows the results of descriptive statistics with the significant test statistic of survey adjusted chi-square test.

Table 2 presents the results of survey ordinal univariate analysis, survey ordinal logistic regression modelling adjusting for random effects and direct and indirect effect.

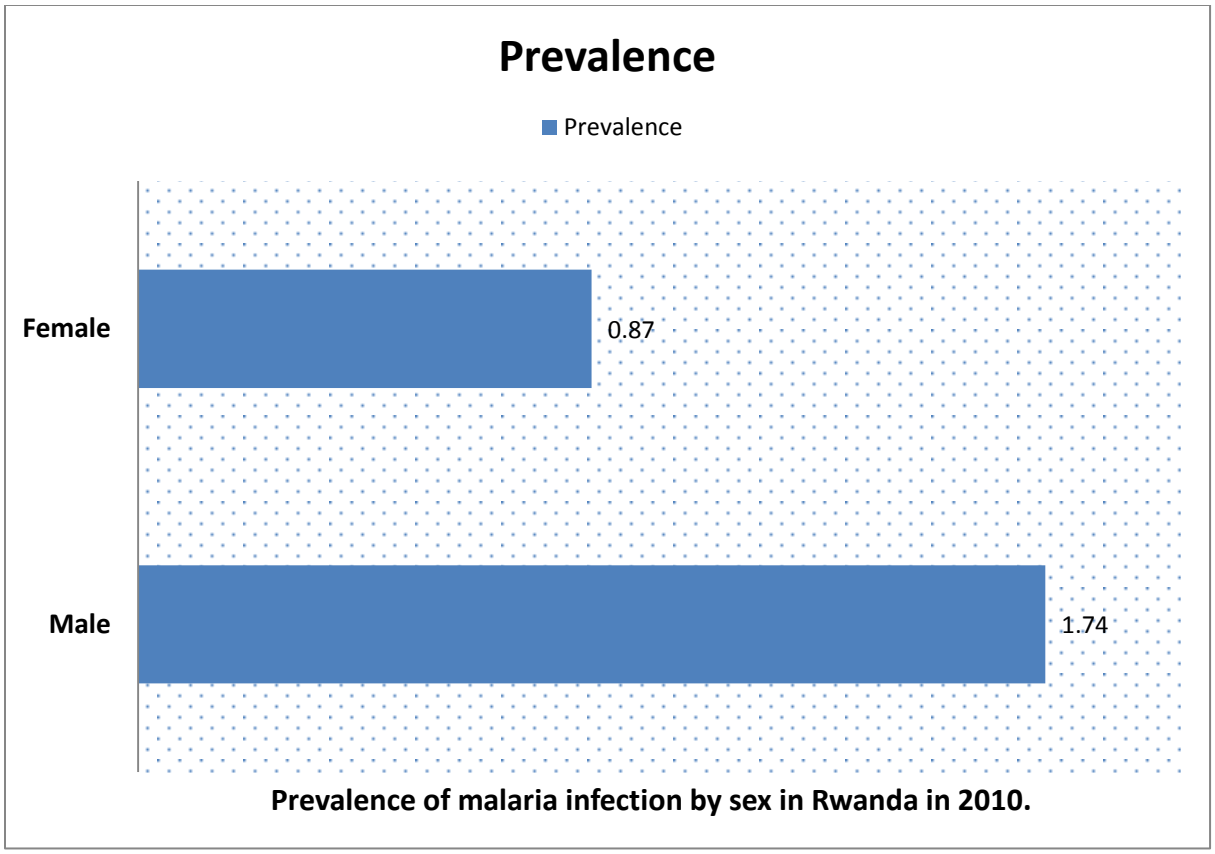


Figure 9: Bar chart showing prevalence of malaria infection by sex in Rwanda

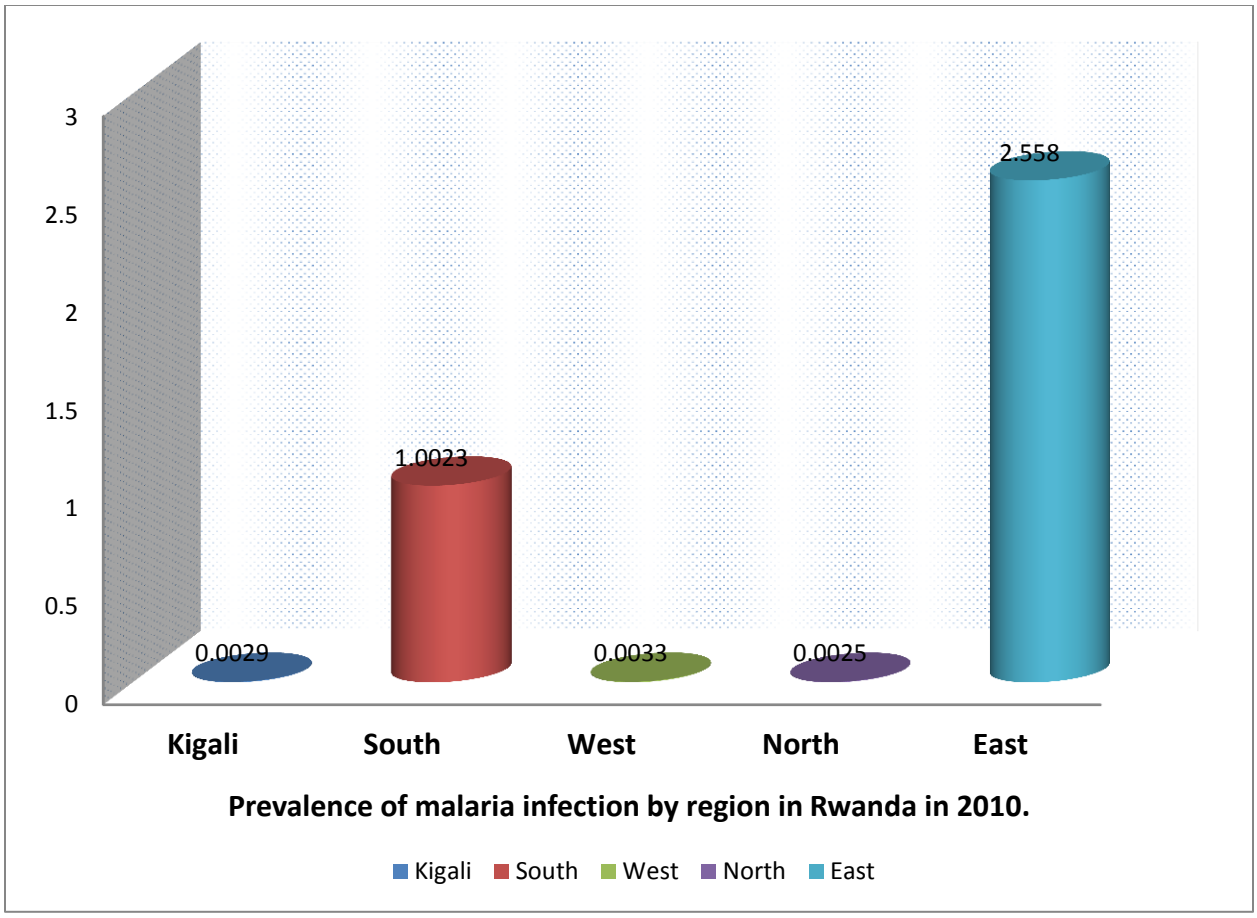


Figure 10: Graph showing distribution of malaria infection by region in Rwanda in 2010

Table 1: Descriptive statistics survey weighted percentages of independent variables for Rwanda in 2010

Independent variables

Variable	Category	Percentage of No Malaria Cases (11,610, 97.67%)	Percentage of Probable Malaria Cases (137, 1.26%)	Percentage of Definite Malaria Cases (118, 1.07%)	Designed-based (Design-based F statistics and p-value)
Sex	Male	20.07	0.27	0.36	F=7.46 (0.001)
	Female	77.42	0.99	0.69	
Education in Years	Mean (SE)*	2.64 (0.05)	1.89 (0.26)	1.38 (0.25)	F=14.50, (<0.000)
Age in years	Mean (SE)*	17.75 (0.11)	14.84 (1.22)	11.92 (1.08)	F=15.64, (0.001)
Social Economic Status	Most Poor	43.1	0.71	0.62	F=5.39 (<0.000)
	Poor	28.65	0.29	0.24	
	Least Poor	0.62	0.33	0.001	
Region	Kigali	10.44	0.0002	0.0003	F=14.55 (<0.000)
	South	22.96	0.38	0.26	
	West	24.25	0.14	0.0008	
	North	16.23	0.0005	0.0004	
	East	23.8	0.66	0.64	
Place of Residence	Urban	13.66	0.0004	0.0005	F=11.59 (<0.000)
	Rural	84.03	1.22	1	
Health Insurance	No	29.83	0.55	0.44	F=7.11 (0.001)
	Yes	67.86	0.71	0.62	

No of rooms	Mean(SE)*	2.30 (0.02)	2.01 (0.11)	2.04 (0.10)	F=6.37, (0.002)
Clean water facility for drinking	No	92.39	1.21	1.02	F=11.02 (<0.000)
	Yes	5.3	0.0005	0.0004	
Cluster altitude (M)	Mean (SE)*	1738.75 (10.78)	1569.15 (19.95)	1524.59 (20.87)	F= 66.59 (<0.000)
Sleep Under treated Net	No	35.96	0.52	0.48	F=2.54 (<0.083)
	Yes	61.73	0.74	0.57	

***SE➔ Standard error**

Table 2: Results of univariate, multivariable analysis adjusted for random effect, direct and indirect effect

Independent variables

Variable	Category	Univariable analysis odds ratio (95% CI), p-value	Multivariable analysis adjusted for random effect, odds ratio (95% CI), p-value	G-SEM direct effect odds ratio (95% CI), p-value	G-SEM indirect effect odds ratio (95% CI), p-value
Education in Years		0.89 (0.85, 0.95), 0.00	1.00 (0.99, 1.00), 0.96	0.98 (0.92, 1.04), 0.48	0.96 (0,94, 0.97), 0.00
Age in years		0.97 (0.96, 0.98), 0.00	0.99 (0.98, 0.99), 0.00	0.98 (0.97, 0.99), 0.03	
Social Economic Status	Most- Poor	1.00	1.00	1.00	
	Poor	0.70 (0.50, 0.98), 0.04	0.98 (0.97, 0.99), 0.04	0.64 (0.47, 0.85), 0.03	
	Least- Poor	0.43(0.26, 0.69), 0.00	0.97 (0.95, 0.98), 0.00	0.44 (0.29, 0.66), 0.00	0.91 (0.85, 0.98), 0.02
Region	Kigali	1.00	1.00	1.00	
	South	5.19 (1.77, 5.22), 0.00	1.02 (0.99, 1.04), 0.05	4.54 (2.03, 10.13), 0.00	
	West	1.78 (0.58, 5.44), 0.31	1.01 (0.99, 1.04), 0.20	2.82 (1.20, 6.67), 0.02	
	North	1.09 (0.34, 3.48), 0.88	1.01 (0.98, 1.03), 0.38	2.28 (0.84, 6.19), 0.10	
	East	10.24 (3.70, 8.34), 0.00	1.05 (1.03, 1.07), 0.00	5.45(2.56, 11.58), 0.00	
Health Insurance	No	1.00	1.00	1.00	
	Yes	0.60 (0.43, 0.80), 0.00	0.99 (0.98, 0.99), 0.04	0.79 (0.61, 1.02), 0.08	0.79 (0.61, 1.02), 0.07

No of rooms		0.72 (0.59, 0.88), 0.00	0.99 (0.98, 1.00), 0.15	0.87 (0.75, 1.00), 0.06	1.41 (1.21, 1.63), 0.00
Clean water facility for drinking	No	1.00	1.00	1.00	
	Yes	0.77 (0.66, 0.89), 0.00	0.98 (0.98, 1.00), 0.71	0.45 (0.21, 0.93), 0.03	
Cluster altitude (M)		0.99 (0.97, 0.99), 0.00	0.99 (0.98, 0.99), 0.00	0.99 (0.97, 0.98), 0.00	
Sleep Under treated Net	No	1.00	1.00	1.00	
	Yes	0.75 (0.56, 1.01), 0.05	0.98 (0.97, 0.99), 0.01	0.69 (0.54, 0.89), 0.01	
Random-effects Parameters Estimates For multivariable analysis					
S.D (hv002)			0.002694, (0.0006)*		
S.D (_cons)			0.059837, (0.0058)*		
S.D (Residual)			0.215894, (0.0016)*		
Inter-class correlation			0.071398**, (0.0130)*		

***Standard error**

****Interclass correlation =** $\frac{sd(hv002)^2 + sd(_cons)^2}{sd(hv002)^2 + sd(_cons)^2 + sd(residual)^2} = \frac{(0.002694)^2 + (0.0.05983)^2}{(0.002694)^2 + (0.0.05983)^2 + (0.215894)^2} =$ **0.071398**

3.2. Result of direct, indirect and total effects using (G-SEM)

3.2.1. Results of direct effects

The direct effects from G-SEM are shown in Table 3. The arrows indicate pathways that were statistically directly significant. Household related variables (number of rooms for sleeping, socio-economic status, health insurance, age in years and education in years), has significantly shown the direct effect on malaria infection. Ecological variables (region and cluster altitude in meters) and behavioural variables (sleep under treated bed net and clean water facility for drinking) also showed the significant direct effect on malaria infection.

Household related variables, least poor (a category of SES) and health insurance were modelled as an exogenous variable, which directly affected negatively on malaria infection (as shown in Table 3) and (as shown in Table 3) adjusting for other household level variables. The number of rooms for sleeping was modelled as an exogenous variable, directly impacted negatively on malaria infection (as shown in Table 3) with total effect (as shown in Table 3).

3.2.2. Results of indirect effects

The indirect effects found from G-SEM are shown in Table 3. The connected arrows show indirect pathways that were statistically significant. Moreover, variable like the number of rooms for sleeping was indirectly influenced by least poor and least poor was indirectly affected by education in years. Education gain in years also affected the health insurance which showed the positive relationship (as shown in Table 3).

Furthermore, when health insurance was treated an endogenous variable, SES variable category “least poor” indirectly impacted malaria infection and had a protective effect (as shown in Table 3). Education in years as an exogenous variable had no direct influence on

malaria infection, but indirectly affected malaria infection through least poor (as shown in Table 3) and had a protective effect on health insurance (as shown in Table 3).

When the number of rooms for sleeping was an endogenous variable, SES variable category least poor was indirectly negatively impacted the malaria infection. However, it positively affected when the no of rooms for sleeping effect was direct (as shown in Table 3).

3.2.3. Total effect

The total effect is an accumulative value of direct and indirect effects of each respective variable. The results of the total effect are shown in Table 3. Least poor category showed a significant total effect of as shown in Table 3 Health insurance also showed a total effect of (as shown in Table 3). Education gain in years showed an indirect effect and resulting total effect was as shown in Table 3.

Table 3: Direct, indirect and total effects of Malaria infection in children in Rwanda 2010						
Variable Category	**Direct Effect on Malaria infection in children Rwanda 2010**				**Indirect Effect on child Malaria infection**	**Total Effect on child Malaria infection**
	Education	**Least Poor**	**No. of Rooms**	**Malaria Diagnose direct effect coef.**		
Education in Years					-0.04074 (0.00836)*	-0.04074** (0.00836)*
Age in years				-0.01869(0.00479)*		-0.01869**(0.00479)*
Social Economic Status						
Poor				-0.46468(0.15131)*		
Least Poor	0.04114 (0.00056)*			-0.84267 (0.20614)*	-0.08464 (0.03717)*	-0.92720** (0.20212)*
Region						
South				1.52598(0.40979)*		1.52598**(0.40979)*
West				1.05460 (0.43893)*		1.05460** (0.43893)*
North				0.84064 (0.50849)*		0.84064** (0.50849)*
East				1.71304 (0.38413)*		1.71304** (0.38413)*
Cluster altitude in meters				-0.00337 (0.00044)*		-0.00337** (0.00044)*
Sleep Under treated Net				-0.36210 (0.13021)*		-0.36210** (0.13021)*
Health Insurance	0.01109 (0.00063)*	0.06660 (0.00472)*		-0.23371 (0.13173)*		-0.3580 **0.1396)*
Number of rooms for sleeping		0.48576 (0.00907)*		-0.14219 (0.07511)*		-0.23297**(0.131793)*
Clean water facility for drinking				-0.80843 (0.20614)*		-0.34357** (0.07566)*

***Standard error**

** Total effect

** **Total effects computed as the product along the related pathways of least poor, i.e.** ((0.06660)*(-0.23371)) + ((0.48576)*(-0.23371)) + (--¬0.84267) = **-0.92720 (0.20212)**

3.3. Results of direct and indirect generalised structural equation modelling (G-SEM)

Generalised structural equation modelling (G-SEM) was based on variables which were statistically significant in regression analyses were chosen for G-SEM pathways as shown in Figure 11 and Figure 12. Results were reported adjusting endogenous and exogenous factors and keeping other factors constant. The results of direct and indirect G-SEM technique showed positive and/or negative effects on the endogenous malaria infection.

Exogenous variables were least poor, health insurance, regions (north, east, west and south), and a number of rooms for sleeping in a household. The indirect effects were modelled on variables education in years, health insurance, least poor and a number of rooms for sleeping.

“Figure 11" highlights the direct pathways of malaria infection (arrows directly linked to the brown square) and the indirect pathways were showed all possible routes of malaria in Figure 12.

Education in years indirectly impacted the malaria infection in two ways least poor (protective) and health insurance (a risk) as shown in Figure 10.

1- Education **=>** least poor **=>** malaria infection = **Protective**

2- Education => health insurance => malaria infection = **Risk**

Eastern region showed greatest total effect on malaria infection (as shown in Table 3), and cluster altitude in meters showed least total effect on malaria infection (as shown in “Table 3”).

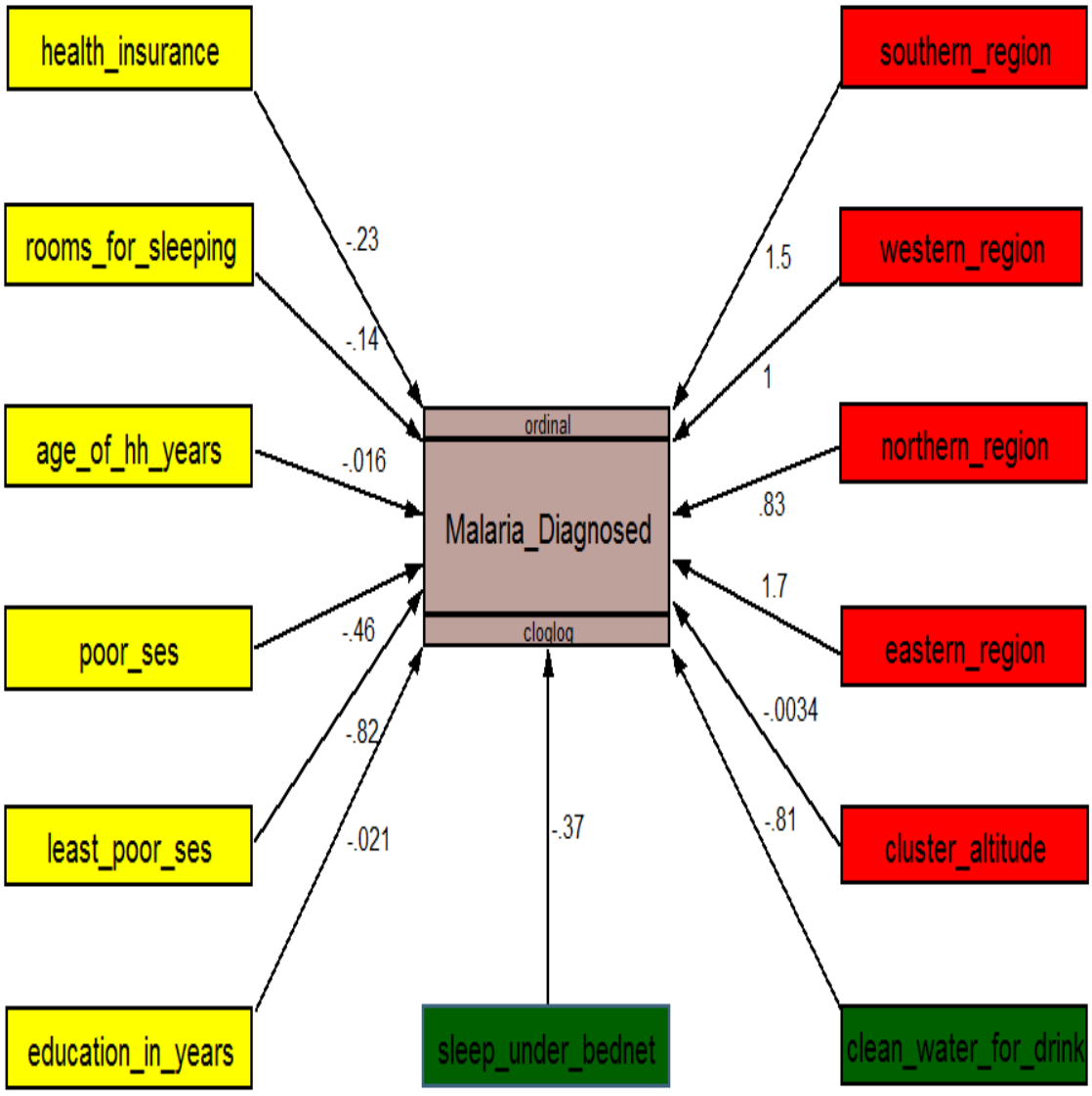


Figure 11: G-SEM pathway diagram shows direct coefficients from ordinal regression analysis of the effects of selected random predictor variables on malaria infection outcome variable result in children and adults in Rwanda in 2010. Key for variables names: individuals covered by health insurance **(health_insurance)**, number of rooms for sleeping in each house **(rooms_for_sleeping)**, age of household members in years **(age_of_hh_yeras)**, poor SES versus most poor SES **(poor_ses)**, least poor SES versus most poor SES **(least_poor_ses)**, education gain of each household member in years **(education_in_years)**, number of household members sleep under treated mosquito bed net **(sleep_under_bednet)**, household members have a clean water excess for drinking **(had_water_excess)**, cluster altitude in meters **(cluster altitude)**, eastern region of Rwanda **(eastern_region)**, northern region of Rwanda **(northern_region)**, western region of Rwanda **(western_region)**, southern region of Rwanda **(southern_region)**. Other: the arrows pointing from the exogenous (explanatory variables) to endogenous (dependent variable).

The result of G-SEM showed both direct and indirect effects on endogenous variable malaria infection. Figure 9 shows the direct G-SEM model and indirect G-SEM model is shown in Figure 10. The endogenous variables; least poor, the number of rooms for sleeping, and health insurance are shown in Figure 10.

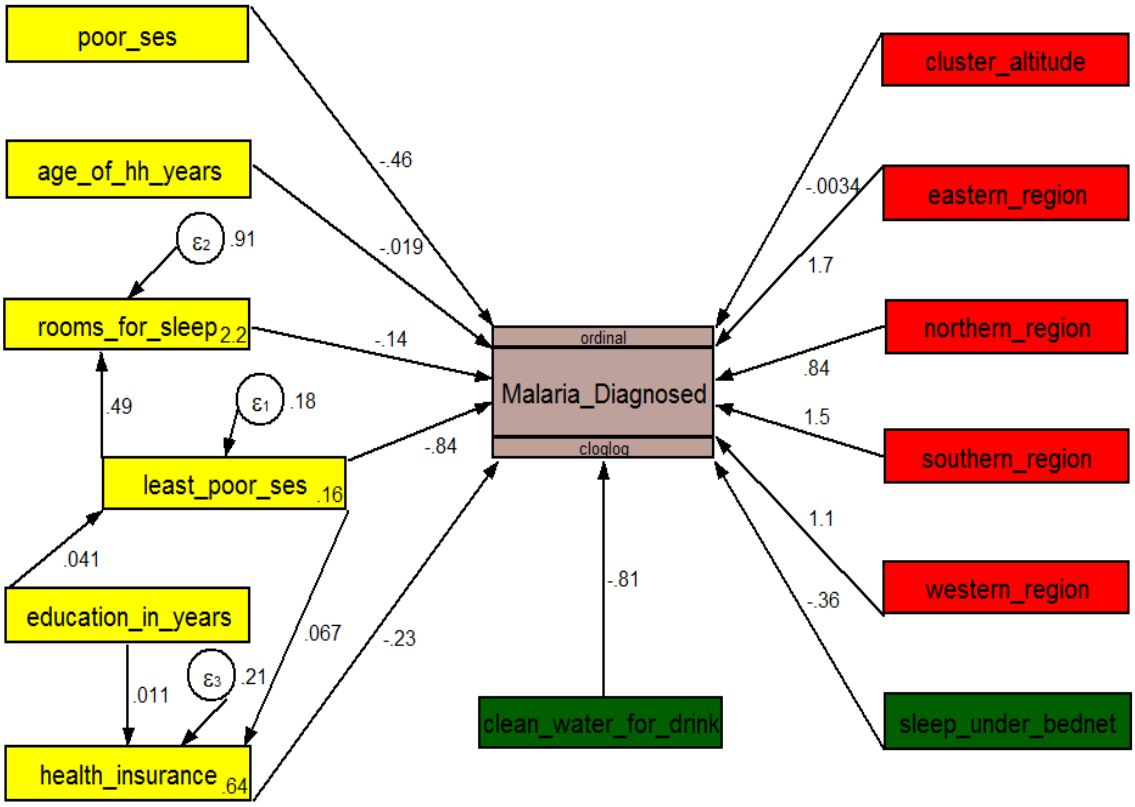


Figure 12: Diagram shows direct and indirect pathways and coefficients from G-SEM based ordinal regression analysis of the effects of selected random predictor variables on malaria infection outcome variable result in children and adults in Rwanda in 2010. Key for variables names: individuals covered by health insurance **(health_insurance)**, number of rooms for sleeping in each house (rooms_for_sleeping), age of household members in years **(age_of_hh_yeras)**, poor SES versus most poor SES **(poor_ses)**, least poor SES versus most poor SES **(least_poor_ses)**, education gain of each household member in years **(education_in_years)**, number of household members sleep under treated mosquito bed net **(sleep_under_bednet)**, household members have a clean water excess for drinking **(had_water_excess)**, cluster altitude in meters **(cluster altitude)**, eastern region of Rwanda **(eastern_region)**, northern region of Rwanda **(northern_region)**, western region of Rwanda **(western_region)**, southern region of Rwanda **(southern_region)**. Other: the arrows pointing from the exogenous (explanatory variables) to endogenous (dependent variable) and the error terms (€) placed on all three endogenous variables.

Chapter 4 Discussion, conclusion and recommendation

This chapter deals with the discussion of the results of this research work and concludes the findings. The chapter also indicates the recommendations of possible future research work.

4.1. Discussion

The study revealed that malaria infection was influenced by the combination of variables such as behaviour, household condition and ecological factors. In 2015, 214 million deaths were recorded due to malaria and 91 % were in sub-Saharan Africa [2]. Social-economic status was a fundamental factor of malaria morbidity in several studies [7,60]. The studies also provided a positive malaria diagnosis.

As mentioned earlier, malaria is associated with poverty [60]. The findings of this work complement the results of the previous studies on malaria morbidity. Previous studies have shown that low socio-economic status increases the prevalence of malaria infection in developing countries [61]. According to the United Nations Accounts (UNA) central aggregated database 2015, Rwanda has low Gross Domestic Product (GDP) [62] which translates into higher malaria infections. This study also confirms the finding. It has also been indicated that the malaria infection is a disease of developing countries putting an additional burden on the healthcare facilities.

Logically the nutritional level is linked with GDP. Therefore, it is obvious that the poorer countries have inadequate resources to improve nutritional levels resulting in poor immunity against malaria disease [40]. Poor SES results into an insufficient use of health-care facilities, therefore increasing the vulnerability of the population to the risk

of malaria. Governments of the poorer countries need rational, optimum and affordable policies to control malaria infection and treatment. This could be achieved by investing in research and data collection to investigate the trends of malaria to make effective and efficient policies and proper utilisation of resources.

Regions (Kigali, south, north, east and west) place-of-residence (urban or rural) and cluster altitude in meters may be interrelated. However, fewer studies indicated an effect on malaria prevalence dependence on altitude [63-65]. Researchers also revealed that individuals living in low altitude areas are more at risk as compared to higher altitude areas [42]. In this work, altitude has shown a marginal reduction in malaria infection.

A study conducted in Thailand concluded that school children could be a better source of anti-malaria education for the family members in contrast to disseminating messages by newsletters [66]. To achieve the significant reduction in malaria morbidity in Rwanda, there is a need of improvement in the education status of the targeted population [67]. Knowledge about malaria prevention might be conveyed in the community by the students, who facilitate the household and families by applying and following influence in the targeted settings.

In this study, Age has shown a significance (p-value = 0.001). Previous studies have shown that children over the age of five were less at risk of malaria infection [13,37]. In this work, increase in age has shown a reduced tendency of malaria infection hence it is less likely to have positive malaria diagnosis as the age increases. Existing literature also

confirms that older people above sixty have the lesser chance of malaria infection due to developed immunity.

Persons who sleep under treated bed net have shown the significance of p-value = 0.004. Results of this study show that individuals who sleep under a treated bed net, are less likely to have positive malaria diagnosis test. It might be due to the fact that they have a lesser chance of having direct contact with infected mosquitos.

Health insurance showed the marginal significance of p-value = 0.06. The result of the study shows that people with health insurance are less likely to get the malaria infection. It is possibly due to health related companies or knowledge of disease provided by the health insurance companies. Health insurance companies also provide preventative methods for protecting against malaria.

Participants who have clean water facility for drinking, are less likely of contracting malaria as shown with significant of p-value = 0.01. The possibilities are that the malaria is an infectious disease and contaminated water is a good inhabitant for mosquito. Therefore, participants who have clean water supply for drinking may be protective as compared who do not.

The number of rooms for sleeping have shown significance (p-value = 0.01). Meaning that people who have more rooms for sleeping they are less likely of getting malaria infection.

The G-SEM's indirect pathways showed a significant association between SES and health insurance, education and health insurance, education and least poor as well as between SES and number of room for sleeping level. G-SEM was used in this study to complement the results from the multiple variable analyses. The results showed that the multiple variable analysis and the G-SEM direct pathways show similar results.

G-SEM can help in diagrammatically measure the effects of the determinants of the outcome and this can assist in the analysis where the variables can be separated into those with a direct effect on the outcome and those with an indirect effect on the outcome. This will help to explain better some factors that might not directly affect the outcome and inform policy on adopting indirect and direct approaches to dealing with the malaria infection in children and adults.

4.2. Strength and limitations of the study

The strength and limitations of this study can be discussed in two categories: classification of independent and dependent variables; confounding and effect modifications.

The main strength of this study was the use of the ordinal outcome variable (malaria diagnosed) based on a rapid malaria diagnostic test as well as a laboratory test result for malaria. The use of ordinal variable was the major strength of this study and prevented "recall bias". However the proportion of "no malaria cases" and "probable cases" weakened the power of the study, this may also be regarded as a limitation. To deal with the confounding variables, survey-adjusted ordinal regression model in addition to structural equation modelling was used in the analysis to cater for direct and indirect determinants.

Multicollinearity was considered as limitation of the study as few variables were dropped from the multivariable analysis which could have resulted in some loss of accuracy and interpretation of the results.

The data used in this study was obtained from a cross-sectional study. The cross-sectional studies mainly measure the prevalence and not incidence. However, this study was looking at incidence (episodes of malaria). Therefore, it may have limited the interpretation of the associations during data analysis. Secondly, no causal sequence can be ascertained from cross-sectional study but in this work causal sequence (influence of direct and indirect factors) was investigated.

4.3. Conclusions

This study shows the importance of socio-economic status as well as influence of education in the fight against malaria. To eliminate malaria morbidity in the population, it is important for the governments to empower the community economically, intellectually and ensure the health education is a part of the efforts to fight the endemic.

Access to health insurance has a positive impact on decreasing malaria infections. Therefore health insurance could be therefore focused as an effective tool in the intervention strategy especially in relatively high-income sectors to reduce the infections significantly. This will assist in the fight to eliminate malaria.

It is important to ensure that the resources are channelled to optimise prevention strategies that are put in place. Once the population is empowered, the preventative strategies can then be implemented successfully. If the population is educated, it can understand the strategies put in place and follow them successfully. Health authorities and Government have to have the latest knowledge of the determinant factors to plan preventive and curative strategies of malaria.

The methods of analysis used in this work could help the health authorities to make effective and efficient strategies against malaria. Hence public health awareness campaigns must be empowered to educate the masses and eliminate malaria morbidity. It is necessary to understand the direct and indirect factors of malaria morbidity so that effective monitoring and evaluation policies for malaria control can be formulated.

The reduction in poverty will go a long way in the fight to eradicate malaria in Africa in particular and globally in general.

4.4. Recommendations

The following recommendations arise from the study.

These are:

1. There must be targeted interventions in disease prevention programs, and concentrate on areas with greater prevalence. It will help to maximise the use of the available resources so that malaria can effectively eliminate.
2. Health education and knowledge about malaria transmission are important in malaria control; therefore health education must be readily and easily available and accessible to the targeted population. This health education can result in behaviour change that results in improved prevention of malaria
3. LLIN are also an important tool in disease control and must be made available to the population in need.
4. There should be programs at the community and individual level to empower the targeted population so that they improve their socio-economic status and this, in turn, helps to reduce the prevalence of malaria.
5. G-SEM is an important tool in disease modelling and can be utilised more in identifying disease determinants.

References

1. Roll back malaria. Available at: http://www.rollbackmalaria.org/about/about-malaria/what-is-malaria 2 October 2016].
2. Roll back malaria. Available from: http://www.rollbackmalaria.org/about/about-malaria/what-is-malaria [cited 2 May 2015].
3. WHO (2005) World malaria report 2005. Available from: <http://rbm.who.int/wmr2005/> [cited 2 May 2015].
4. Health in the Millennium Development Goals. Available from: http:// www.who.int/mdg [cited 2 May 2015].
5. WHO (2014) World malaria report 2014. Available from: http://rbm.who.int/wmr2014/ [cited 2 May 2015].
6. National Institute of Statistics of Rwanda. Fourth Population and Housing Census. Thematic Report: Characteristics of households and housing. Ministry of Finance and Economic Planning; 2012 [cited 2 May 2015].
7. President's Malaria Initiative. Malaria Operational Plan (MOP). Kigali, Rwanda: Rwanda FY 2014; 2014 [cited 2 May 2015].
8. Karema C, Aregawi MW, Rukundo A, Kabayiza A, Mulindahabi M, et al. (2012) Trends in malaria cases, hospital admissions and deaths following scale-up of anti-malarial interventions, 2000–2010, Rwanda. Malar J 11: 10.1186.
9. Otten M, Aregawi M, Were W, Karema C, Medin A, et al. (2009) Initial evidence of reduction of malaria cases and deaths in Rwanda and Ethiopia due to rapid scale-up of malaria prevention and treatment. Malar J 8: 14.
10. Abuja declaration and the plan of action. Available from: <http://www.rbm.who.int/docs/abuja_declaration_final.htm [cited 2 May 2015].
11. Feachem RG, Phillips AA, Hwang J, Cotter C, Wielgosz B, et al. (2010) Shrinking the malaria map: progress and prospects. Lancet 376: 1566-1578.
12. Smith T, Hii JL, Genton B, Muller I, Booth M, et al. (2001) Associations of peak shifts in age--prevalence for human malarias with bednet coverage. Trans R Soc Trop Med Hyg 95: 1-6.
13. Winskill P, Rowland M, Mtove G, Malima RC, Kirby MJ (2011) Malaria risk factors in north-east Tanzania. Malar J 10: 98.
14. Lengeler C (2004) Insecticide-treated bed nets and curtains for preventing malaria. Cochrane Database Syst Rev: Cd000363.
15. President's Malaria Initiative (PMI). Malaria Operational Plan: Rwanda FY 2012. Washington, DC: PMI, 2011. Available from: http://www.pmi.gov/countries/ mops/fy12/rwanda_mop_fy12.pdf [cited 2 May 2015].
16. Bloland PB, Boriga DA, Ruebush TK, McCormick JB, Roberts JM, et al. (1999) Longitudinal cohort study of the epidemiology of malaria infections in an area of intense malaria transmission II. Descriptive epidemiology of malaria infection and disease among children. Am J Trop Med Hyg 60: 641-648.
17. Ingstad B, Munthali AC, Braathen SH, Grut L (2012) The evil circle of poverty: a qualitative study of malaria and disability. Malar J 11: 15.
18. World Bank. http://siteresources.worldbank.org/EXTANNREP2010/Resources/WorldBank-AnnualReport2010.pdf. [Cited 07 January 2017].
19. Kundu R, Ganguly N, Ghosh TK, Choudhury P, Shah RC (2005) Diagnosis and management of malaria in children: recommendations and IAP plan of action. Indian Pediatr 42: 1101-1114.

20. Bennett A, Kazembe L, Mathanga DP, Kinyoki D, Ali D, et al. (2013) Mapping malaria transmission intensity in Malawi, 2000-2010. Am J Trop Med Hyg 89: 840-849.
21. Snow RW, Craig M, Deichmann U, Marsh K (1999) Estimating mortality, morbidity and disability due to malaria among Africa's non-pregnant population. Bull World Health Organ 77: 624-640.
22. Demographic and Health Survey report 2010. Available from: https://dhsprogram.com/pubs/pdf/FR259/FR259.pdf. Accessed 26 July 2016.
23. World Health Organization (Rwanda: Country Health Profile). Available from: http://www.who.int/countries/rwa/en/. Accessed 8 July 2016.
24. Ernst KC, Lindblade KA, Koech D, Sumba PO, Kuwuor DO, et al. (2009) Environmental, socio-demographic and behavioural determinants of malaria risk in the western Kenyan highlands: a case-control study. Trop Med Int Health 14: 1258-1265.
25. Rogers DJ, Randolph SE, Snow RW, Hay SI (2002) Satellite imagery in the study and forecast of malaria. Nature 415: 710-715.
26. Stratton L, O'Neill MS, Kruk ME, Bell ML (2008) The persistent problem of malaria: addressing the fundamental causes of a global killer. Soc Sci Med 67: 854-862.
27. WHO. (2008) World malaria report 2008. Available from: Geneva World Health Organization [cited 2 May 2015].
28. WHO. (2013a) Global Health obervatory Data Repository. Rwanda statistics summary. Available from. http://apps.who.int/gho/data/node.country.country-RWA?lang=en [cited 2 May 2015].
29. Donnelly MJ, McCall PJ, Lengeler C, Bates I, D'Alessandro U, et al. (2005) Malaria and urbanization in sub-Saharan Africa. Malar J 4: 12.
30. Yamamoto S, Louis VR, Sie A, Sauerborn R (2010) Household risk factors for clinical malaria in a semi-urban area of Burkina Faso: a case-control study. Trans R Soc Trop Med Hyg 104: 61-65.
31. Cheesbrough Monica (2006). District laboratory practice in tropical countries. New York-Cambridge press Part1, 2nd edition Pp249-258. Arora DR and Arora B (2008). Medical Parasitology. 2nd edition.Pp.67-76.
32. Afolabi BM, Salako LA, Mafe AG, Ovwigho UB, Rabiu KA, et al. (2001) Malaria in the first 6 months of life in urban African infants with anemia. Am J Trop Med Hyg 65: 822-827.
33. Coluzzi M (1999) The clay feet of the malaria giant and its African roots: hypotheses and inferences about origin, spread and control of Plasmodium falciparum. Parassitologia 41: 277-283.
34. Noor AM, Gething PW, Alegana VA, Patil AP, Hay SI, et al. (2009) The risks of malaria infection in Kenya in 2009. BMC Infect Dis 9: 180.
35. Cibulskis RE, Aregawi M, Williams R, Otten M, Dye C (2011) Worldwide incidence of malaria in 2009: estimates, time trends, and a critique of methods. PLoS Med 8: e1001142.
36. Reiter P (2001) Climate change and mosquito-borne disease. Environ Health Perspect 109 Suppl 1: 141-161.
37. Mawili-Mboumba DP, Bouyou Akotet MK, Kendjo E, Nzamba J, Medang MO, et al. (2013) Increase in malaria prevalence and age of at risk population in different areas of Gabon. Malar J 12: 3.
38. O'Meara WP, Bejon P, Mwangi TW, Okiro EA, Peshu N, et al. (2008) Effect of a fall in malaria transmission on morbidity and mortality in Kilifi, Kenya. Lancet 372: 1555-1562.
39. Reiter P (2008) Global warming and malaria: knowing the horse before hitching the cart. Malar J 7 Suppl 1: S3.

40. Caulfield LE, Richard SA, Black RE (2004) Undernutrition as an underlying cause of malaria morbidity and mortality in children less than five years old. Am J Trop Med Hyg 71: 55-63.
41. Bates I, Fenton C, Gruber J, Lalloo D, Medina Lara A, et al. (2004) Vulnerability to malaria, tuberculosis, and HIV/AIDS infection and disease. Part 1: determinants operating at individual and household level. Lancet Infect Dis 4: 267-277.
42. Abeku TA, van Oortmarssen GJ, Borsboom G, de Vlas SJ, Habbema JD (2003) Spatial and temporal variations of malaria epidemic risk in Ethiopia: factors involved and implications. Acta Trop 87: 331-340.
43. WHO. (2012). World Malaria Report 2012. Rwanda [cited 8 May 2015].
44. Liu L, Johnson HL, Cousens S, Perin J, Scott S, et al. (2012) Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet 379: 2151-2161.
45. World Health Organization. WHO guidelines for the treatment of malaria. 3rd ed Geneva, Switzerland: WHO, 2015. [Cited, 12 January 2017].
46. Wingfield T, Boccia D, Tovar M, Gavino A, Zevallos K, et al. (2014) Defining Catastrophic Costs and Comparing Their Importance for Adverse Tuberculosis Outcome with Multi-Drug Resistance: A Prospective Cohort Study, Peru. PLoS Med 11.
47. Guerra CA, Gikandi PW, Tatem AJ, Noor AM, Smith DL, et al. (2008) The limits and intensity of Plasmodium falciparum transmission: implications for malaria control and elimination worldwide. PLoS Med 5: e38.
48. Mosley WH, Chen LC (1984) An analytical framework for the study of child survival in developing countries. Population and development review 10: 25-45.
49. Lewis JJ, Donnelly CA, Mare P, Mupambireyi Z, Garnett G, et al. (2007) Evaluating the proximate determinants framework for HIV infection in rural Zimbabwe. Sexually transmitted infections.
50. Center for disease control. Available from: https://wwwn.cdc.gov/nndss/conditions/malaria/case-definition/2014/. [Cited 6 January 2016].
51. National Institute of Statistics of Rwanda. Fourth Population and Housing Census. Thematic Report: Characteristics of households and housing. Ministry of Finance and Economic Planning; 2012. Available from: http://statistics.gov.rw/file/2907/download?token=i09m0Bly. Accessed 7 July 2016.
52. Ministry of Health, National Malaria Control Programme, MEASURE DHS, ICF International: Rwanda Malaria Indicator Survey (MIS) 2010. https://dhsprogram.com/pubs/pdf/MIS16/MIS16.pdf. Assessed 8 July 2016.
53. Demoraphic and Health Survey 2010 final reportAvailable from: https://dhsprogramcom/pubs/pdf/FR259/FR259pdf Assessed 8 July 2016.
54. Gwatkin DR, Rutstein S, Johnson K, Pande R, Wagstaff A (2000) Socio-economic differences in health, nutrition, and population. Washington, DC: World Bank.
55. Center for Disease Control. Available from; https://www.cdc.gov/malaria/diagnosis_treatment/rdt.html. [Cited 13 January 2017].
56. (World Health Organization. Annex 1. Defining the term “malaria case”. Available from: http://www.who.int/malaria/mpac/mpac-sept2015-terminology-annex1.pdf [Cited 10 January 2017].).
57. Stata ado-file st02862: A menu-driven facility for sample-size calculations in cluster randomized controlled trials. K. Hemming and J. Marsh. Stata Journal 14: 701; 13: 114–135.

58. Grace JB (2008) Structural equation modeling for observational studies. The Journal of Wildlife Management 72: 14-22.
59. Hooper D, Coughlan J, Mullen M (2008) Structural equation modelling: guidelines for determining model fit. Articles: 2.
60. Snow RW, Craig MH, Newton C, Steketee RW (2003) The public health burden of Plasmodium falciparum malaria in Africa. Working Paper 11. Disease Control Priorities Project, Fogarty International Center, National Institutes of Health, Bethesda
61. Sachs J, Malaney P (2002) The economic and social burden of malaria. Nature 415: 680-685.
62. Map of Rwanda. Available from: https://www.google.co.za/search?q=Rwanda+map&rlz=1C1GNAM_enZA681ZA681&source=lnms&tbm=isch&sa=X&ved=0ahUKEwiJruC5rN3OAhWD7RQKHRmSDXwQ_AUICCgB&biw=1440&bih=775#imgrc=t8bYuxvUxLWxHM%3A . Assessed 8 August 2016.
63. Drakeley CJ, Corran PH, Coleman PG, Tongren JE, McDonald SL, et al. (2005) Estimating medium- and long-term trends in malaria transmission by using serological markers of malaria exposure. Proc Natl Acad Sci U S A 102: 5108-5113.
64. Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW (2004) The global distribution and population at risk of malaria: past, present, and future. Lancet Infect Dis 4: 327-336.
65. Lindsay SW, Martens WJ (1998) Malaria in the African highlands: past, present and future. Bull World Health Organ 76: 33-45.
66. Okabayashi H, Thongthien P, Singhasvanon P, Waikagul J, Looareesuwan S, et al. (2006) Keys to success for a school-based malaria control program in primary schools in Thailand. Parasitol Int 55: 121-126.
67. O'Meara WP, Mangeni JN, Steketee R, Greenwood B (2010) Changes in the burden of malaria in sub-Saharan Africa. Lancet Infect Dis 10: 545-555.
68. Stata 13 manual. Seemingly unrelated estimation (suest) procedures. Available http:www.stata.com/manual13/rsuest.pdf. [13 January 2017].

Appendix

1.1: Table 4: Sensitivity analysis using malaria ordinal variable, binary RDT variable and binary blood smear test

Table 5: Sensitivity analysis of malaria ordinal variable with binary variable blood smear and rapid malaria test results of univariate.

Independent variables

Variable	Category	Univariable analysis odds ratio (95% CI), p-value with malaria ordinal variable	Univariable analysis odds ratio (95% CI), p-value with blood smear test	Univariable analysis odds ratio (95% CI), p-value with rapid malaria test
Education in Years		0.89 (0.85, 0.95), 0.00	0.89 (0.83, 0.97), 0.00	0.91 (0. 88, 0.96), 0.00
Age in years		0.97 (0.96, 0.98), 0.00	0.97(0.96, 0.99), 0.00	0.98 (0.97, 0.98), 0.00
Social Economic Status	Most- Poor	1.00	1.00	
	Poor	0.70 (0.50, 0.98), 0.04	0.85 (0.55, 1.30), 0.45	0.85 (0.62, 1.62), 0.31
	Least- Poor	0.43(0.26, 0.69), 0.00	0.36 (0.19, 0.69), 0.00	0.49 (0.34, 0.71), 0.00
Region	Kigali	1.00	1.00	
	South	5.19 (1.77, 5.22), 0.00	2.28 (0.874, 7.05), 0.15	2.85 (1.50, 5.41), 0.00
	West	1.78 (0.58, 5.44), 0.31	0.87 (0.25, 3.02), 0.83	1.43 (0.72, 2.84), 0.30
	North	1.09 (0.34, 3.48), 0.88	0.82 (0.25, 2.75), 0.75	2.24 (1.09, 4.57), 0.03
	East	10.24 (3.70, 8.34), 0.00	5.23 (1.85, 14.77), 0.00	3.63 (1.95, 6.73), 0.00
Health Insurance	No	1.00	1.00	
	Yes	0.60 (0.43, 0.80), 0.00	0.66 (0.46, 0.95), 0.03	0.81 (0.62, 1.06), 0.13

No of rooms		0.72 (0.59, 0.88), 0.00	0.78 (0.63, 0.98), 0.03	0.81 (0.70, 0.93), 0.00
Clean water facility for drinking	No	1.00	1.00	
	Yes	0.77 (0.66, 0.89), 0.00	0.93 (0.77, 1.11), 0.42	0.57 (0.31, 1.06), 0.08
Cluster altitude (M)		0.99 (0.97, 0.99), 0.00	0.99 (0.99 , 1.00), 0.00	0.99 (0.99, 1.00), 0.00
Sleep Under treated Net	No	1.00	1.00	
	Yes	0.75 (0.56, 1.01), 0.05	0.67 (0.46, 0.97), 0.03	0.74 (0.58, 0.95), 0.02

Table 5: Sensitivity analysis of malaria ordinal variable with binary variable blood smear and rapid malaria test results of multivariate analysis adjusted for random effect.

Independent variables

Variable	Category	Univariable analysis odds ratio (95% CI), p-value with malaria ordinal variable	Multivariable analysis adjusted for random effect, odds ratio (95% CI), p-value with malaria ordinal variable	Multivariable analysis adjusted for random effect, odds ratio (95% CI), p-value with malaria blood smear test	Multivariable analysis adjusted for random effect, odds ratio (95% CI), p-value with rapid malaria test
Education in Years		0.89 (0.85, 0.95), 0.00	1.00 (0.99, 1.00), 0.96	1.00 (0.99, 1.03), 0.69	1.00 (0.99, 1.01), 0.48
Age in years		0.97 (0.96, 0.98), 0.00	0.99 (0.98, 0.99), 0.00	0.99 (0.99, 1.03), 0.34	0.99 (1.00, 1.02), 0.03
Social Economic Status	Most- Poor	1.00	1.00	1.00	1.00
	Poor	0.70 (0.50, 0.98), 0.04	0.98 (0.97, 0.99), 0.04	0.99 (0.97, 1.01), 0.37	1.01 (1.03, 1.06), 0.03
	Least- Poor	0.43(0.26, 0.69), 0.00	0.97 (0.95, 0.98), 0.00	0.98 (0.96, 1.00), 0.08	0.95 (0.90, 1.01), 0.00
Region	Kigali	1.00	1.00	1.00	1.00
	South	5.19 (1.77, 5.22), 0.00	1.02 (0.99, 1.04), 0.05	0.98 (0.96, 1.01), 0.44	1.01 (0.92, 1.11), 0.00
	West	1.78 (0.58, 5.44), 0.31	1.01 (0.99, 1.04), 0.20	0.99 (0.96, 1.02), 0.53	0.99 (0.89, 1.10), 0.02
	North	1.09 (0.34, 3.48), 0.88	1.01 (0.98, 1.03), 0.38	0.99 (0.96, 1.02), 0.66	1.11 (0.99, 1.24), 0.10
	East	10.24 (3.70, 8.34), 0.00	1.05 (1.03, 1.07), 0.00	1.01(0.98, 1.04), 0.44	0.95 (0.87, 1.04), 0.00
Health Insurance	No	1.00	1.00	1.00	1.00
	Yes	0.60 (0.43, 0.80), 0.00	0.99 (0.98, 0.99), 0.04	0.99 (0.98, 1.03), 0.88	1.02(0.97, 1.06), 0.00

No of rooms		0.72 (0.59, 0.88), 0.00	0.99 (0.99, 1.00), 0.15	0.99 (0.99, 1.01), 0.89	0.99 (0.97, 1.01), 0.00
Clean water facility for drinking	No	1.00	1.00	1.00	1.00
	Yes	0.77 (0.66, 0.89), 0.00	0.98 (0.98, 1.00), 0.71	1.03 (0.99, 1.07), 0.06	0.97 (0.87, 1.08), 0.03
Cluster altitude (M)		0.99 (0.97, 0.99), 0.00	0.99 (0.98, 0.99), 0.00	0.99 (0.99, 1.00), 0.39	0.99 (0.99, 1.00), 0.00
Sleep Under treated Net	No	1.00	1.00	1.00	1.00
	Yes	0.75 (0.56, 1.01), 0.05	0.98 (0.97, 0.99), 0.01	0.99 (0.97, 1.00), 0.15	0.97 (0.94, 1.01), 0.00

Appendix 1.2: Histogram of factor score

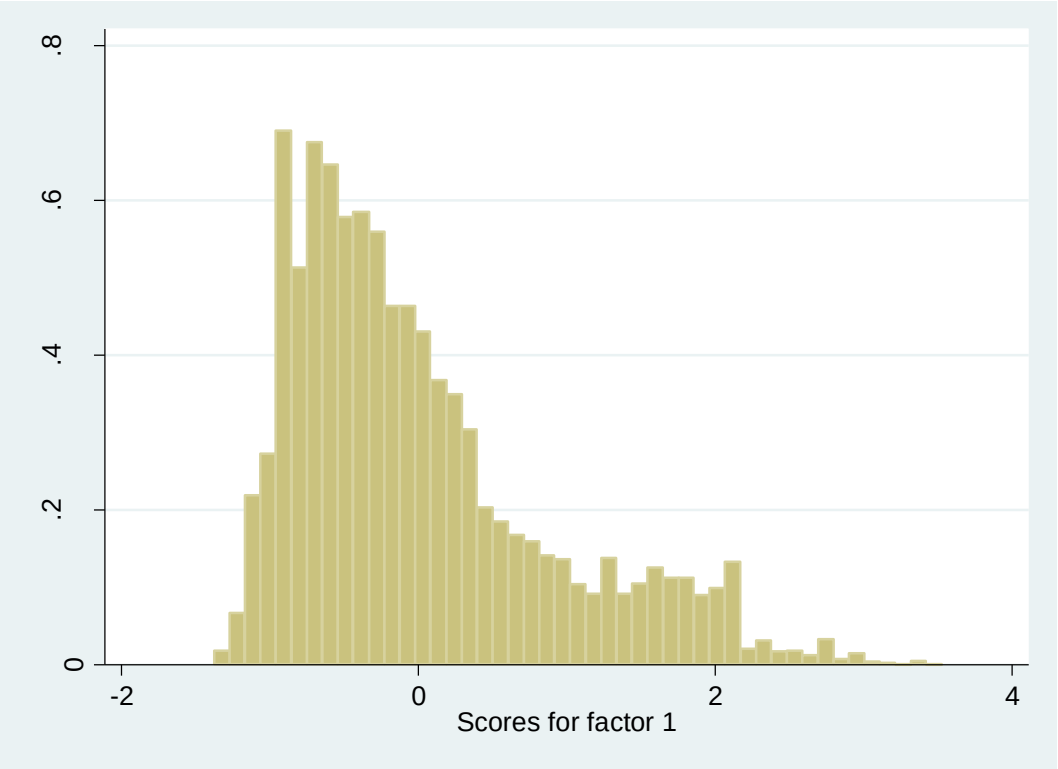


Figure 13: Appendix A1.1: Histogram of factor scores for the creation of socio-economic status

Appendix A2: Stata codes of statistical analysis

A2.1: Power calculation

clustersampsi, binomial power p1(.021) p2(.03) m(115) k(492) rho(0.071) size_cv(0) alpha(0.05) base_correl(0)

significance level:0.05

baseline measures adjustment (correlation):0.00

average cluster size:115

number of clusters per arm:492

coefficient of variation (of cluster sizes):0.00

intra-cluster correlation (ICC):0.0710

clustersampsi estimated parameters:

Firstly, assuming individual randomisation:

power: 1.00

Then, allowing for cluster randomisation:

design effect: 9.09

power:0.89

A2.2: Factor analysis for the creation of socio-economic status

factor source_of_water Type_of_Toilet_Facility Has_Radio Has_Bicycle Has_Motorcycle Has_Car Has_Telephone Share_toiler_with_HH Has_Mobile Has_watch Own_Land Own_cattle Own_goats Own_sheeps Own_chicken Own_bulls Own_pigs Owns_rabbits Has_bankaccount Main_Floor_Material Main_wall_material Main_Roof_Material Type_of_CookingFuel

predict scorefactor_new

sum scorefactor_new, detail

tab scorefactor_new

histogram scorefactor_new

**************Factorscore has been finalized************

recode scorefactor_new (min/-0.333878=1) (-0.333879/0.3148308=2) (0.3148308/max=3), gen (SES_new)

tab SES_new

label define SES_new 1 "Most Poor" 2 "Poor" 3 "Least Poor"

label value SES_new SES_new

```
. tab SES_new
```

RECODE of scorefactor _new (Scores for factor 1)	Freq.	Percent	Cum.
Most Poor	24,875	44.52	44.52
Poor	15,750	28.19	72.71
Least Poor	15,247	27.29	100.00
Total	55,872	100.00	

A2.3: Fitting of final Direct modeling manually

xi: svy: ologit Malaria_Diagnosed Education_in_Years Health_Insurance clus_altitude_meter No_of_rooms Slept_under_Net Age_of_HH poor_ses least_poor_ses south_ref_Kigali west_ref_Kigali north_ref_Kigali east_ref_Kigali has_water_ref_No water_missing Sex Place_of_Residence Boil_Water, or

est store A

xi: svy: ologit Malaria_Diagnosed Education_in_Years Health_Insurance clus_altitude_meter No_of_rooms Slept_under_Net Age_of_HH poor_ses least_poor_ses south_ref_Kigali west_ref_Kigali north_ref_Kigali east_ref_Kigali has_water_ref_No water_missing, or

est store B

A2.4: Checking the Goodness of fit of survey final model using suest test

**********Checking the Goodness of fit of survey final model*****

suest B A, svy

**********Suest test for goodness of fit**********

**********Testing of Models**

test [B_Malaria_Diagnosed=A_Malaria_Diagnosed], common

**********Testing of Coeficients*******

test ([B_cut1]_cons=[A_cut2]_cons) ([B_cut2]_cons=[A_cut1]_cons)

A2.5: Direct model using GSEM

*sem (clus_altitude_meter -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (No_of_rooms -> Malaria_Diagnosed, famiy(ordinal) link(cloglog)) (Slept_under_Net -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (poor_ses -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (least_poor_ses -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (south_ref_Kigali -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (west_ref_Kigali -> Malaria_Diagnosed, family(ordinal)link(cloglog)) (north_ref_Kigali -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (east_ref_Kigali -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (Has_water_for_Handwash -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (water_missing -> Malaria_Diagnosed, family(ordinal) link(**cloglog)) (Health_Insurance -**alaria_Diagnosed, family(ordinal) link(cloglog)) (Education_in_Years -> Malaria_Diagnosed, family(ordinal) link(cloglog)) (Age_of_HH -> Malaria_Diagnosed, family(ordinal) link(cloglog)), nocapslatent*

estat eform

gsem, coeflegend

A2.6: Indirect model using GSEM

***\

nlcom

*_b[least_poor_ses:Education_in_Years]*_b[Malaria_Diagnosed:least_poor_ses]nlcom*

*_b[least_poor_ses:Education_in_Years]*_b[No_of_rooms:least_poor_ses]*_b[Malaria_D*

iagnosed:No_of_rooms]

*******Total Effect of least_poor_ses***********

nlcom

*_b[Health_Insurance:least_poor_ses]*_b[Malaria_Diagnosed:Health_Insurance]+_b[No_*

*of_rooms:least_poor_ses]*_b[Malaria_Diagnosed:No_of_rooms]+_b[Malaria_Diagnosed*

:least_poor_ses]

Appendix 3: Mathematical presentation of Rwanda survey adjusted random effect model

The model for Rwanda can be expressed with equations:

$$\log it\left(y_{ij}\right) = X_{ij}^{T}\beta + \phi_{ij} + \varepsilon_{ij}$$

Where Y_{ij} , i=1, 2, 3… nt. is the ordinal outcome of the ith participant from location j. ϕ_{ij} Contains the values of the cluster and household (structured) random effect, and ε_{ij} is the vector of the residuals non-random effect.

Appendix 3.1: Mathematical presentation of Rwanda direct, indirect and total effect

Mathematically direct, indirect and total effect presented as:

G-SEM can fit models of the form

$$Y = BY + \tau X + \alpha + \xi$$

Where $B = \left[\beta_{ij}\right]$ is the matrix of coefficients on endogenous variables predicting other endogenous variables, $r = \left[\gamma_{ij}\right]$ is the matrix of coefficient on exogenous variables, $\alpha = \left[\alpha_{i}\right]$ is the vector of intercepts for the endogenous variables, and $\left[\xi\right]$ is assumed to have mean 0 and

$$Cov\left(X, \xi\right) = 0$$

The direct effects are

$$E_{d} = \left[\hat{B} \quad \hat{\tau}\right]$$

And the indirect effects are

$$E_i = E_t - E_d .$$

The total effects are

$$E_t = \left[(I \quad \hat{B})^{-1} - I, \hat{\tau}(I - \hat{B})^{-1}\tau \right]$$

Appendix 4: Formulae for Odds Ratio Calculation and Conversion of ologit coefficients

Odds Ratio Calculation

The study utilized odds ratios which is the odds of an event occurring in one group to the odds of it occurring in another group (the other group usually termed the reference group).

$$\text{OR} = \frac{\text{odds of event occurring in one group}}{\text{odds of event occurring in another group}}$$

$$\text{P1}/1 - (\text{P1} \,/\, \text{P2})/1 - \text{P2}$$

$$((\text{P1}/1 - \text{P1}))/((\text{P2}/\text{P0})/1 - \text{P2})$$

$$\text{e\^{}}(\beta 0 + \beta 1\text{xi}/1+) = 1 + \text{e\^{}}\beta 0 + \beta 1\text{x1} \div /\text{e\^{}}\beta 0 \ + \beta 1\text{xi}/1 + \text{e\^{}}\beta 0 + \beta 1\text{xi}$$

Converting the ologit coefficient to an odds ratio

The structural equation modeling reported the ologit coefficients and we converted them to odds ratios for consistency in our reporting as follows:

Step 1. oLogit P(x1)= β0 + β1 xi

Step 2. $\text{oLog}[\frac{\text{P(x1)}}{1-\text{P(x1)}}] = \beta 0 + \beta 1$ xi

Step 3. $\text{oLog}[\frac{\text{P(xi)}}{1-\text{P(xi)}}] = \text{e}^{\beta 0+\beta 1\ \text{x1}\ldots\beta\text{nxn}}$

Where: xi= number of covariates in the fitted model

β0= intercept of the fitted model

βi= fitted model parameters

Appendix 5: Plagiarism form



Plagiarism declaration for written work: Master of Science in Epidemiology

I **Muhammad Abu Bakar** (Student number: **1139039** am a postgraduate student registered

for degree / Programme Masters in Epidemiology in the Wits School of Public Health.

I am submitting my written work for assessment for the module:

Research Report

I hereby declare the following:

- I am aware that plagiarism is the use of someone else's work without their permission and/or without acknowledging the original source).
- I am aware that plagiarism is wrong.

- I confirm that the work submitted for assessment for the above course is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a
  Belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature: M. Abu Bakar Date: January-16-2017

Appendix 6: Ethical approval certificate

R14/49 Mr Muhammad Abu Bakar

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M151040

NAME: (Principal Investigator)	Mr Muhammad Abu Bakar
DEPARTMENT:	Epidemiology and Biostatistic University of the Witwatersrand
PROJECT TITLE:	Determinants of Childhood Malaria Morbidity in Rwanda 2013: A Spartial Cross Sectional Survey Study
DATE CONSIDERED:	30/10/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Eustassius Musenge
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	23/11/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 7: Change of title of research certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

27 September 2016
Person No: 1139039
TAA

Mr M Abu Bakar
P. O Box 490
Wits
Johannesburg
RSA
2050
South Africa

Dear Mr Abu Bakar

Master of Science in Epidemiology: Change of title of research

I am pleased to inform you that the following change in the title of your Research Report for the degree of **Master of Science in Epidemiology** has been approved:

From:	**Determinants of childhood malaria morbidity in Rwanda 2013: a spatial cross sectional survey study**
To:	**Factors influencing Malaria morbidity in Rwanda 2010: a cross-sectional survey study using generalised structural equation modelling**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences