

https://dspace.org/

Determinants of malaria episodes in children under 5 in Malawi in 2012

Chitunhu, Simangaliso

2015-04-17
http://hdl.handle.net/10539/17442

Downloaded from a DSpace repository. https://dspace.org/



Determinants of malaria episodes in children under 5 in Malawi in 2012

By

Simangaliso Chitunhu

A Thesis Submitted to the Faculty of Health Sciences,

University of the Witwatersrand in partial fulfilment of

the requirements for the Degree of

Master of Science in Epidemiology

Major Area-Subject: Biostatistics and Epidemiology

November 2014

Declaration

I, Simangaliso Chitunhu declare that this research report is my own work.

It is being submitted for fulfillment of the requirements for the degree of Master of Science in Epidemiology major subject area: Epidemiology and Biostatistics at the University of the Witwatersrand, Johannesburg.

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

.....

S Chitunhu

19 November 2014

Dedication

I dedicate this thesis to my late parents who instilled in me the hunger for education as well as my husband and children for standing by me throughout this course, without your support I would not have made it.

Abstract

Background:

Malaria is a serious public health challenge in sub-Saharan Africa with children under five being the most vulnerable, and a child dies every 30 seconds from it. Therefore, it is important to investigate malaria's direct and indirect determinants in specific sub-Saharan populations as well as identifying malaria hotspots in order to have informed and targeted preventative interventions.

Rationale:

Given the extent and seriousness of malaria in Southern Africa, understanding fully the factors associated with malaria is important in successfully fighting it. Therefore, understanding the determinants of malaria in children under five is important in working towards eliminating malaria in sub-Saharan populations.

Objectives:

This study's objectives were:

- To describe demographic, behavioral and environmental determinants (factors) associated with malaria episodes in under fives in households in Malawi in the year 2012
- To investigate the determinants of malaria episodes in children under five years in Malawi in 2012
- To compare spatial distribution of malaria episodes in households in Malawi in 2012.

Methods:

This study was a secondary data analysis based on data from the Malawi 2012 Malaria Indicator Survey (MIS) obtained from Demographic and Health Survey (DHS) program website. The outcome variable was positive blood smear result for malaria in children less than five years, after an initial positive rapid malaria diagnostic test done at the homestead. We controlled for confounders after propensity score matching in order to reduce selection bias. Cases and controls were matched based on their propensity scores. Statistical modelling was done using logistic regression as well as generalized structural equation modeling (G-SEM) to model direct and indirect effects on the outcome. Poisson regression was done to determine associations between the outcome (positive blood smear malaria result) and selected explanatory variables at household level and we then introduced a structured and unstructured random effect to measure spatial effects if any of malaria morbidity in children under the age of five.

Results:

The matched data had 1 325 children with 367 (24.3%) having blood smear positive malaria. Female children made up approximately 53% of the total study participants. Child related variables (age, haemoglobin and position in household) as well as wealth index were significant (directly and indirectly) with p values <0.001. Socio-economic status (SES) [Odds ratio (OR) = 0.96, 95% Confidence interval (CI) = 0.92, 0.99] and primary level of education [OR = 0.50, 95%CI = 0.32, 0.77] were important determinants. The spatially structured effects accounted for more than 90% of random effects as these had a mean of 1.32 (95% Credible Interval (CI) =0.37, 2.50) whilst spatially unstructured had a mean of 0.10(CI=$9.0x10^{-4}$, 0.38). The spatially adjusted

significant variables on malaria morbidity were; type of place of residence (Urban or Rural) [posterior odds ratio (POR) =2.06; CI = 1.27, 3.34], not owning land [RR=1.77; CI= 1.19, 2.64], not staying in a slum [RR=0.52; CI= 0.33, 0.83] and enhanced vegetation index [RR=0.02; CI= 0.00, 1.08]. A trend was observed on usage of insecticide treated mosquito nets [POR=0.80; CI= 0.63, 1.03].

Conclusion:

Socio-economic status (directly and indirectly) and education are important factors that influence malaria control. The study showed malaria as a disease of poverty with significant results in slum, type of place of residence as well as ownership of land. It is important that these factors be taken into consideration when planning malaria control programs in order to have effective programs. Direct and indirect effect modelling can also provide an alternative modelling technique that incorporates indirect effects that might not be of significance when modeled directly. This will help in improving malaria control. Enhanced vegetation index was also an important factor in malaria morbidity but precipitation and temperature suitability index were not significant factors.

Definition of terms

Determinant – a determining or causal factor

Environmental determinants – factors found in the environment that influence malaria infection like temperature, vegetation or precipitation

Behavioural determinants – factors that can be attributed to behaviour of humans for example use of insecticide treated nets (ITNs)

Spatial determinants – factors that can be attributed to the location of affected individuals

Malaria episode – case of clinical malaria experienced by a child (yes/no –binary variable) or number of children in household (count variable) under the age of five as well as case of clinical malaria experienced in a household

Spatial analysis – Analytical technique that accounts for spatial variations due to unmeasured random effects

Structural equation modelling – Analytical technique using direct and indirect modelling to analyse the complex relationships between selected variables

Preface

This research report covers an important aspect in 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 as well as pregnant women are the most affected by malaria. The lack of resources both at national and household level makes fighting this disease difficult. This paper analyses the direct and indirect determinants of malaria as well as the structured and unstructured spatial effects of malaria in Malawi in 2012 in children less than five in order 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.

Acknowledgements

I would like to acknowledge and express my sincere gratitude to Dr. Eustasius Musenge my supervisor, for his guidance, tremendous assistance and indescribable patience with me during the writing of this research. I have not only greatly enhanced my statistical skills but also acquired greater knowledge for biostatistical analysis of which, I am deeply indebted to him. May God richly bless you.

I also would like to thank the division of Epidemiology and Biostatistics at the School of Public Health, the University of the Witwatersrand, all the lecturers as well as the course administrator for the support that they offered during this course in ensuring that everything ran smoothly during the course of this degree.

I would like to thank the Department of Science and Technology/National Research Foundation (DST/NRF) South African Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) for providing funding that made this research work possible.

I would also like to appreciate Ms Lucy Chimoyi for the invaluable assistance that she offered in preparing the choropleth maps that were used to visualize the spatial effects in this study.

I would also like to appreciate Dr. Thomas Achia for the assistance that he offered in Bayesian modelling that helped me greatly in my structured and unstructured models, the knowledge that you shared with me was quite invaluable.

My contributions in the thesis papers

My contributions as the first author in the thesis papers in chapters 2 to 3 were as follows:

- Chapter 2: Conceptualisation of research question based on main concept provided by supervisor, structuring of the paper, running the statistical analysis, writing of all drafts of the paper, addressing peer reviewers' and co-authors' comments. Fully responsible for registering with the journal and submitting the paper for review.
- Chapter 3: Conceptualisation of research question based on main concept provided by supervisor, structuring of the paper, running the statistical analysis, writing of all drafts of the paper, addressing peer reviewers' and co-authors' comments. Also intend to be fully responsible for registering with the journal and submitting the paper for review.
- I was also partly responsible for selection of the journals for submission of papers and was the corresponding author in all the articles.

Table of Contents

Declaration ..... **ii**

Dedication ..... **iii**

Abstract ..... **iv**

Definition of terms ..... **vii**

Preface ..... **viii**

Acknowledgements ..... **ix**

My contributions in the thesis papers ..... **x**

Table of Contents ..... **xi**

List of Figures ..... **xiii**

List of Tables ..... **xiv**

Abbreviations ..... **xv**

Chapter 1 Introduction **16**

1.1 Background Information *16*
1.2 Statement of the problem *17*
1.3 Justification of the study *18*
1.4 Literature review *19*
1.4.1 Malaria transmission and illness 19
1.4.2 Factors associated with malaria illness 20
1.5 Thesis framework *23*
1.6 Aim and specific objectives *26*
1.7 Ethical considerations *27*
1.8 Organisation of the research report *27*

Chapter 2 Determinants of Malaria Morbidity in Malawian Children under 5 ..... **28**

Abstract *29*
2.1 Introduction *31*
2.2 Materials and methods *33*
2.2.1 Study area 33
2.2.2 Malawi Malaria Indicator Survey Data 35
2.2.3 Statistical analysis methods 36
2.2.4 Ethics approval 37
2.3 Results *38*
2.4 Discussion and conclusion *46*
2.5 Acknowledgments *49*

Chapter 3 Spatially adjusted socio-demographic and environmental factors of household malaria morbidity in Malawi 51

Abstract *52*
3.1 Introduction *54*
3.2 Materials and Methods *56*
3.2.1 Study area 56
3.2.2 Malawi Malaria Indicator Survey Data 57
3.2.3 Statistical analysis methods 59
3.2.4 Ethics approval 65
3.3 Results *65*
3.4 Discussion and conclusion *72*
3.5 Acknowledgments *74*

Chapter 4 Discussion and conclusions 76

4.1 Behavioural determinants *76*
4.2 Environmental determinants *78*
4.3 Spatial hotspots *78*
4.4 Recommendations *79*
4.5 Conclusions *80*

References 83

5.0 Appendices: 110

Appendix 1: WinBUGS code 111

Appendix 2: BayesX code 113

Appendix3: INLA code 114

Appendix4: Run-times and number of iterations for the different methods used in analysis 116

Appendix 5: WinBUGS maps 117

Appendix6: Human Research Ethics Clearance Certificate 118

List of Figures

Figure 1-1: Map of Africa showing distribution of *Plasmodium falciparum* malaria in Africa (Malaria Atlas Project (MAP) 2010)(The Malaria Atlas Project, 2010)..... 16
Figure 1-2: Conceptual diagram illustrating the possible association between malaria episodes in households and behavioural, environmental and spatial factors 24
Figure 2-1: Map of Malawi showing districts as well as the major water bodies 34
Figure 2-2: Graph showing Propensity scores that were calculated to adjust for differences in use of mosquito bed nets amongst the study participants..... 36
Figure 2-3: G-SEM path diagram showing coefficients from binomial logistic regression analysis of the direct effects of selected random variables on a blood smear positive malaria result in children under five in Malawi in 2012. 43
Figure 2-4: G-SEM path diagram of selected random variables showing both direct and indirect pathways related to blood smear positive malaria results for children less than five years in Malawi in 2012. 44
Figure 3-1: Map of Malawi with the location of the 140 enumeration areas as well as well as the major water bodies. 58
Figure 3-2: Structured spatial effects on coefficients of blood smear positive malaria results showing both mean and median as well as 95% probabilities of malaria risk 70
Figure 3-3: Unstructured spatial effects on coefficients of blood smear positive malaria results showing both mean and median as well as 95% probabilities of malaria risk 71

List of Tables

Table 1-1: Thesis papers titles, status, comparative features and summary of key results. 25
Table 2-1: Descriptive statistics of the variables of interest (initial and propensity matched data)..... 39
Table 2-2: Univariate and multiple variable analyses results of unmatched data 40
Table 2-3: Propensity score matched univariate and multivariable results 42
Table 3-1: Comparative results between STATA, WINBUGS, R-INLA and BayesX for the Multiple variable Poisson regression analysis without the spatial random effect. 66
Table 3-2: Bayesian structured and unstructured spatial results. 67
Table 3-3: Posterior estimates of the convolution model 69

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
CAR	Conditional Autoregressive Model
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
DHS	Demographic and Health Survey
DIC	Deviance Information Criteria
EA	Enumeration Area
EVI	Enhanced Vegetation Index
GDP	Gross Domestic Product
GIS	Geographic information System
GLM	Generalised Linear model
GMRF	Gaussian Markov Random Field
G-SEM	Generalized Structural Equation Modelling
HIV	Human Immunodeficiency Virus
INLA	Integrated Nested Laplace Approximations
ITNs	Insecticide treated bed nets
MCMC	Markov Chain Monte Carlo
MDGs	Millennium Development Goals
MIS	Malaria Indicator Survey
MH	Metropolis-Hastings
MLE	Maximum Likelihood Estimation
OR	Odds ratio
PCI	Posterior Credibility Interval
POR	Posterior odds ratio
SEM	Structural equation modelling
SES	Socio- Economic Status
SSA	sub-Saharan Africa
TSI	Temperature Suitability Index
UN	United Nations
WinBUGS	Windows Bayesian inference using Gibbs Sampling
WHO	World Health Organisation

Chapter 1 Introduction

1.1 Background Information

The poorest countries of the world are the most affected by malaria (Mhalu, 2005), with most of these being in sub-Saharan Africa (Ricci, 2012). Nine out of every ten cases of malaria and malaria mortality take place in Africa (Dzinjalamala, 2009). This makes it one of the most important current global health challenges (World Health Organization). Figure 1-1 below is a map of Africa showing the countries where malaria is endemic. From the map, Malawi is in the intermediate risk range with malaria incidence higher than 5% but less than 40%.

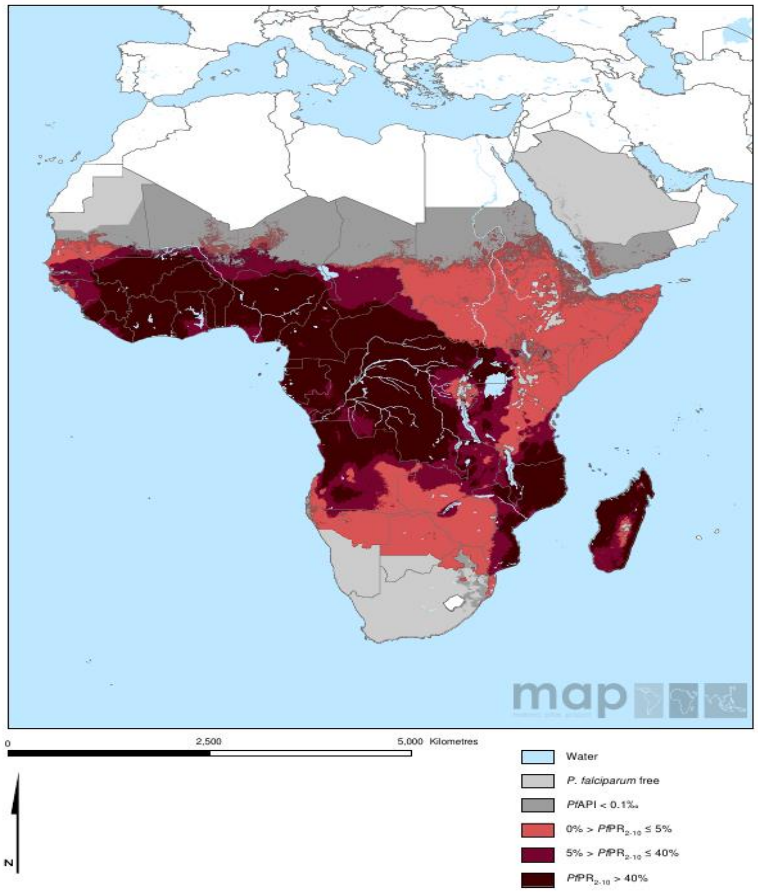


Figure 1-1: Map of Africa showing distribution of *Plasmodium falciparum* malaria in Africa (Malaria Atlas Project (MAP) 2010)(The Malaria Atlas Project, 2010)

2010 estimates as reported by the WHO of the global *Plasmodium falciparum* malaria illness burden showed that malaria deaths accounted for about 570 000 deaths in children under five and most were from Africa (World Health Organization).

Malaria is endemic throughout the country of Malawi and is a major public health problem in that country (Wilson et al., 2012). In the year 2010 in Malawi, malaria accounted for the third highest number of deaths (Institute for Health Metrics and Evaluation, 2012).
Climate factors including temperature, humidity, and rainfall are the main determinants of transmission (Connor et al., 2006). Other factors that also determine transmission include socio-economic status, knowledge on malaria prevention methods and access to treatment (Kiang et al., 2009). The extent and distribution of these factors influence the prevalence rate of malaria. Transmission is highest in areas that experience high temperature and frequent rainfall from October through to April (Bloland et al., 1999).

1.2 Statement of the problem

Malaria illness is a serious public health challenge in sub-Saharan Africa. This condition also seems to be associated with the socio-economic status (SES) of countries. Given the extent of malaria in southern Africa, a full understanding of the factors associated with malaria morbidity is important. This study will examine to what extent environmental, spatial and behavioural factors influence malaria episodes in households in children under five in Malawi in 2012 using the malaria indicator survey data. The study will also try to identify the malaria hotspots in Malawi

1.3 Justification of the study

Sub-Saharan Africa carries the highest burden of malaria with 86% of all global malaria cases being reported in sub-Saharan Africa in 2008 (Bloland et al., 1999). In Malawi, malaria is endemic in more than 95% of the country (Kazembe et al., 2006b). Malaria causes serious health problems in Malawi with the whole population at risk of contracting the disease (Ingstad et al., 2012). Malawians are among the poorest in Africa (World Bank Group, Wilson et al., 2012) with a per capita gross domestic product (GDP) of 388 US dollars for 2011 compared to South Africa's 8 090US dollars (United Nations) resulting in about 65% of the population being unable to meet their daily food requirements (Palmer, 2006). Eighty percent of the people live in rural areas, with about 74% living below the poverty datum line (United Nations Development Programme, 2011). Over half the 15 million population depends on smallholder agriculture for sustenance (Cromwell and Kyegombe, 2005, Palmer, 2006). In 2011 according to WHO, Malawi experienced 5 338 701 episodes of malaria (World Health Organization, 2012). This puts pressure on its management of health-care resources as the GDP is not adequate to cover sufficiently and effectively its health problems. The presence of water bodies is an important factor in the transmission of malaria. Lake Malawi covers almost the whole length of Malawi and is an important source of income and food for many families through fishing (Ingstad et al., 2012) as well as an important transport route and this puts the people living along the lake under high risk (Bennett et al., 2013, Okiro et al., 2014).

Malaria is endemic throughout Malawi but areas close to Lake Malawi and the low lying areas which are to the south of Lake Malawi and along the Shire valley are most affected (Dzinjalamala, 2009). Children under five constitute about 50% of the total suspected malaria

cases and nearly 60% of all hospital deaths in children under five are as a result of malaria and anemia (Connor et al., 2006). Understanding the determinants of malaria in children under five is also important in working towards achieving millennium development goal 4 which states "reduce child mortality" (Net ODA, 2011).

There is need to fully understand the determinants of malaria in order to reduce the burden that malaria puts on the health care system as well as the economic system. Being endemic in sub-Saharan Africa, there is need for adequate information about malaria for effective health policies to be put in place. Policies that the poor countries and communities can afford are vital as they will be easy to implement, compared to policies that require the intervention of donors.

Studies carried out previously show that the environment (temperature, humidity and rainfall) is also an important driver of malaria (Kazembe et al., 2006a, Snow et al., 1999).

Determining the spatial distribution of malaria is also important in ensuring that areas with high incidence are prioritized in the distribution of resources as well as in malaria prevention programs.

Therefore, this study seeks to determine the environmental, spatial and behavioural determinants of malaria episodes in children less than five years in households in the country of Malawi in 2012 using malaria indicator survey (MIS) data that is accessible from the measure Demographic and Health Survey (DHS) website.

1.4 Literature review

1.4.1 Malaria transmission and illness

Malaria is caused by four species of parasites of the genus Plasmodium that affect humans (*P. falciparum, P. vivax, P. ovale*, and *P. malariae*). Malaria is mainly found in tropical

areas(Mendis and Carter, 1995). Malaria due to *P. falciparum* is the most dangerous form and it is mainly found in Africa; *P. vivax* is less dangerous but more widespread, and the other two species are found much less frequently (World Health Organization). *P. falciparum* is responsible for almost all the malaria mortality cases in Sub-Saharan Africa and it is often stated that the continent bears over 90 percent of the global *P. falciparum* burden (Snow and Omumbo, 2006). Malaria infection is caused by mosquito bites and manifests itself in different ways. Severe malaria can result in severe anaemia, respiratory distress in relation to metabolic acidosis, or cerebral malaria. In adults, multi-organ involvement is also frequent. Immunity may develop in malaria endemic areas, resulting in mild infections to occur, particularly in adults. No clinical syndrome is entirely specific for malaria (Ayeni, 2011, World Health Organisation, 2011).

1.4.2 Factors associated with malaria illness

Malaria transmission is controlled by environmental factors which affect the intensity of distribution, seasonality and transmission (Snow and Omumbo, 2006). Malaria thrives in conditions that promote the growth of the vector of malaria which is the mosquito. Studies have shown that a dirty environment can result in increased malaria transmission (Cibulskis et al., 2011). Other factors are temperature, humidity, rainfall, forest clearance, agriculture and non-availability of insecticide treated mosquito nets (Cibulskis et al., 2011, Reiter, 2001), rainfall leaves pools of stagnant water that are good breeding for mosquitoes, clearing of forests results in light being able to penetrate into the forest and therefore providing ideal breeding for mosquitoes and in Malawi, firewood is the main source of fuel (Jumbe and Angelsen, 2011, Mapira and Munthali, 2011). This leads to the destruction of forests and thereby promoting mosquito breeding. Agricultural methods that involve irrigation as well as the building of dams also promote the breeding of mosquitoes therefore these results in increased malaria transmission (Reiter, 2001, Cibulskis et al., 2011). All these factors

promote malaria illness as these result in increased chances of a person being bitten by mosquitoes.

Another study suggested that temperature, rainfall and humidity cannot be looked at in isolation but there is need to also investigate the behavior of humans (Reiter, 2008). Human behaviour seems to play a role in making sure that the ideal conditions for mosquito breeding are met therefore there is need to control for human behaviour in order to ensure that malaria illness is adequately controlled.

Socio-economic status (SES), immunization, knowledge, humidity and temperature and general under nutrition also play a role in increasing malaria illness and mortality. Nutrition is linked to economic status if one is economically sound then they are able to provide adequately for themselves and therefore resulting in a well-nourished body. A well-nourished body is immune competent to fight off malaria infection by mounting an adequate response to infection as compared to an immune vulnerable undernourished body (Caulfield et al., 2004). Malaria severely affects nutrition by limiting food intake through lack of appetite and vomiting; Nutritional status also affects responses to anti-malarial medication (Hess et al., 1997) resulting in drug resistance. Approximately 67% of anaemia cases in children in malaria-endemic countries are thought to be the result of malaria (Bates et al., 2004a). Health status is also linked to economic status and malaria is also affected by the economic status of an individual as well as country (Stratton et al., 2008). A poor economic status results in inadequate health care facilities and therefore increasing vulnerability of the population to malaria. A review of literature on SES and malaria showed that malaria and low SES were interlinked (Worrall et al., 2005).

Age and gender are the other important factors that are also associated with malaria illness with the majority of malaria illness and deaths occurring in children under the age of five. Studies carried out in Gabon and Tanzania showed that children over the age of five were most at risk in the transmission of malaria (Mawili-Mboumba et al., 2013, Winskill et al., 2011). In the Tanzania study, males were more at risk of malaria illness compared to females (Winskill et al., 2011). A study carried out in rural Nigeria did not show any difference between the sexes but showed that prevalence of malaria was highest in 11 to 20 years age group (Kalu et al., 2012). Another study carried out in Kenya showed that parasitaemia decreased with age with children in the 1-4 year age group having the highest prevalence at 83% and decreasing to 60% in the 10-14 year age group (O'Meara et al., 2008). In Malawi it has been shown that children under five carry the heaviest burden of malaria (Dzinjalamala, 2009), this is because their immune system is not yet fully developed.

Studies also suggest that location also plays an important role in malaria transmission. In one study carried out in Ethiopia, clustering or hot spots of malaria were revealed (Yeshiwondim et al., 2009). Another study carried out in Ghana showed that distance from a water body plays an important role in malaria prevalence (Prosper and Duker, 2012). A review of literature on factors that influence vulnerability to malaria showed that malaria is climate sensitive (Bates et al., 2004b). Altitude is also another factor that has been shown to be important in malaria transmission, with low lying areas being at a higher risk compared to higher altitude areas (Abeku et al., 2003, Okello et al., 2006, Drakeley et al., 2005b, Kazembe, 2007, Alegana et al., 2014).This shows that spatiality is an important aspect in malaria transmission.

1.5 Thesis framework

Based on the conceptual framework shown below, three themes that concern public health policy and interventions have been extracted:

- Determinants of malaria morbidity in children under five years of age.
- Direct and indirect determinants of malaria morbidity in children under five years of age.
- Structured and unstructured spatial modelling of malaria morbidity in resource limited settings.

Figure 1-2 below shows the conceptual diagram of the possible associations between malaria and the different determinants of malaria morbidity.

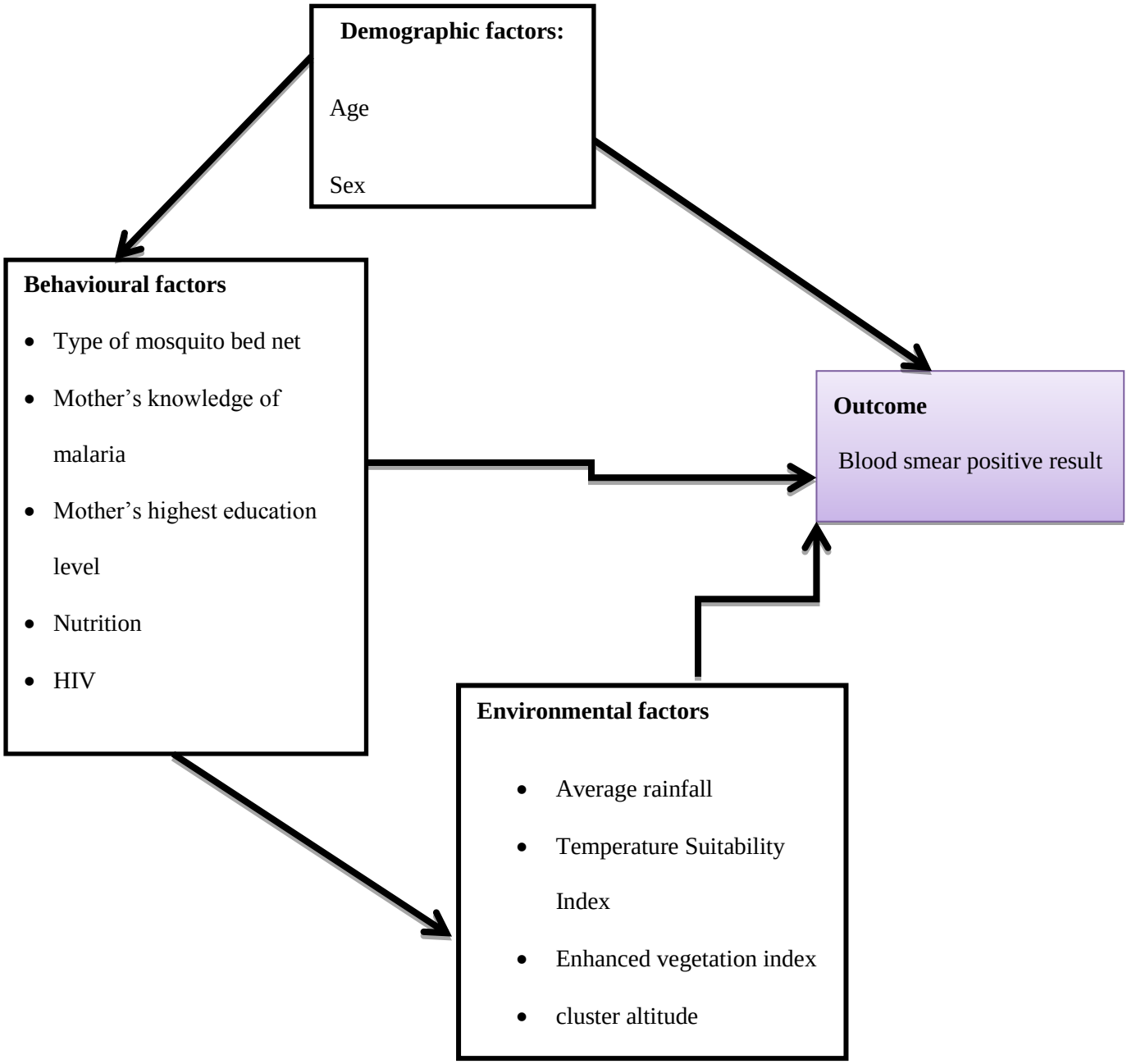


Figure 1-2: Conceptual diagram illustrating the possible association between malaria episodes in households and behavioural, environmental and spatial factors

Table 1.1 below shows detail on how the themes link up with the papers and the fields of Epidemiology and Biostatistics.

Table 1-1: Thesis papers titles, status, comparative features and summary of key results.

Paper	Title, type and status	Key comparative features of papers: Design, sample-size, outcome and explanatory variables	Analyses methods used and duration of computing	Key result findings
1	- Direct and indirect determinants of childhood (0 to under 5 years) malaria morbidity in Malawi using Malaria indicator survey data for 2012 - Application **Submitted to Malaria Journal.**	Cross-sectional, propensity score matched data had 1 325 children. The outcome was a positive laboratory blood smear result for malaria. Behavioural determinants were explanatory variables	Statistical modelling using logistic regression as well as generalized structural equation modeling (G-SEM) (took 3 days computing duration)	The matched data had 1 325 children with 367 (24.3%) having blood smear positive malaria. Child related variables (age, haemoglobin and position in household) as well as wealth index were significant (directly and indirectly)
2	- Spatial and socio-economic effects on malaria morbidity in children under 5 years in Malawi in 2012 -Application and Methodology **Journal to be advised.**	Cross-sectional, 1 900 households from 140 clusters, outcome number of confirmed malaria cases per household	Structured and unstructured random effects of malaria morbidity. Inference done using Bayesian MCMC for spatial models (took 7days computing duration).	1878 households in 140 clusters. The spatially structured effects accounted for more than 90% of random effects.

1.6 Aim and specific objectives

The aim of the study was to describe and analyse environmental, spatial and behavioural determinants of malaria episodes in children less than five years in households in the Malawian population in 2012.

	Specific objectives	Paper
1.	To describe demographic, behavioural and environmental factors associated with malaria episodes in children less than five years in households in Malawi in the year 2012	➡ **Paper 1**: Direct and indirect determinants of childhood (0 to under 5 years) malaria morbidity in Malawi using Malaria indicator survey data for 2012
2.	To investigate the determinants of malaria episodes in children under five years in Malawi in 2012.	➡ **Paper 1**: Direct and indirect determinants of childhood (0 to under 5 years) malaria morbidity in Malawi using Malaria indicator survey data for 2012
3.	To investigate and compare spatial distribution of malaria episodes in households in Malawi in 2012.	➡ **Paper 2** : Spatial and socio-economic effects on malaria morbidity in children under 5 years in Malawi in 2012

1.7 Ethical considerations

This study was granted ethics approval by the University of the Witwatersrand's Human Research Ethics Committee (Medical) (Clearance Certificate No. M130962). Approval to use the MIS data was obtained from the measure DHS website. The primary study, where the data was collected, verbal informed consent for testing of children was obtained from the child's parent or guardian at the end of the household interview. The survey was also anonymised so that household or individual information is not identifiable(Ministry of Health et al., 2012) .

1.8 Organisation of the research report

The rest of the research paper is organized as follows:

- In chapter 2 we present the paper on direct and indirect determinants of malaria morbidity in children under five in Malawi in the year 2012.
- In Chapter 3 we present the paper on the effect of unstructured and structured spatial random effects on socio-demographic as well as environmental factors on malaria morbidity in children under five in Malawian households in the year 2012
- In Chapter 4 we present the discussion, conclusions and recommendations from this study
- Appendices show the code used for analysis, the run-times, WinBUGS maps and copy of the Human research ethics clearance certificate

Chapter 2 Determinants of Malaria Morbidity in Malawian Children under 5

2.0: Direct and indirect determinants of childhood (0 to under 5 years) malaria morbidity in Malawi using Malaria indicator survey data for 2012

Simangaliso Chitunhu, Eustasius Musenge

Biostatistics and Epidemiology Division, School of Public Health, Faculty of Health Sciences,

University of the Witwatersrand, Johannesburg, South Africa

This paper has been submitted to Malaria journal and is currently under review.

Abstract

Introduction

Children under the age of five are most vulnerable to malaria (malaria is a major health challenge in sub-Saharan Africa) with a child dying every 30 seconds from malaria. Hampered socio-economic development, poverty, diseconomies of scale, marginalization, and exploitation are associated with malaria. Therefore establishing determinants of malaria in affected sub-Saharan populations is important in order to come up with informed interventions that will be effective in malaria control, our study focuses on Malawi.

Materials and methods

The study was a secondary data analysis of survey data from the Malawi 2012 Malaria indicator Survey obtained from Demographic and Health Survey (DHS) program website. The outcome variable was positive laboratory based blood smear result for malaria in children less than five years, after an initial positive rapid malaria diagnostic test done at the homestead. We controlled for socio-demographic determinants, confounders after propensity score matching to reduce selection bias. Statistical modelling was done using survey logistic regression as well as generalized structural equation modeling (G-SEM) to analyse direct and indirect effects of malaria morbidity.

Results

The propensity score matched data had 1325 children with 367 (24.3%) having blood smear positive malaria. Female children made up approximately 53% of the total study participants. Child related variables (age, haemoglobin and position in household) and household wealth

index were significant directly and indirectly. Further on G-SEM based multivariable analysis showed socio-economic status (SES) [Odds ratio (OR) = 0.96, 95% Confidence interval (CI) = 0.92, 0.99] and primary level of education [OR = 0.50, 95%CI = 0.32, 0.77] were important direct and indirect determinants of malaria morbidity.

Discussion and conclusion

Socio-economic status (directly and indirectly) and education are important factors that influence malaria control. Effective malaria control programs must consider these factors in coming up with control strategies. Direct and indirect effect modelling can also provide an alternative modelling technique that incorporates indirect effects that might not be of significance when modelled directly. This holistic approach is useful in improving malaria control.

Key words

Childhood malaria, Direct determinant, Indirect determinant, Propensity score matching, Structural equation modelling

2.1 Introduction

Malaria causes illness and death mainly in the poorest countries of the world (Mhalu, 2005). Most poor countries in sub-Saharan Africa are affected, with nine out ten cases of the global malaria morbidity (Dzinjalamala, 2009). This makes it one of the most important global health problems (World Health Organization). Malaria is a serious problem in developing countries and this is acknowledged by United Nations (UN) as the millennium development goal 6 aims to "Combat HIV/AIDS, malaria and other diseases" and millennium development goal 4 targets to "reduce child mortality" (World Health Organization) . Addressing the challenge of malaria in developing countries will significantly address these two millennium development goals. In areas that are malaria endemic, children less than five years of age are the most vulnerable to malaria infection, the World Health Organisation (WHO) records that every 30 seconds a child in this age group dies of malaria (World Health Organization). A report on the global impact of malaria produced by the Centers for Disease Control (CDC) and prevention stated that children under the age of five accounted for 86% of all the malaria deaths reported in 2010 (CDC). More than 3 billion people live in malaria endemic areas and the disease causes between 1 million and 3 million deaths each year (Herrero et al., 2007, Snow et al., 2003b) with approximately 80% of cases and 90% of deaths estimated to occur in the sub-Saharan Africa (Breman et al., 2004).

Malaria is endemic and a major public health problem to Malawi, a low income country that is in sub-Saharan Africa (Dzinjalamala, 2009, Lowe et al., 2013). It is estimated that Malawi experiences about 6 million episodes of malaria annually (Snow et al., 2003b). In the year 2010, malaria accounted for the third highest number of deaths in the country (Institute for Health

Metrics and Evaluation, 2012). In 2011 according to WHO, Malawi experienced 5 338 701 episodes of malaria (World Health Organization, 2012).

Malaria is caused by Plasmodium parasites (*P. falciparum, P. vivax, P. ovale,* and *P. malariae*) (Breman, 2001). It is transmitted through the bite of a plasmodium carrying anopheles mosquito (Snow and Omumbo, 2006). Transmission is mainly determined by climatic factors: temperature, humidity, and rainfall (Patz and Olson, 2006). Other factors that also determine transmission include socio-economic status, knowledge on malaria prevention methods as well as access to health services (Somi et al., 2007). The extent and distribution of these factors influence the prevalence rate. Transmission is highest in areas of high temperature and frequent rainfall from October through April (Price et al., 2001).

Malaria is a disease and cause of poverty and has determinants of vulnerability (Snow et al., 2003b), because poor communities cannot afford malaria prevention and treatment tools as well as housing that is protective from mosquitoes (The Global Poverty Project). According to a report on the epidemiological profile of malaria and its control in Malawi (Okiro et al., 2014), the country is low-income and is amongst one of the poorest nations of the world. Poverty levels are extremely high with about 65% of the population being classified as poor (Word Bank, 2013).In 2012, Malawi was classified as one of the ten poorest countries in the world (Heilig, 2012). Also urbanisation is very low in Malawi (Okiro et al., 2014).Therefore, there is need to fully understand the determinants of malaria in order to reduce the burden that malaria puts on the health care system due to the poverty levels. Identifying direct and indirect determinants of malaria in a low income malaria endemic country will assist in the identification of important

determinants of the disease and this will help in the development of health programs that target those determinants in order to effectively reduce the burden of malaria with the available resources and also inform health policy (Guerra et al., 2008). Policies that the poor countries can afford are important as they may be easier to implement (Feachem et al., 2010).

The aim of this paper is to investigate the direct and indirect determinants of malaria morbidity in the under 5 year olds using pathway analysis using data from Malawi malaria indicator survey collected in 2012. This age group was selected as it is the most vulnerable age group to malaria in malaria endemic areas (World Health Organization).

2.2 Materials and methods

2.2.1 Study area

Malawi (figure 2-1) is a country in southern Africa that has an area of approximately 120 000km^2 and is bordered by Zambia to the west, Mozambique to the south and Tanzania to the north of the country (Lowe et al., 2013). The presence of many water bodies especially on the eastern side makes the nation vulnerable to malaria morbidity and mortality.

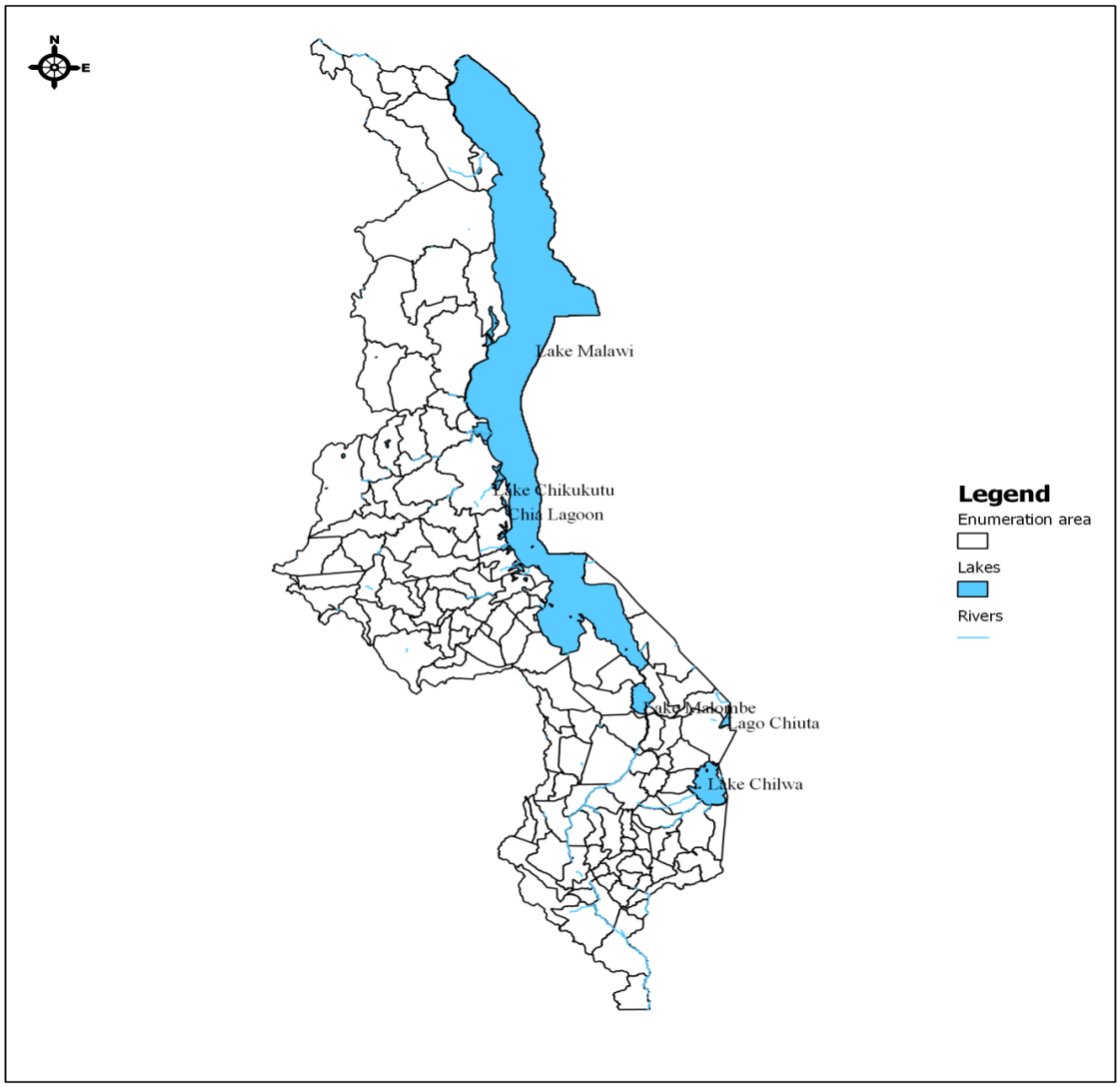


Figure 2-1: Map of Malawi showing districts as well as the major water bodies

2.2.2 Malawi Malaria Indicator Survey Data

The malaria data used in this study were obtained from the 2012 malaria indicator survey (MIS) and were obtained from the Demographic and Health Survey (DHS) program website. The original study collected data on basic demographic and health indicators, malaria prevention, treatment and morbidity. A total of 3,500 households were selected for data collection. A two stage cluster sampling technique was used to select the households. The first stage selected 140 enumeration areas (EAs) with 96 from rural areas and 44 from urban areas. At the second stage, 25 households per EA were selected. The data were obtained through use of a household questionnaire that collected housing characteristics, and identified all household members and their basic characteristics. Data for children less than five were collected from their mothers. Population sampling adjustments weights were done for the 140 clusters (EAs) to account for differences due to the unequal proportions selected per cluster (Ministry of Health et al., 2012, Lowe et al., 2013). Malaria morbidity on children under five at the households was tested using a rapid malaria diagnostic test and those who tested positive had their blood collected for a confirmatory blood smear laboratory test (Ministry of Health et al., 2012). A positive blood smear laboratory test was used as the main outcome variable in our data analysis. The variables used were region, type of place of residence, cluster altitude, wealth index of household, position of child in the family, child's age in month, use of mosquito bed net the previous night before the study, mother's knowledge of malaria, mother's level of education, child's altitude adjusted haemoglobin level and time to get to the source of water. The sample size was determined during the primary study; we established that data we used had a greater than 80% power.

2.2.3 Statistical analysis methods

Since the data were observational, we adjusted for selection bias using propensity score matching on some unbalanced selected variables (Austin, 2011, Sarna et al., 2013). Matching cases and controls helps to balance known confounders (Peikes et al., 2008, Caliendo and Kopeinig, 2008). Caliper matching was used to match the data. As a proxy for use of preventative methods in malaria control, we utilized the variable on use of mosquito bed net the previous night by children under five. This was then used as the treatment variable and propensity scores were extracted post multivariable logistic regression. Figure 2-2 shows the propensity scores that were calculated to adjust for differences in use of mosquito bed nets amongst the study participants. (Rubin and Thomas, 1996).

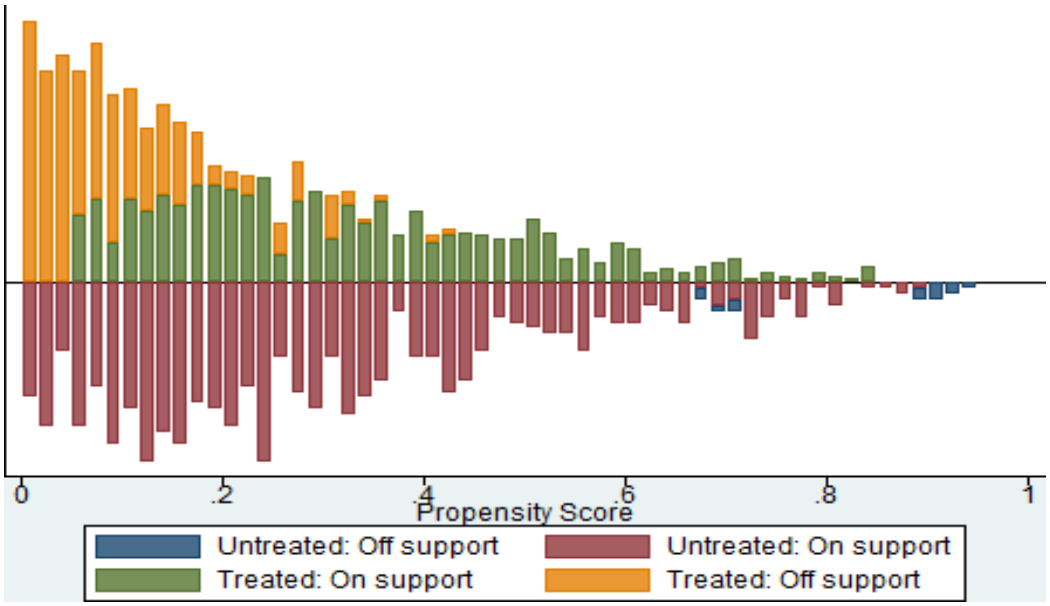


Figure 2-2: Graph showing Propensity scores that were calculated to adjust for differences in use of mosquito bed nets amongst the study participants

Survey adjusted bi-variate analyses, namely Pearson's Chi-Square and Student's t-test were carried out. Variables that were selected for multivariable analysis were based on their significant association with the outcome variable. Smear positive malaria result was modeled using survey logistic regression in order to determine the associations between the independent variables that were selected for analysis. Clustered robust method was used in analysing the data and the cluster was the primary sampling unit also used as the weighting variable. Generalized structural equation modelling (G-SEM) was used to model the direct and indirect pathways (Ullman and Bentler, 2003). This direct and an indirect model was developed to analyse the complex relationships between selected variables and the pathways that the authors conceptualized as having had an impact on a child having malaria in a household in 2012. All statistical analyses for this paper were carried out using Stata®13.1 (Copyright 1985-2013, StataCorp LP).

2.2.4 Ethics approval

This study was granted ethics approval by the University of the Witwatersrand's Human Research Ethics Committee (Medical) (Clearance Certificate No. M130962). Approval to use the MIS data was obtained from the measure DHS website. The primary study, where the data was collected, verbal informed consent for testing of children was obtained from the child's parent or guardian at the end of the household interview. The survey was also anonymised so that household or individual information is not identifiable(Ministry of Health et al., 2012) .

2.3 Results

The total number of children who were used in the study was 1 898 and their ages ranged from 6 months to 59 months with a mean age of 32.06 months. This was the number of children who were tested for malaria using a laboratory based test, of whom 468 (24.7%) had a positive result for malaria and 1 430 (75.3%) had a negative result for malaria. The Central Province had 53.3% of the total cases; the Southern Province had 37.4% and the Northern Province had 9.3% of total cases. There were less children [522 (27.1%)] from urban areas compared with children from the rural areas [1 376(72.9%)]. Female children made up approximately 53% of the total study participants. Most of the mother's in this study had no education (71.7%) but 55.4% of the mothers were able to read whole sentences.

In the matched data, a total of 1 392 children were analysed with 367 (27.7%) having blood smear positive malaria and 1 025 (72.3%) having no malaria. Table 2-1 shows the descriptive statistics for both matched and unmatched data that were selected for analysis looking at the association between the selected variable and positive blood smear for malaria. An association was considered significant if it had a p-value of less than 0.05.

Table 2-1: Descriptive statistics of the variables of interest (initial and propensity matched data)

Independent variables		**Unmatched data**			**Propensity score matched data**		
Variable	**Category**	**Blood smear positive** (n = 468(24.7%))	**Blood smear negative** (n = 1430 (74.9%))	**test statistic (p-value[a])**	**Blood smear positive** [n =367 (24.3%)]	**Blood smear negative** [n = 958 (75.7%)]	**test statistic (p-value)**
***Child's age in months**	mean ± SE	34.79±0.56	31.25±0.40	t = -5.08 (<0.001)	34.7±0.64	31.7±0.52	t=-3.60 (<0.001)
Position of child in household	1 2 3	290 (54.1%) 168 (32.6%) 66 (13.3%)	1103 (68.0%) 311 (20.2%) 174 (11.8%)	χ^2 = 11.17 (<0.01)	224(59.8%) 135 (38.1%) 8 (2.1%)	723 (74.3%) 217 (24.0%) 18 (1.7%)	χ^2 = 7.20 (<0.001)
Child's altitude adjusted haemoglobin level	mean ± SE	9.2±0.96	10.4±0.56	t = 11.90 (<0.01)	9.2±0.91	10.3±0.63	t=10.7 (<0.001)
***Children under 5 slept under mosquito bed net last night**	No Yes	204 (41.3%) 262 (58.7%)	488 (34.1%) 938 (65.9%)	χ^2 = 1.89 (0.15)	184 (47.4%) 183 (52.6%)	481 (48.8%) 477 (51.2%)	χ^2 = 0.36 (0.691)
***Region**	Northern Central Southern	60 (9.3%) 234 (53.3%) 174 (37.4%)	266(15.4%) 525 (38.0%) 639 (46.6%)	χ^2 = 3.64 (0.01)	47 (9.6%) 181 (51.4%) 139 (39.0%)	176 (15.4%) 348 (36.6%) 434 (48.1%)	χ^2 = 3.27 (0.015)
Type of place of residence	Urban Rural	54(5.0%) 414(95.0%)	468(16.4%) 962(83.6%)	χ^2 = 9.82 (<0.01)	48(5.9%) 319 (94.1%)	278(14.3%) 680(85.7%)	χ^2 = 5.96 (0.003)
Cluster altitude (kilometres)	mean ± SE	0.90 ±0.03	0.89±0.03	t = -0.49 (0.623)	0.90 ± 0.03	0.88 ± 0.03	t = -0.43 (0.667)
***Mother's highest education level**	None Primary Secondary	415 (88.9%) 47 (9.9%) 6 (1.2%)	949 (73.1%) 361 (21.5%) 120 (5.4%)	χ^2 = 7.30 (<0.01)	329 (89.6%) 34 (9.3%) 4 (1.1%)	700 (78.8%) 221 (18.9%) 37 (2.3%)	χ^2 = 3.54 (0.012)
Mother has heard of malaria	No Yes	47(10.5%) 421(89.5%)	62(4.9%) 1368(95.1%)	χ^2 = 4.27 (0.02)	38(11.0%) 329(89.0%)	50(5.9%) 908(94.1%)	χ^2 = 3.09 (0.048)
***Wealth index score**	mean ± SE	-5.58 ± 0.25	-2.47 ±0.32	t = 8.05 (<0.01)	-5.68 ± 0.35	-3.56 ± 0.36	t = 6.41 (<0.001)
***Time in hours to get to water source**	Mean ± SE	5.23 ±0.52	6.63 ±0.47	t = 2.71 (<0.01)	5.05 ± 0.55	6.18 ± 0.49	t = 1.92 (0.057)

*variables that were used in propensity score matching [a] significance was calculated at 5%

SE (standard error)

Univariate and multiple variable analyses were done to establish the relationships between blood smear positive malaria and selected variables and how they influence blood smear positive malaria in children under 5 years old. The results are shown in table 2-2.

Table 2-2: Univariate and multiple variable analyses results of unmatched data

	Univariate analysis	**Multivariable analysis**
Variable	**Odds ratio(95% CI), p-value**	**Odds ratio(95% CI), p-value**
Child's age in months	1.02(1.00, 1.02) ,<0.01	1.03(1.02, 1.04) ,<0.01
[!]**Child's position in household**		
1	1.00	1.00
2	2.03(1.59, 2.60), <0.01	1.43(1.04, 1.96), 0.03
3	1.46(1.08, 1.99), 0.02	0.99(0.40, 2.45), 0.98
Child slept under mosquito bed net		
No		
Yes	1.00	1.00
	0.74(0.54, 1.03), 0.07	0.77(0.60, 0.99), 0.04
Child's haemoglobin level	0.95(0.95, 0.96), <0.01	0.95(0.94, 0.96), <0.01
Region		
Northern	1.00	1.00
Central	2.43(1.24, 4.74), 0.01	1.79(1.24, 2.59), <0.01
Southern	1.36(0.69, 2.68) ,0.89	0.89(0.58, 1.39), 0.62
Type of place of residence		
Urban	1.00	1.00
Rural	3.87(2.22, 6.73),<0.01	1.83(1.18, 2.83), <0.01
Cluster altitude in kilometres	1.11(0.63, 1.96), 0.73	0.72(0.45, 1.12), 0.15
Mother's highest education level		
None		
Primary	1.00	1.00
Secondary	0.40(0.28, 0.57) ,<0.01	0.53(0.37, 0.76), <0.01
	0.18(0.08, 0.42), <0.01	0.57(0.23, 1.47), 0.25
Wealth index score	0.90(0.87, 0.94) ,<0.01	0.95(0.93, 0.98), <0.01
Time to water source	0.98(0.96, 1.00), 0.01	0.97(0.96, 0.99), <0.01

* The indirect effect of cluster altitude on malaria was calculated by multiplying the OR of altitude on region and OR of region on smear and adding this to the product of OR of altitude on type of place of residence and OR of type of place of residence on smear

[!] The position of child is for births in the last five years

Table 2-2 shows results of the univariate survey logistic regression, multiple variable survey logistic regression as well as the results of the G-SEM. The table 2-3 below shows the results of the propensity score matched results of the same data.

These results from logistic regression model as well as the generalized structural equation modelling show that socio-economic status (SES) represented by wealth index; region, time to water source, mother's highest level of education, child haemoglobin level (OR= 0.95 CI = 0.94, 0.96) as well as child's age were important determinants of malaria episodes in children aged between 6 and 59 months in Malawi in the year 2012. Of these, SES, child's age, rural residents, central region residents and child's haemoglobin level had p values less than 0.01. Age also showed (OR = 1.03 CI = 1.02, 1.04) that positive blood smear malaria increased with increasing age and the analysis on the position of the child showed that a child in the second position was almost one and half times likely (OR = 1.43 CI = 1.04, 1.96) as a child in first position to get malaria. Time to water source was also significant in this study (OR = 0.97 CI = 0.96 - 0.99).Table 2-3 shows the matched results of both univariate and multiple variable analysis.

Table 2-3: Propensity score matched univariate and multivariable results

	Univariate analysis	Multivariable analysis	G-SEM direct effects	G-SEM indirect effects
Variable Category	**Odds ratio(95% CI), p-value**	**Odds ratio(95% CI), p-value**	**Odds ratio(95% CI), p-value**	**Odds ratio(95% CI), p-value**
Child's age in months	1.01(1.01, 1.02), <0.01	1.03(1.02, 1.04) ,<0.01	1.03(1.02, 1.04), <0.01	
Position of child in household				
1	1.00	1.00	1.00	
2	1.91(1.39, 2.63), <0.01	1.49(1.05, 2.10), 0.02	1.49(1.04, 2.14), 0.03	1.03(1.01, 1.05), <0.01
3	1.73 (0.73, 4.09), 0.21	1.12(0.41, 3.08), 0.82	1.12(0.42, 2.99), 0.82	
Child's altitude adjusted haemoglobin level	0.95(0.94, 0.96), <0.01	0.94(0.93, 0.95), <0.01	0.94(0.93, 0.95), <0.01	
Children slept under mosquito bed net				
No	1.00	1.00	1.00	
Yes	1.07(0.77, 1.50), 0.69	0.77(0.58, 1.01), 0.06	0.77(0.56, 1.04), 0.09	
Region				
Northern	1.00	1.00	1.00	
Central	2.33(1.22, 4.48), 0.01	1.92(1.26, 2.92), <0.01	1.92(1.03, 3.55), 0.04	
Southern	1.32(0.69, 2.56), 0.394	0.96(0.58, 1.59), 0.88	0.96(0.48, 1.91), 0.91	
Type of place of residence				
Urban	1.00	1.00	1.00	
Rural	2.74(1.55, 4.88), <0.01	1.58(0.97, 2.56), 0.07	1.58(0.84, 2.94), 0.15	
Cluster altitude in kilometres	1.11 (0.59, 2.06), 0.75	0.75(0.44, 1.29), 0.30	0.75(0.31, 1.84), 0.53	1.24(0.87, 1.62), <0.01
Mother's highest education level				
None	1.00	1.00	1.00	
Primary	0.45 (0.31, 0.66), <0.01	0.50(0.32, 0.77), <0.01	0.50(0.32, 0.76), <0.01	0.50(0.28, 0.71), <0.01
Secondary	0.40 (0.14, 1.19), 0.10	0.71(0.20, 2.52), 0.60	0.71(0.19, 2.71), 0.62	
Wealth index score	0.91(0.88, 0.95), <0.01	0.96(0.92, 0.99), 0.01	0.96(0.92, 0.99), 0.01	
Time to get to water source	0.98 (0.96, 1.00), 0.07	0.97 (0.95, 0.99) ,<0.01	0.97 (0.95, 0.99) ,<0.01	

Table 2-3 shows that type of place of residence (urban or rural) has a significant effect on childhood malaria. Those who stay in the rural areas were more likely to have a positive blood smear result for malaria as compared to their counterparts in the urban areas (OR = 1.83 CI = 1.18, 2.83). Region of residence was also an important factor in this study (p = <0.01). The

central region of Malawi was the most affected with a 79% greater odds of malaria morbidity compared to the northern and southern regions (1.79(CI = 1.24, 2.59)).

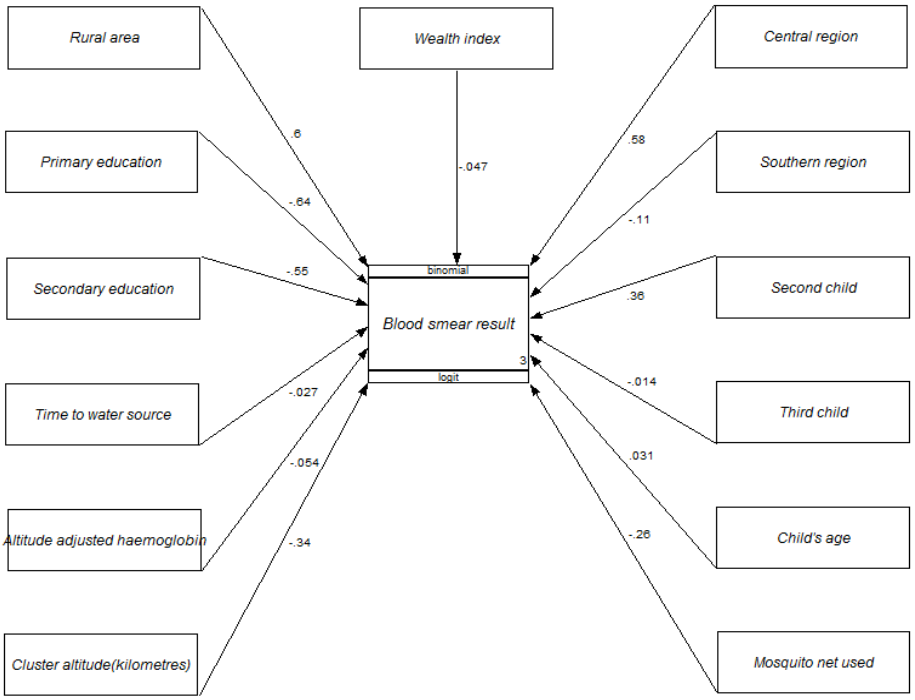


Figure 2-3: G-SEM path diagram showing coefficients from binomial logistic regression analysis of the direct effects of selected random variables on a blood smear positive malaria result in children under five in Malawi in 2012.

The results of the G-SEM show both direct and indirect effects on the variable blood smear positive malaria. The figures 2-3 and 2-4 show the G-SEM models. Figure 2-3 showing the direct G-SEM and figure 2-4 showing the indirect G-SEM. Exogenous variables; rural area means type of place of residence and primary education represents mother's level of education.

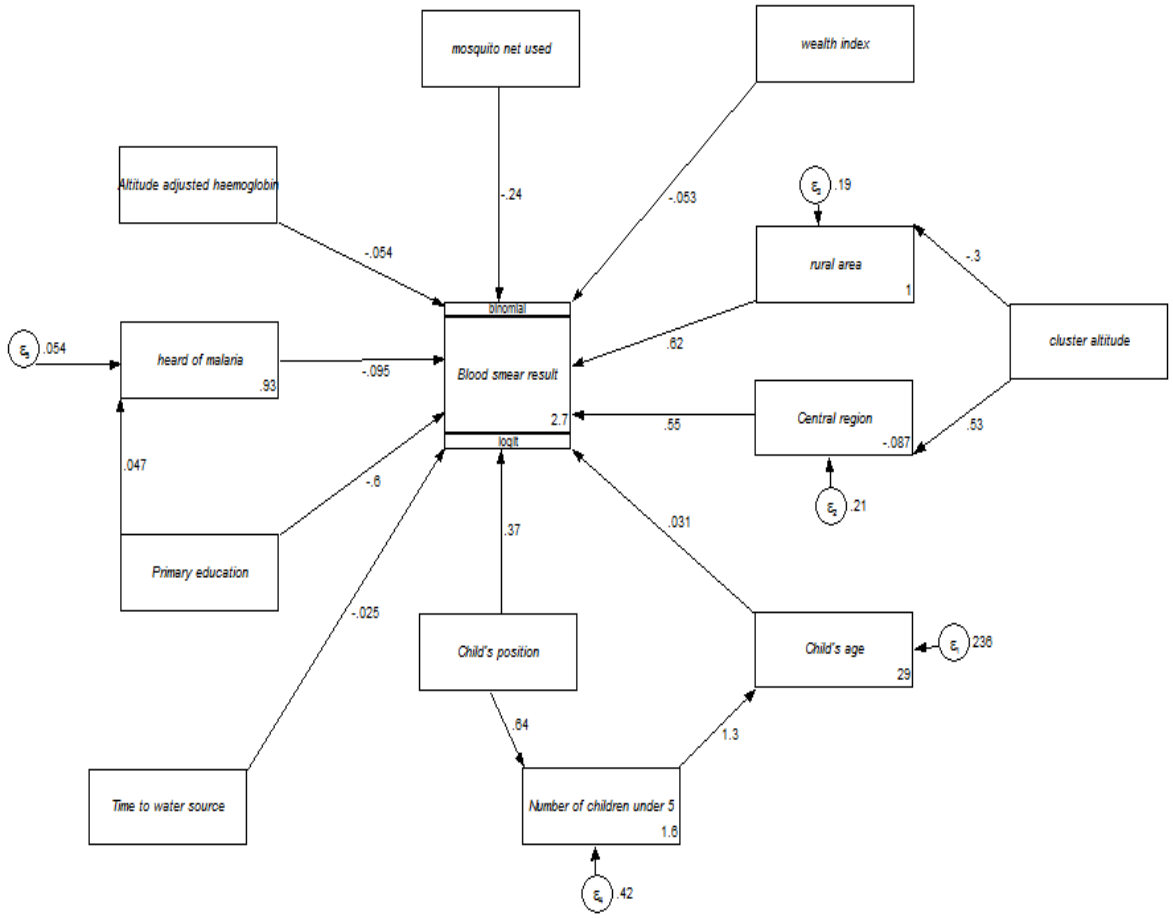


Figure 2-4: G-SEM path diagram of selected random variables showing both direct and indirect pathways related to blood smear positive malaria results for children less than five years in Malawi in 2012.

The indirect effects were modelled on the variables; cluster altitude, mother's highest education level and the wealth index score. Cluster altitude and knowledge of malaria were identified as variables that can indirectly affect malaria morbidity in children less than five.

Strengths and limitations

Strengths and limitations were looked at with regards to data, study design, confounding, measurement of outcome as well as the robustness of analysis (Musenge et al., 2013b). Some of the study limitations were that the data could not be verified and was used as it was and this might have limited the analysis as well. Multi-collinearity was another limitation of the study as some variables could not be used and were dropped from the multivariable analysis; this might have resulted in loss of useful information and might have affected the interpretation of the results. In this study, we used data from a cross sectional study so although the study was looking at episodes of malaria, cross sectional studies mainly measure prevalence and not incidence. This therefore limited the interpretation of the associations that were observed during data analysis. There was no temporal sequence that could be ascertained from this type of study design. This study was a secondary data analysis therefore the data used in this study was collected for other purposes and not for the purposes of this study therefore this could have affected the quality of the results that were produced.

Strengths of the study were our use of propensity score matching in order to deal with selection bias and ultimately confounding. Cases and controls were matched according to propensity scores with insecticide treated mosquito net usage as the matching variable. This variable was selected because it had the potential of confounding the outcome.

The outcome was based on a rapid diagnostic test result as well as a laboratory test result for malaria so this was strength of the study in that the outcome was based on laboratory confirmed results and not affected by recall bias.

We also used survey adjusted multiple logistic regression as well as structural equation modeling in our analysis to cater well for direct and indirect determinants.

2.4 Discussion and conclusion

SES is an important determinant of malaria and other studies (Snow et al., 2003a, Messina et al., 2011, The Global Poverty Project) also showed that SES is an important factor in malaria episodes. As mentioned earlier malaria is a disease of poverty (Snow et al., 2003a, Akazili et al., 2008) so this finding compliments what other studies have shown with regards to this particular variable on malaria morbidity. One review article on economic and social burden of malaria stated that malaria thrives in poor countries (Sachs and Malaney, 2002). The results from this study support this review because Malawi has a low GDP(United Nations); this means malaria puts an extra burden on the government as well as an extra burden on the population in terms of accessing healthcare. The government needs to ensure that the resources are available for diagnosis as well as treatment and the population must have the necessary financial means in order to access the treatment(Sachs and Malaney, 2002). If the population cannot afford this treatment, then the government is forced to provide the treatment at affordable costs and this might affect the government's self sufficiency. Since malaria is endemic in Malawi; the government needs to put in place measures to control malaria. These include providing insecticide treated mosquito nets, indoor residual spraying as well as providing anti-malaria tablets(Okenu, 1999) and these activities strain the budget of the country and other economic building activities will not be prioritized and therefore this affects the overall development of the country. In order to balance the spending on malaria treatment and the spending on other developmental activities, it is important for the country to know the malaria trends so that the use of resources is optimized.

GDP also affects nutrition, because nutrition is linked to economic status if one is economically sound then they are able to provide adequately for themselves and therefore resulting in a well-nourished body. A well-nourished body is better able to fight malaria infection by mounting an adequate response to infection as compared to an undernourished body (Caulfield et al., 2004). Health status is also linked to economic status and malaria is also affected by the economic status of an individual as well as country (Stratton et al., 2008). A poor economic status results in inadequate health care facilities and therefore increasing vulnerability of the population to malaria.

Type of place of residence as well as region could be linked to the altitude, where some studies (Drakeley et al., 2005a, Hay et al., 2004, Lindsay and Martens, 1998) found an effect on malaria prevalence depending on the altitude. It is important for the government to know the areas that are malaria "hotspots" so that malaria prevention resources can be allocated to the areas that have higher malaria morbidity as compared to the rest of the country. Malaria endemicity is also influenced by temperature and rainfall and altitude also influences temperature and rainfall (Cibulskis et al., 2011, Reiter, 2001), this is explored in our further work using spatial modelling. Water bodies especially stagnant water sources (Cibulskis et al., 2011, Reiter, 2001)are known as breeding places for mosquitoes therefore this study showed that those who were nearer to water sources were at a higher risk for malaria.

Education level of the mother also showed significance ($p = <0.001$). The results showed that the more educated a mother was, the less likely the child was to have malaria. This could be due to

the fact that an educated mother better understands information on malaria and are more likely to implement properly the preventive measures that they are taught. And also that educated mothers a more likely to be employed or be entrepreneurs, hence getting income to sustain the family and children better.

Child related variables (haemoglobin level, position of child and age of child) were also significant in influencing malaria in children under five. Studies(Price et al., 2001, Oladeinde et al., 2012, Takem et al., 2010, Carneiro et al., 2006) have shown that anaemia is a complication of malaria so this study confirms this and children with a low haemoglobin level had higher chances of having malaria as compared to children with normal haemoglobin levels From the descriptive statistics only 32.3% were not anemic and this might be linked to the low SES resulting in poor nutrition (Caulfield et al., 2004).

The G-SEM's indirect pathways also showed a significant association between cluster altitude and region as well as between SES and education level. G-SEM was used in this study to complement the results from the multiple variable analysis and the results showed that the multiple variable analysis and the G-SEM direct pathways show similar results. G-SEM can help in diagrammatically conceptualizing the effects of the determinants on the outcome and this helps in analysis where the variables can then 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 disease in children.

It is important to understand the determinants of malaria so that effective monitoring and evaluation of malaria can be carried out. This study showed the importance of socio-economic status as well as education in the fight against malaria. In order for malaria to be eliminated in the population it is important for the government to empower the population economically and also ensure that health education is a part of the efforts that are put in place to fight malaria. This will assist in the fight to eliminate malaria. It is important to ensure that resources are channeled in order to optimize prevention strategies that are put in place. Once the population is empowered, then preventative strategies for malaria elimination can then be implemented successfully and if the population is educated, then it is able to understand better the strategies in place and implement them successfully. The other important determinates also are linked to socio-economic status, therefore reduction of poverty will go a long way in the fight to eliminate malaria.

2.5 Acknowledgments

The authors would like to thank the division of Epidemiology and Biostatistics at the School of Public Health, the University of the Witwatersrand for the support that they offered in the drafting of this paper and ensuring that the study received ethics approval. We also would like to thank the DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) for providing funding that made this research work possible.

Chapter 3 Spatially adjusted socio-demographic and environmental factors of household malaria morbidity in Malawi

3.0 Spatial and socio-economic effects on malaria morbidity in children under 5 years in Malawi in 2012

Simangaliso Chitunhu, Eustasius Musenge

Biostatistics and Epidemiology Division, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

This is a draft version.

Abstract

Introduction

Malaria is a major health challenge in sub-Saharan Africa with children under five being most vulnerable to it. Therefore it is important to identify malaria hotspots as this will be important in having targeted preventative interventions.

Materials and methods

This study analysed malaria morbidity using data from the Malawi 2012 Malaria Indicator Survey that were obtained from the Demographic and Health Survey (DHS) program website which captured malaria related information on children under age of five. Poisson regression was done to determine associations between the outcome (number of children under five positive for malaria in household) and selected explanatory variables and we then introduced a structured and unstructured random effect using Bayesian geostatistical modelling to measure the spatial effects on those selected variables.

Results

There were a total of 1878 households in 140 clusters. The total number of children under age of five was 1900. The spatially structured effects accounted for more than 90% of random effects as these had a mean of 1.32 (95% Credible Interval (CI) =0.37, 2.50) whilst spatially unstructured had a mean of 0.10(CI=9.0×10^{-4}, 0.38). The spatially adjusted significant variables on malaria

morbidity were; type of place of residence (Urban or Rural) [posterior odds ratio (POR) =2.06; CI = 1.27, 3.34], not owning land [RR=1.77; CI= 1.19, 2.64], not staying in a slum [RR=0.52; CI= 0.33, 0.83] and Enhanced vegetation index [RR=0.02; CI= 0.00, 1.08]. A trend was observed on usage of insecticide treated mosquito nets [POR=0.80; CI= 0.63, 1.03].

Discussion and conclusion

This study showed that malaria is a disease of poverty with significant results in slum, type of place of residence as well as ownership of land. Enhanced vegetation index was also an important factor in malaria morbidity but precipitation and temperature suitability index were not significant factors. The central region of the country was identified as the spatial hotspot for malaria.

3.1 Introduction

Malaria is a serious problem in developing countries and many studies have been carried out in these countries to identify factors that are associated with the disease (Bell et al., 2005, Bowie, 2007, Breman et al., 2004, Brooker et al., 2008, Omumbo et al., 2005, Kazembe et al., 2006b, Messina et al., 2011, Snow et al., 2003b, Noor et al., 2009, Bennett et al., 2013). Factors that have been identified are both natural and human related and these include climatic, geographic and SES variables (Chirombo et al., 2014). Temperature and precipitation are major environmental risk factors (Nobre et al., 2005). Human related factors include use of bed nets, access to anti-malarial drugs, poor access to health services, inadequate case management, poor immunological competence because of malnutrition and socioeconomic factors (Cox et al., 2007, Bowie, 2007, Omumbo et al., 2005, Snow et al., 2003b). The human related factors have a strong link with poverty and vulnerability(Snow et al., 2003b, The Global Poverty Project). Therefore, the impact of malaria is strongly felt in low income countries.

In the fight against malaria, there is need to ensure that adequate information on the disease and prevalence in specific areas (Snow et al., 1996) is available and this is based on the notion that people living in a household and those that live close together have exposures that are similar (Musenge et al., 2013b, Elliott et al., 1995).

Transmission of malaria varies from place to place, mapping this variation is important in identifying populations at different risk levels, comparing and interpreting malaria interventions in different places, and evaluating options for controlling the disease (Gething et al., 2011, Lowe et al., 2013). Disease maps can be used and these show how the disease is geographically distributed by highlighting the areas with high and low incidence of the disease (Sun et al., 2000,

Musenge et al., 2013b). This is important in order to target the available limited resources to areas of where they are required the most for the greatest effect (Kazembe, 2007). Geographical information system (GIS) and spatial statistical methods are used in identifying areas with increased risk of disease and determining spatial associations between disease and risk factors (Omumbo et al., 2005, Goovaerts, 2006, Webster et al., 2006, Hay et al., 2009). GIS techniques generate maps which can provide a comprehensive display of disease pattern and magnitude (Law et al., 2004). Therefore, disease-specific maps play an important role in disease control activities including monitoring changes in disease epidemiology and guiding the allocation of resources (Hay et al., 2009, Noon and Hankins, 2001).Disease specific maps also assist in planning, monitoring and evaluating cost-effective strategies for disease (Gosoniu et al., 2012).

Bayesian statistical methods are applied in spatial analysis and disease mapping because they enable the integration of spatial correlation and modelling of fixed variables and random effects(Lawson et al., 1999, Wakefield, 2007). Spatial modelling introduces a random effect and this creates a spatial correlation on the distribution of the random effects thus providing correct estimates of parameters being tested (Clements et al., 2006, Riedel et al., 2010, Gosoniu et al., 2006). MCMC methods are used in Bayesian statistics. MCMC methods are used in sampling probability distributions beginning with an initial value with conditional probabilities being used in generating new values (Lawson, 2013). MCMC methods deliver dependent outcomes, which are auto-correlated (Banerjee et al., 2004). Gibbs sampling and MH are some of the ways used in MCMC (Fruhwirth-Schnatter, 2013, Geman and Geman, 1993, Casella and George, 1992, Chib and Greenberg, 1995). Gibbs sampling is used when the joint distribution is unknown or is difficult to sample directly, but the conditional distribution of each variable is known and is from a normal distribution or normal related distributions (Arminger and Muthén, 1998, Geman and

Geman, 1993). MH is applied whenever direct sampling is difficult even for a single variable. These methods are going to be utilized in this paper.

This paper aims to understand the spatial associations between malaria morbidity and environmental and behavioural determinants of malaria in Malawi in the year 2012. This will be achieved through applying a Bayesian geostatistical model that can deal with spatial random effects. Three different Bayesian approaches are going to be implemented and this will assist in fully understanding the determinants of malaria as well as the influence of different geographical areas and environmental effects in malaria prevalence.

Understanding fully the determinants of malaria in a low income sub-Saharan country will assist in the development of health programs that will help to reduce the burden of malaria with the available resources and interventions will be targeted at the areas that need the interventions the most in order to reduce the burden of malaria on the population.

3.2 Materials and Methods

3.2.1 Study area

Malawi is a landlocked country located in southern Africa with an area of approximately 120 000km^2 and is divided into three regions (Northern, Southern and Central). The country is bordered by Zambia, Mozambique and Tanzania (Lowe et al., 2013). Malawi has a sub-tropical climate with a rainy season from November to May and a dry season from May to November (Bennett et al., 2013). The presence of many water bodies especially on the eastern side with Lake Malawi being the most prominent at 580km makes the nation vulnerable to malaria morbidity and mortality (Bowie, 2007, Dzinjalamala, 2009, Bennett et al., 2013).

3.2.2 Malawi Malaria Indicator Survey Data

The 2012 Malaria Indicator Survey (MIS) data that were used in this study came from a sample of households that were selected throughout the three regions (Northern, Central and Southern) of Malawi, and were obtained from the measure Demographic and Health Survey (DHS) website. A two stage cluster sampling technique was used to select the households. Weighting was carried out to adjust for the differences in the sampling of clusters. The original study collected data on basic demographic and health indicators, malaria prevention and treatment, anaemia, and malaria. These were extracted for analysis using Stata®13.1 (Copyright 1985-2013, StataCorp LP).

The figure 3-1 below shows the country of Malawi with the 140 enumeration areas as well as the major water bodies.

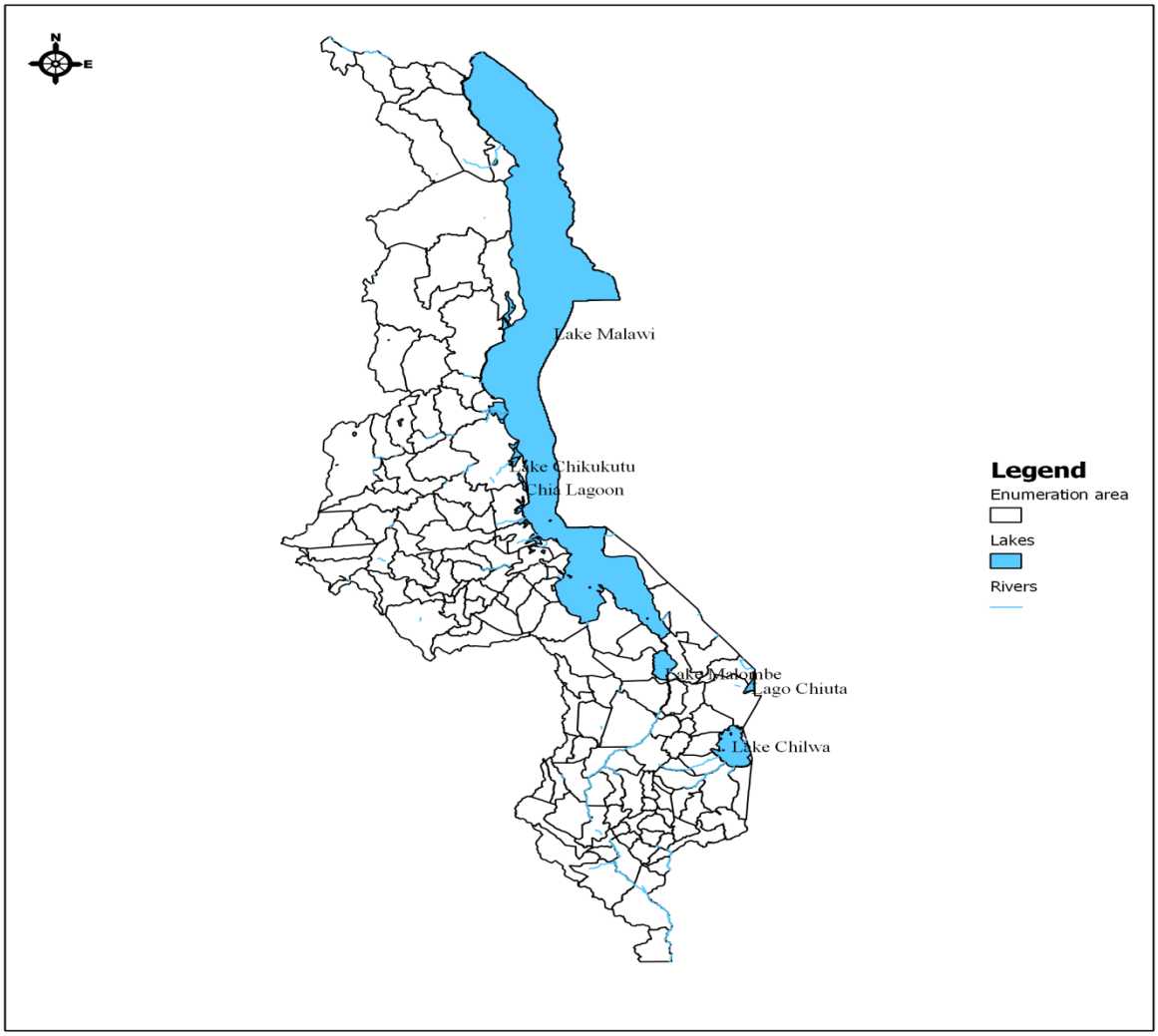


Figure 3-1: Map of Malawi with the location of the 140 enumeration areas as well as well as the major water bodies.

NB: Enumeration areas were selected according to the population of the area so the major cities Lilongwe (central) and Blantyre (southern) had more enumeration areas as compared with the other areas.

3.2.3 Statistical analysis methods

Outcome and explanatory variables

The outcome variable was number of malaria positive children under five in the household in 2012.

The fixed variables were selected based on significant correlation with the outcome. A special variable that was used as proxy for socio-economic status was created. This variable was based on presence of tap water, toilet and electricity in the household. Presence of all three was defined as none slum and absence of one or more of these variables was defined as slum. This was based on a study that was done in rural South Africa (Musenge et al., 2013a) that used this approach. The other variables that were used were type of place of residence whether it is urban or rural, cluster altitude, use of insecticide treated mosquito net and the ownership of land that is suitable for agriculture.

Environmental variables that were used in this analysis were temperature suitability index (TSI), annual mean precipitation and enhanced vegetation index (EVI) (Huffman and Bolvin, 2013, The Malaria Atlas Project, 2010, World Climate, 2012, MODIS, 2011) and they are known to influence malaria transmission (Noor et al., 2012, Alegana et al., 2014, Snow et al., 2012). The EVI was a measure of the amount of vegetation in the country and how the vegetation influences propagation of mosquitoes and thus malaria transmission, the TSI was a measure of the suitability of the temperature in promoting the growth of mosquitoes (Bennett et al., 2013).

These variables were selected after doing stepwise Poisson modelling and obtaining the variables with the best fit. These variables were then used as they were with the three different Bayesian approaches that were used in this study. A spatial random effect was then introduced at cluster

level and the random effect was both structured and unstructured. This was done to see if there was any spatial effect on the malaria episodes in the households in the different clusters.

Statistical modelling

Generalised linear models

Bayesian geostatistical modelling was done to investigate effects of structured and unstructured random effects by allowing for the joint analysis of the fixed effects and the random effects (Belitz et al., 2012). The following models are described according to the WinBUGS code shown in Appendix 1. The regression model that was used to fit the data was the Poisson because the outcome was a count which was the number of malaria positive cases in each household. The total number of children under five was used as the offset variable in data analysis. The Poisson distribution is given by (Banerjee et al., 2004, Lawson, 2013, Carlin and Louis, 2000, Ntzoufras, 2011):

$$y_i \sim Poisson(\lambda_i) \qquad \text{where} \quad i = 1, 2, ..., n \qquad \text{(Equation 1)}$$

with probability $P(y_i) = \frac{\lambda^{y_i} e^{-\lambda_i}}{y_i!}$ and mean $E(y_i) = \lambda_i$ and variance $\text{var}(y_i) = \lambda_i$

In this distribution the predictor is given by the following $\psi_i = X_i^T \beta + \phi_i + \theta_i$

where the X_i^T is the design matrix $\underset{\sim}{\beta}$ is the vector of fixed coefficients, $\underset{\sim}{\theta}$ is the vector of structured random effect and $\underset{\sim}{\phi}$ is the vector of unstructured random effect.

The link function links the mean of the distribution $\lambda_i = E(y_i)$ with the linear predictor under general linear models (Cameron and Trivedi, 2013). This is the mean but with the GLM. This is a member of the exponential family of distributions as is in our case we have a log link function. This log link function is given by $\psi_i = \ln \mu_i$. Exponentiating both sides ensures that the mean is always positive (Guikema and Goffelt, 2008) and this gives $\mu_i = e^{\psi_i}$

In our case we are using the number of children in the household as those exposed; we introduced the offset variable as such $\lambda_i = E_i \mu_i = E_i e^{\psi_i}$. This gives us:

$$\lambda_i = E_i e^{\psi_i} = E_i e^{X_i^T \beta + \phi_i + \theta_i} \qquad \text{(Equation 2)}$$

The Bayesian mode of parameter estimation involves us expressing this as follows:

$$Posterior\left[p(parameters \mid data) \right] \propto Likelihood \times priors$$

(and their corresponding hyper-priors)

The posterior likelihood for our data is thus:

$$L\left(\Omega \equiv \{\underset{\sim}{\beta}, \underset{\sim}{\phi}, \underset{\sim}{\theta}\} \mid y_i\right) = \prod_{i=1}^{n} P\left(y_i \mid \Omega\right) \times P\left(\underset{\sim}{\beta}, \underset{\sim}{\phi}, \underset{\sim}{\theta}\right)$$

The full conditional for this model would need to be done using the following equation:

$$\begin{aligned} p\left(\underset{\sim}{\phi}, \underset{\sim}{\theta}, \underset{\sim}{\beta} \mid y_i\right) &\propto p\left(\Omega \mid y\right) = L\left(y \mid \Omega\right) \times p(\underset{\sim}{\beta} \mid \sigma_\beta) \times p\left(\underset{\sim}{\theta} \mid \tau_c\right) \times p\left(\underset{\sim}{\phi} \mid \tau_h\right) \\ &= L\left(y \mid \Omega\right) \times p(\underset{\sim}{\beta} \mid \sigma_\beta) \times p\left(\underset{\sim}{\theta} \mid \tau_c\right) \times p\left(\tau_c\right) \times p\left(\underset{\sim}{\phi} \mid \tau_h\right) \times p\left(\tau_h\right) \end{aligned} \qquad \text{(Equation 3)}$$

Therefore the likelihood:

$$\prod_{i=1}^{n} P\left(y_i \mid \underset{\sim}{\beta}, \underset{\sim}{\phi}, \underset{\sim}{\theta}\right) = \prod_{i=1}^{n} \frac{e^{-\lambda_i} \lambda^{y_i}}{y_i!} = \frac{\lambda_i^{\sum_{i=1}^{n} y_i} e^{-\lambda_i n}}{\prod_{i=1}^{n} y_i}$$

Therefore substituting λ_i from equation 2 we get:

$$L\left(y_i \mid \Omega\right) \propto \left[E_i e^{X_i^T \beta + \phi_i + \theta_i} \right]^{\sum_{i=1}^{n} y_i} e^{-n\left(E_i e^{X_i^T \beta + \phi_i + \theta_i}\right)} \qquad \text{(Equation 4)}$$

The prior for the beta coefficients for the k-1 fixed covariates is:

$$\beta_k \overset{iid}{\sim} N\left(\mu_\beta, \sigma_\beta^2\right) \text{ therefore } p\left(\beta_k\right) = \frac{1}{\sqrt{2\pi\sigma_\beta^2}} \exp\left[-\frac{1}{2}\left(\frac{\beta_k - \mu_\beta}{\sigma_\beta} \right)^2 \right] \qquad \text{(Equation 5)}$$

The parameters were treated as constant in most of our models.

Working on the random effects, for unstructured part we have $p\left(\underset{\sim}{\phi} \mid \tau_h\right)$ therefore:

$$\phi_i \overset{iid}{\sim} N\left(0, \frac{1}{\tau_h}\right) \text{therefore } p\left(\phi_i \mid \tau_h\right) = \frac{1}{\sqrt{\frac{2\pi}{\tau_h}}} \exp\left[-\frac{1}{2}\left(\frac{\phi_i - 0}{1 \big/ \sqrt{\tau_h}} \right)^2 \right]$$

where a conjugate gamma hyper prior on τ_h is given by (Banerjee et al., 2004)

$$\tau_h \sim G\left(\alpha_h, \beta_h\right) \text{therefore } P\left(\tau_h\right) = \frac{\left(\beta_h\right)^{\alpha_h}}{\Gamma\left(\alpha_h\right)} . \tau_h^{\alpha_h - 1} . e^{-\beta_h \tau_h} \text{ therefore:}$$

$$P(\phi_i \mid \tau_h)P(\tau_h) \propto e^{\left(-\frac{1}{2}\phi_i\tau_h^{\frac{1}{2}}\right)}\tau_h^{\alpha_h-1}e^{-\beta_h\tau_h} \qquad \text{(Equation 6)}$$

The CAR prior for θ_i is given by (Banerjee et al., 2004, Lawson, 2013) $\theta_i \sim CAR(\tau_c)$ and this CAR prior is given by $\theta_i \sim N\left(\frac{\theta_i}{\overline{\theta}_i}, \frac{1}{\tau_c m_i}\right)$ therefore

$$p(\theta_i \mid \tau_c) = \frac{1}{\sqrt{\frac{2\pi}{\tau_c m_i}}} \exp\left[-\frac{1}{2}\left(\frac{\theta_i - \frac{\theta_i}{\overline{\theta}_i}}{\sqrt{\frac{1}{\tau_c m_i}}}\right)^2\right]$$

Hence the likelihood of all neighbouring households is

$P(\theta_1.....\theta_n \mid \tau_c) = P(\underset{\sim}{\theta} \mid \tau_c) \propto \exp\left\{-\frac{\tau_c}{2}\sum_{i=1}^{n} w_{ij}\left(\theta_i - \theta_j\right)^2\right\}$ where w_{ij} denotes the adjacency matrix, ij denotes that region j is a neighbour of region i and m_i is the number of neighbours of region i.

a conjugate hyperprior on τ_c is given by $\tau_c \sim G(\alpha_c, \beta_c)$

therefore $P(\tau_c) = \frac{(\beta_c)^{\alpha_c}}{\Gamma(\alpha_c)}.(\tau_c)^{\alpha_c-1}.e^{-\beta_c\tau_c}$ therefore

$$P(\underset{\sim}{\theta} \mid \tau_c)P(\tau_c) \propto \exp\left\{-\frac{\tau_c}{2}\sum_{i=1}^{n} w_{ij}\left(\theta_i - \theta_j\right)^2\right\}(\tau_c)^{\alpha_c-1}e^{-\beta_c\tau_c} \qquad \text{(Equation 7)}$$

Combining equations 4, 5, 6 and 7 we obtain our posterior function as follows:

$$P\left(\underset{\sim}{\beta},\underset{\sim}{\phi},\underset{\sim}{\theta}\mid y_i\right)\propto\left[E_i e^{X_i^T\beta+\phi_i+\theta_i}\right]^{\sum_{i=1}^{n}y_i} e^{-n\left(E_i e^{X_i^T\beta+\phi_i+\theta_i}\right)}\times\exp\left[-\frac{1}{2}\left(\frac{\beta_k-\mu_\beta}{\sigma_\beta}\right)^2\right]$$
$$\times\exp\left(-\frac{1}{2}\phi_i\tau_h^{1/2}\right)\tau_h^{\alpha_h-1}e^{-\beta_h\tau_h}\times\exp\left\{-\frac{\tau_c}{2}\sum_{i=1}^{n}w_{ij}\left(\theta_i-\theta_j\right)^2\right\}\left(\tau_c\right)^{\alpha_c-1}e^{-\beta_c\tau_c} \quad \text{(Equation 8)}$$

This can be solved for the parameters $\underset{\sim}{\beta},\underset{\sim}{\phi},\underset{\sim}{\theta}$ using GIBBS sampling and where there is no closed form of the distribution we use MCMC with Metropolis- Hastings algorithms.

Data analysis methods

Poisson regression analysis was done using Stata®13.1 (Copyright 1985-2013, StataCorp LP). Bayesian spatial Poisson conditional autoregressive (CAR) model using WinBUGS (Lunn et al., 2000), R-INLA [R-Cran software version 2.15.2 (R Development Core Team, 2012)] as well as R2BayesX [(R-Cran software version 2.15.2 (R Development Core Team, 2012)] (Team, 2012) was also carried out. The models' goodness of fit for the Bayesian models was assessed using the Deviance Information Criterion (DIC) whereby adding a spatial random effect was evaluated to see if it improves the unstructured model (Best et al., 2005). The software producing the lowest DIC was the software that was selected as the best fitting software.

All output maps were produced using a projected co-ordinate system, WGS Zone 84 in Quantum GIS version 1.8.0 (QGIS, 2013) (Quantum, 2011), WinBUGS as well as R2BayesX.

3.2.4 Ethics approval

This study was granted ethics approval by the University of the Witwatersrand's Human Research Ethics Committee (Medical) (Clearance Certificate No. M130962). Approval to use the MIS data was obtained from the measure DHS website. The primary study, where the data was collected, verbal informed consent for testing of children was obtained from the child's parent or guardian at the end of the household interview. The survey was also anonymised so that household or individual information is not identifiable(Ministry of Health et al., 2012) .

3.3 Results

Data were analysed at household level with a total of 1878 households in 140 clusters. The total number of children under the age of five was 1900. Table 3-1 below shows the comparative results between the different methods that were used in analysing the data. These results are from data that were analysed without the random effects. Significance was set at 5% level.

Table 3-1: Comparative results between STATA, WINBUGS, R-INLA and BayesX for the Multiple variable Poisson regression analysis without the spatial random effect.

Variable	Stata Coefficient (CI)	WINBUGS Posterior coefficient (CI 2.5, 97.5)	INLA Posterior coefficient (CI 2.5, 97.5)	BAYES-X Posterior coefficient (CI 2.5, 97.5)
Number children sleeping under net				
0 (reference)				
1	-0.22(-0.47, 0.03)	-0.39(-0.62, -0.16)*	-0.30(-0.52, -0.09)*	-0.22(-0.42,-0.02)*
2 or more	-0.21(-0.47,0.04)	-0.04(-0.26, 0.19)	-0.29(-0.50,-0.07)*	-0.22(-0.41,-0.01)*
Cluster altitude	0.0004(-0.001,0.02)	0.0007($1.29x10^{-6}$, 0.0016)*	0.0005(0.0001,0.0012)*	0.0004(-0.0002,0.0011)
Precipitation	-0.004(-0.01,0.01)	-0.003(-0.01, 0.004)	-0.003(-0.008, 0.003)	-0.004 (-0.009,0.001)
EVI	-4.19(-8.45,0.08)	-3.63 (-6.67, -0.60)*	-3.92(-6.65,-1.25)*	-4.25(-6.87, -1.69)*
TSI	1.54(-1.04,4.12)	2.21(0.57, 4.50)*	1.97(0.37,3.58)*	1.55(-0.003,3.13)
Owns land for crops				
No (reference)				
Yes	0.57(0.17,0.97)*	0.72(0.24, 1.09)	0.71(0.36,1.07)	0.58(0.27,0.92)*
Type of residence				
Urban (reference)				
Rural	0.72(0.24,1.20)	0.60(0.28, 1.15)	0.59(0.27,0.92)*	0.74(0.34,1.16)
Slum				
Yes (reference)				
No	-0.65(-1.12,-0.18)*	-0.79(-1.35, -0.21)*	-0.75(-1.29,-0.27)*	-0.68(-1.26,-0.16)*

Stata CI = 95% confidence interval

WINBUGS, INLA, BAYES-X CI = 95% Credibility Interval

BAYES-X and STATA are weighted

*significant at 5% level

From the table 3-1 the variable that showed significance at 5% with all the methods of analysis used was whether respondents stay in a slum or not. The other variables were not significant across all the testing methods used but EVI and 1 child sleeping under an ITN showed significance with all the Bayesian methods. Owning land for crops was significant with Stata and BayesX.

Table 3-2 shows results of the same variables but now with the structured and unstructured random effects and these were done using the three methods that is WinBUGS, INLA and BayesX. The structured and unstructured random effects were run separately. From the table 3-2, type of place of residence showed significance with all the three methods with both the structured and unstructured random effects. DIC was used to measure the model with the best fit (Ntzoufras, 2011). WinBUGS had the models with the least fit and BayesX had models with the best fit.

Table 3-2: Bayesian structured and unstructured spatial results.

Analysis method	**WINBUGS (Posterior coefficients (CI 2.5,97.5))**		**INLA (Posterior coefficients (CI 2.5, 97.5))**		**BAYESX (Posterior coefficients (CI 2.5, 97.5))**	
Variable	**Unstructured**	**Structured**	**Unstructured**	**Structured**	**Unstructured**	**Structured**
Number children sleeping under net						
0 (reference)						
1	-0.31(-0.54,-0.09)*	-0.35(-0.56,-0.13)*	-0.27(-0.49,-0.05)*	-0.28(-0.50,-0.06)*	-0.19(-0.39,0.02)	-0.21(-0.42,-0.002)*
2 or more	-0.10(-0.33,0.13)	-0.09(-0.32,0.14)	-0.33(-0.56,-0.10)*	-0.35(-0.57,-0.12)*	-0.29(-0.50,-0.07)*	-0.31(-0.52,-0.09)*
Cluster altitude	-0.003(-0.02,0.01)	0.0006(-0.0007,0.002)	0.001(-0.0003,0.001)	0.0001(-0.001,0.001)	0.001(-0.0004,0.003)	0.0003(-0.002,0.002)
Precipitation	-0.04(-0.16,0.06)	0.002(-0.01,0.01)	-0.001(-0.01,0.01)	0.001(-0.01,0.01)	-0.001(-0.01,0.01)	0.01(-0.01,0.02)
EVI	9.57(-26.42,60.51)	-2.18(-6.82,2.50)	-4.59(-9.53,0.20)	-2.65(-7.12,1.77)	-5.34(-10.54,-0.38)*	0.91(-4.19,5.96)
TSI	5.26(-32.86,47.44)	1.87(-1.10,4.69)	3.30(0.26,6.42)	0.88(-1.84,3.61)	3.28(0.06,6.64)	2.83(-1.02,6.94)
Owns land for crops						
No (reference)						
Yes	0.31(-0.06,0.71)	0.59(0.22,0.97)*	0.49(0.13,0.88)*	0.58(0.22,0.96)*	0.37(0.03,0.72)*	0.45(0.11,0.81)*
Type of residence						
Urban (reference)						
Rural	11.39(0.88,21.0)*	0.83(0.39,1.31)*	0.84(0.37,1.33)*	0.79(0.34,1.25)*	0.88(0.32,1.44)*	0.78(0.29,1.31)*
Slum						
Yes (reference)						
No	-0.25(-0.84,0.30)	-0.67(-1.23,-0.15)*	-0.60(-1.17,-0.08)*	-0.66(-1.22,-0.14)*	-0.54(-1.14,0.01)	-0.55(-1.14,0.01)
Deviance information criterion (DIC)	2041.83	2157.62	2138.07	2142.12	1278.61	1269.02

PCI = 95% posterior credibility interval

Number of children was used as an offset variable in all the models.

BAYES-X was weighted to take into account the survey data

*significant at 5% level

Table 3-3 below shows the model where both structured and unstructured random effects were run in the same model.

Table 3-3: Posterior estimates of the convolution model

Variable	WINBUGS (Posterior coefficients (PCI 2.5,97.5))	INLA (Posterior coefficients (PCI 2.5,97.5))	BayesX (Posterior coefficients (PCI 2.5,97.5))
Number children sleeping under net			
0 (reference)			
1	-0.34 (-0.56, -0.13)*	-0.27 (-0.49, -0.05)*	-0.21 (-0.42, 0.001)
2 or more	-0.09 (-0.31, 0.14)	-0.33 (-0.56, -0.10)*	-0.30 (-0.52, -0.09)*
Cluster altitude	-0.0009 (-0.0006,0.002)	0.001(-0.0003, 0.002)	0.0003(-0.002, 0.002)
Precipitation	-0.0009 (-0.011, 0.009)	-0.001(-0.01, 0.01)	0.005 (-0.007, 0.02)
EVI	-3.19 (-8.52, 1.66)	-4.59 (-9.54, 0.20)	0.40 (-4.90, 5.73)
TSI	2.67 (-0.61, 5.91)	3.29 (0.26, 6.44)	2.79 (-1.19, 6.96)
Owns land for crops			
No (reference)			
Yes	0.55 (0.18, 0.94)*	0.50 (0.13, 0.88)*	0.44 (0.10, 0.79)*
Type of residence			
Urban (reference)			
Rural	0.83 (0.34, 1.32)*	0.84 (0.37, 1.34)*	0.79 (0.30, 1.31)*
Slum			
Yes (reference)			
No	-0.63 (-1.21, -0.11)*	-0.60 (-1.17,- 0.08)*	-0.53 (-1.14, 0.01)
Deviance information criterion (DIC)	2 089.36	2 138.79	1 268.77

PCI = 95% posterior credibility interval

*significant at 5% level

Table 3-3 shows that significance with the variables owning land for crops and type of place of residence at 5% level with all three methods. Using ITNs and living in a slum were significant

with two of the methods. Again DIC was used as a measure of best model fit and from the table 3-3 BayesX showed the best fit and INLA had the least fit.

Mapping was done using BayesX and WinBUGS. Figures 3-2 and 3-3 below show the posterior mean and median of both the structured and unstructured models. The WinBUGS maps are shown in appendix 5. From these maps, the central region of Malawi shows an increased risk of malaria. The maps with the structured random effects show clearly that the central region is where the problem of malaria is concentrated although there are some spots in the Southern parts of the country where malaria is also high.

The figures 3-2 and 3-3 below show the maps of the posterior estimates using BayesX

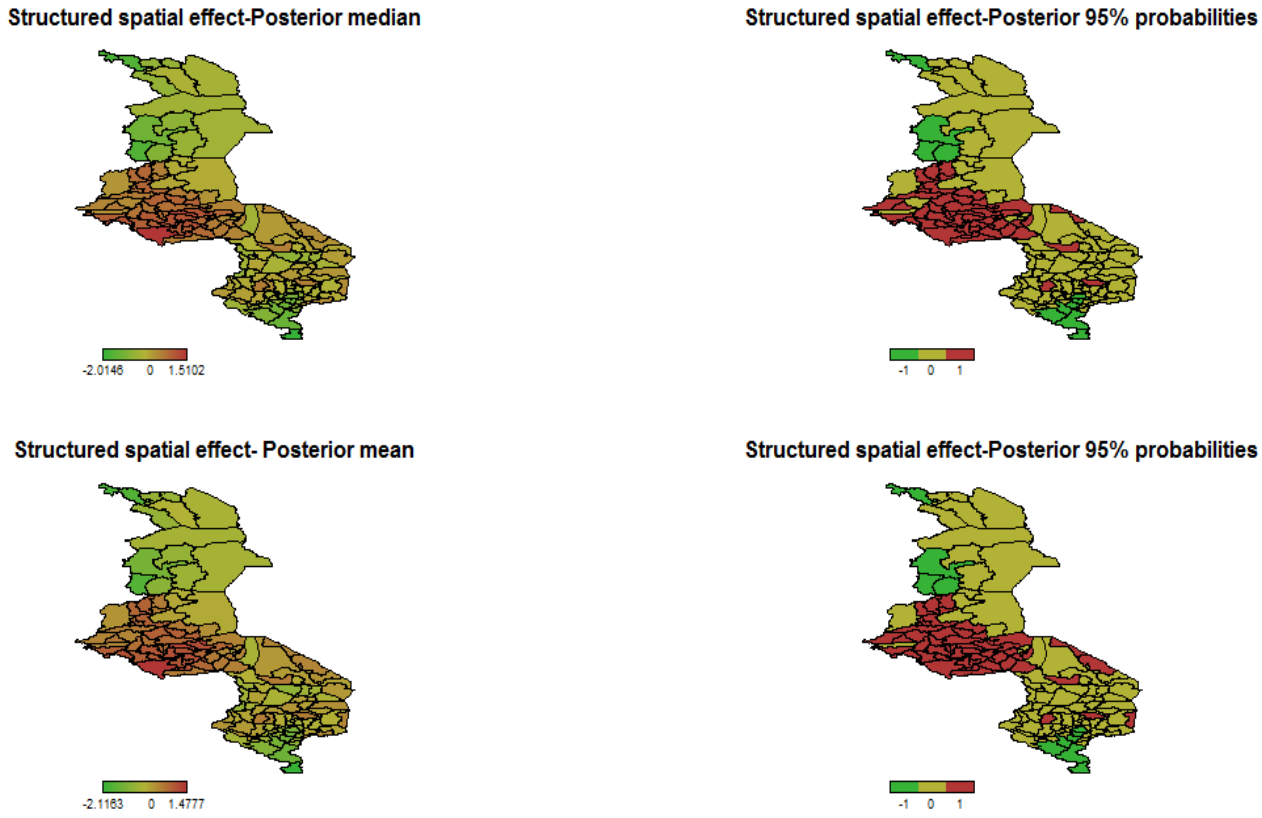


Figure 3-2: Structured spatial effects on coefficients of blood smear positive malaria results showing both mean and median as well as 95% probabilities of malaria risk

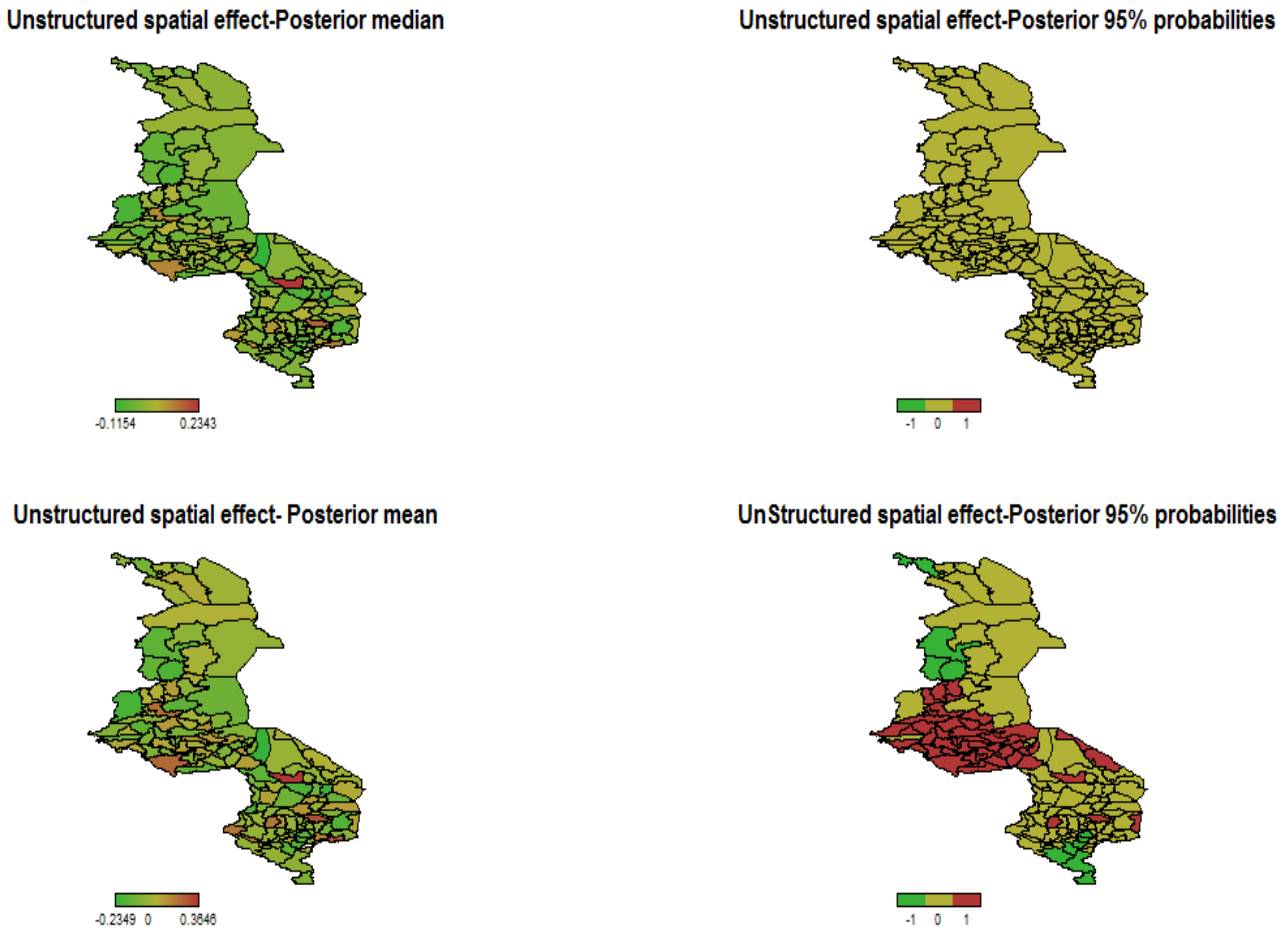


Figure 3-3: Unstructured spatial effects on coefficients of blood smear positive malaria results showing both mean and median as well as 95% probabilities of malaria risk

The other maps that were done using WinBUGS are presented in Appendix 5 and they show the means as well as the probabilities of malaria risk for both structured and unstructured random effects. Maps from both softwares show that the central region is the hotspot for malaria in Malawi.

3.4 Discussion and conclusion

This paper is a follow up on an earlier study that looked at the direct and indirect determinants of malaria morbidity in children under five years in Malawi in the year 2012. SES was an important driver of malaria morbidity. Ownership of land, type of place of residence and residing in a slum or not were significant factors in malaria morbidity. These factors are strongly correlated with SES. This finding confirms what other studies have shown with regards to malaria morbidity. A number of studies that have been carried out have also confirmed that malaria is poverty related (Sachs and Malaney, 2002, Gallup and Sachs, 2001, Teklehaimanot and Paola Mejia, 2008, Malaney et al., 2004, Pattanayak et al., 2006, Worrall et al., 2005).

The environmental factors that were analysed in this study were precipitation, temperature suitability index as well as enhanced vegetation index as these environmental factors have been shown to be important drivers of malaria (Alegana et al., 2013, Weiss et al., 2014, Alegana et al., 2014). These environmental factors were not statistically significant using the modelling techniques that were used in this study.

Looking at the structured and unstructured distribution of the posterior estimates of smear positive malaria results, the central region is the region that is most affected. This finding complements other studies that have been done on malaria in Malawi that showed that the central region is the one that is most affected (Bennett et al., 2013, Dzinjalamala, 2009, Kazembe et al., 2006a). One study explained that this trend was due to the central region being covered by large portions of inland plain land as well as low lying areas along the lake Malawi (Chirombo et al., 2014). The central region of Malawi is the region that has the capital city of Malawi (Lilongwe).

According to a report by UN habitat, 70% of the population in Lilongwe lives in informal settlements with high numbers of people living in those areas living in slum conditions (United Nations and Habitat, 2011)and therefore this increases their vulnerability to malaria infection.

This study also compared frequentist method (STATA) with Bayesian approaches (WINBUGS, INLA and BAYES-X). STATA and BAYES-X were able to incorporate sample population sampling adjustments weights that were done for the 140 clusters (EAs) to account for differences due to the unequal proportions selected per cluster (Ministry of Health et al., 2012, Lowe et al., 2013) which was an advantage for these two methods as this was able to reduce bias associated with survey data. The disadvantage of STATA was that we were unable to incorporate the structured and unstructured spatial effects. The major disadvantage of the WINBUGS method was that it took a long time to run the models. INLA had the quickest time in analysis but the disadvantage that we noticed with this method was that the user had no control over the number of iterations that the method can be done in running the models as the number of iterations was determined internally by the method.

The strengths of this study are; the study was based on the Bayesian goestatistical approach in modelling. This approach is advantageous because structured and unstructured random effects can be introduced into the models and this can help improve the interpretation of the results as spatial correlation may arise because of unobserved variables, and incorporating the spatial random effect in the model can help to account for them (Kazembe et al., 2006a). This study compared models that adjust for sample weights and models that do not adjust for weight and were able to select the best model that took into consideration the sample weights and therefore

adjusting for bias that might result from the use of survey data. Bayesian approaches are able to provide inferences that are conditional on the data but the inferences can be affected by the prior that is used which is a limitation of this analysis method (Musenge et al., 2011). This study also used the CAR model and this approach helps to reduce bias and variance of the posterior estimates (Earnest et al., 2007).

The limitations of this study are; this study only concentrated on spatial aspect but did not look also at the temporal aspect and this could have affected the effects of the random effects as the temporal aspect was lacking. The environmental covariates need to be examined further and could have been affected by the lack of a temporal aspect because environmental covariates are time varying therefore the average annual values that were used in this analysis might be biased therefore resulting in unreliable results.

3.5 Acknowledgments

The authors would like to thank the division of Epidemiology and Biostatistics at the School of Public Health, the University of the Witwatersrand for the support that they offered in the drafting of this paper and ensuring that the study received ethics approval. We also would like to thank the Department of Science and Technology/National Research Foundation (DST/NRF) South African Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) for providing funding that made this research work possible. The Authors would also like to

appreciate Ms Lucy Chimoyi for the invaluable assistance that she offered in preparing the choropleth maps that were used to visualize the spatial effects in this study.

Chapter 4 Discussion and conclusions

This chapter discusses the findings of the research study on the malaria episodes in children under five years in Malawi in the year 2012. The purpose of the research was to analyse the demographic, behavioural as well as the environmental determinants of malaria episodes in children under five years and also investigate if any random effects of malaria episodes and how these affect the prevalence of disease in the selected population.

The findings are going to be categorised according to the behavioural determinants, environmental determinants, and spatial hotspots. The strengths of this study are also going to be discussed. The recommendations from this study will be discussed as well as the conclusions that were obtained from this study.

4.1 Behavioural determinants

This study showed that malaria has got important behavioural related drivers in the disease. A higher SES is associated with a number of factors that lead to lowered malaria transmission, like increased literacy levels, higher access to malaria health awareness campaigns and health education, as well as being able to afford disease prevention methods and treatment (Imbahale et al., 2010, Ademowo et al., 1995, Tarimo et al., 2000). This results in improved malaria control in those of a higher SES. The findings from both chapter 2 and chapter 3 complement each other as far as SES is concerned. Both studies show that SES was an important determinant in malaria morbidity in Malawi in children under 5 in the year 2012. Ownership of land, type of place of residence and whether the household was a slum or not where significant factors in malaria morbidity. These factors and SES are strongly correlated. So this finding confirms what other studies have shown. A number of studies that have been

carried out have also confirmed that malaria is poverty related (Sachs and Malaney, 2002, Gallup and Sachs, 2001, Teklehaimanot and Paola Mejia, 2008, Malaney et al., 2004).

The type of place of residence whether its urban area or rural area as well as region could be linked to the altitude, where some studies (Drakeley et al., 2005a, Hay et al., 2004, Lindsay and Martens, 1998) found an effect on malaria prevalence depending on the altitude. This study also showed that those dwelling in rural areas had a higher risk of contracting malaria as compared to those living in urban areas. This could also be linked to the fact that those living in rural areas are generally of a low economic status compared to their counterparts living in urban areas in one report on malaria and poverty it was shown that poverty results in people living in conditions that promote mosquito breeding (Teklehaimanot and Paola Mejia, 2008). Generally the population of Malawi is mainly rural (Luka, 2010)and this also explain the problem of malaria in Malawi as it is more common in rural populations as this study showed. The higher SES of urban residents contributes to a reduced risk of contracting malaria (Somi et al., 2007); within cities, SES factors contribute to increased transmission in poorer areas with slum conditions. This study showed in that those who dwelt in slum-like conditions were at a higher risk of contracting malaria as compared to those whose dwellings were not classified as slum.

Use of insecticide treated bed nets was also an important factor in malaria control with households that had more children sleeping under ITNs having less cases of malaria in the household. This finding is corroborated by other studies (Maxwell et al., 2002, Deressa et al., 2007, Mmbando et al., 2011) that also found that the use of ITNs is important in malaria

control. This again links to SES as those households with a higher SES are the households that are able to provide ITNs for their children.

The G-SEM's indirect pathways also showed a significant association between cluster altitude and region as well as between SES and education level. G-SEM was used in this study to complement the results from the multiple variable analysis and the results showed that the multiple variable analysis and the G-SEM direct pathways show similar results.

4.2 Environmental determinants

Temperature and rainfall influence malaria endemicity. Altitude is a known factor in influencing temperature and rainfall (Cibulskis et al., 2011, Reiter, 2001). The environmental factors that were analysed in this study were precipitation, TSI as well as EVI as these environmental factors have been shown to be important drivers of malaria (Alegana et al., 2013, Weiss et al., 2014, Alegana et al., 2014). TSI, EVI and precipitation were generated from long-term annual average temperature, vegetation and precipitation and represent estimates of a year (Noor et al., 2013).

These environmental factors that were used in this study were not statistically significant. Cluster altitude was an important variable in the G-SEM models but with Bayesian models, it was not a significant covariate in malaria morbidity.

4.3 Spatial hotspots

Looking at the structured and unstructured distribution of the posterior estimates of smear positive malaria results, the central region is the region that is most affected. This finding

complements other studies that have been done on malaria in Malawi that showed that the central region is the one that is most affected (Bennett et al., 2013, Dzinjalamala, 2009, Kazembe et al., 2006a). One study explained that this trend was due to the central region being covered by large portions of inland plain land as well as low lying areas along lake Malawi (Chirombo et al., 2014). The central region of Malawi is the region that has the capital city of Malawi (Lilongwe) According to a report on Malawi by UN habitat approximately 76 percent of Lilongwe's population lives in informal settlements with poverty standing at about 25 percent and unemployment at 16 percent (Luka, 2010). These poor SES conditions might influence the vulnerability of the city to malaria. In chapter 2, the central region was shown to be the one most affected by malaria and this was done without introducing structured random effects and with the introduction of random effects, this confirmed what the first study showed but now with structured random effects that make the results more precise.

4.4 Recommendations

The following recommendations arise from the findings of this study. These are:

- There must be targeted interventions in malaria prevention programs and concentrate on areas with high prevalence as this will help to maximise the use of the available resources so that malaria can be effectively eliminated
- Health education is important in malaria control, therefore health education materials must be readily available and easily accessible to the targeted population. This health education can result in behaviour change that results in improved prevention of malaria

- ITNs are also an important tool in malaria control and must be made available to the population in need. Funding must be made available in order to provide the required ITNs and programs must prioritise their availability and need to have in place a budget to adequately supply ITNs to the population
- There must be programs to empower the communities so that they improve their SES and this in turn helps to reduce prevalence of malaria
- It is important that care-givers especially mothers have access to information on malaria and how to identify signs and symptoms so that suspicious cases can be quickly identified and appropriate action is taken in order for the children to get the treatment that they need
- Bayesian geostatistical modelling helps to model random effects and should be used more in disease modelling.
- G-SEM is an important tool in disease modelling and can be utilised more in identifying disease determinants.

4.5 Conclusions

It is important to understand the determinants of malaria so that effective monitoring and evaluation of malaria can be carried out. This study showed the importance of socio-economic status as well as education in the fight against malaria. In order for malaria to be eliminated in the population it is important for the government to empower the population economically and also ensure that health education is a part of the efforts that are put in place to fight malaria. This will assist in the fight to eliminate malaria. It is important to ensure that resources are channeled in order to optimize prevention strategies that are put in place. Once the population is empowered, then preventative strategies for malaria elimination can then be

implemented successfully and if the population is educated, then it is able to understand better the strategies in place and implement them successfully. The government must be economically sound in order to effectively implement the malaria control strategies so resources must be in place to implement malaria control strategies as well as sustaining them. The other important determinates also are linked to socio-economic status, therefore reduction of poverty will go a long way in the fight to eliminate malaria.

More work needs to be done on the identification of hotspots and identifying the determinants in specific populations. This will help in ensuring that the interventions are not generic but specific for a given population.

References

ABEKU, T. A., VAN OORTMARSSEN, G. J., BORSBOOM, G., DE VLAS, S. J. & HABBEMA, J. D. F. 2003. Spatial and temporal variations of malaria epidemic risk in Ethiopia: factors involved and implications. *Acta Tropica,* 87**,** 331-340.

ADEMOWO, O., FALUSI, A. & MEWOYEKA, O. 1995. Prevalence of asymptomatic parasitaemia in an urban and rural community in south western Nigeria. *The Central African journal of medicine,* 41**,** 18-21.

AKAZILI, J., AIKINS, M. & BINKA, F. N. 2008. Malaria treatment in Northern Ghana: What is the treatment cost per case to households? *African Journal of Health Sciences,* 14**,** 70-79.

ALEGANA, V. A., ATKINSON, P. M., WRIGHT, J. A., KAMWI, R., UUSIKU, P., KATOKELE, S., SNOW, R. W. & NOOR, A. M. 2013. Estimation of malaria incidence in northern Namibia in 2009 using Bayesian conditional-autoregressive spatial–temporal models. *Spatial and spatio-temporal epidemiology,* 7**,** 25-36.

ALEGANA, V. A., WRIGHT, J. A., NAHZAT, S. M., BUTT, W., SEDIQI, A. W., HABIB, N., SNOW, R. W., ATKINSON, P. M. & NOOR, A. M. 2014. Modelling the Incidence of Plasmodium vivax and Plasmodium falciparum Malaria in Afghanistan 2006–2009. *PloS one,* 9**,** e102304.

ARMINGER, G. & MUTHÉN, B. O. 1998. A Bayesian approach to nonlinear latent variable models using the Gibbs sampler and the Metropolis-Hastings algorithm. *Psychometrika,* 63**,** 271-300.

AUSTIN, P. C. 2011. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behavioral Research,* 46**,** 399-424.

AYENI, A. 2011. Malaria morbidity in Akure, southwest Nigeria: A temporal observation in a climate change scenario. *Trends in Applied Sciences Research,* 6**,** 488-494.

BANERJEE, S., GELFAND, A. E. & CARLIN, B. P. 2004. *Hierarchical modeling and analysis for spatial data*, Crc Press.

BATES, I., FENTON, C., GRUBER, J., LALLOO, D., LARA, A. M., SQUIRE, S. B., THEOBALD, S., THOMSON, R. & TOLHURST, R. 2004a. Vulnerability to malaria, tuberculosis, and HIV/AIDS infection and disease. Part 1: determinants operating at individual and household level. *The Lancet Infectious Diseases*, 4**,** 267-277.

BATES, I., FENTON, C., GRUBER, J., LALLOO, D., LARA, A. M., SQUIRE, S. B., THEOBALD, S., THOMSON, R. & TOLHURST, R. 2004b. Vulnerability to malaria, tuberculosis, and HIV/AIDS infection and disease. Part II:

determinants operating at environmental and institutional level. *The Lancet Infectious Diseases,* 4**,** 368-375.

BELITZ, C., BREZGER, A., KNEIB, T., LANG, S. & UMLAUF, N. 2012. *BayesX - Software for Bayesian inference in structured additive regression models Version 2.1. 2.1* [Online]. Munich Germany. Available: http://www.stat.uni-muenchen.de/~bayesx/bayesxdownload.html.

BELL, D. R., JORGENSEN, P., CHRISTOPHEL, E. M. & PALMER, K. L. 2005. Malaria risk: estimation of the malaria burden. *Nature,* 437**,** E3-4; discussion E4-5.

BENNETT, A., KAZEMBE, L., MATHANGA, D. P., KINYOKI, D., ALI, D., SNOW, R. W. & NOOR, A. M. 2013. Mapping malaria transmission intensity in Malawi, 2000-2010. *Am J Trop Med Hyg,* 89**,** 840-9.

BEST, N., RICHARDSON, S. & THOMSON, A. 2005. A comparison of Bayesian spatial models for disease mapping. *Statistical methods in medical research,* 14**,** 35-59.

BLOLAND, P. B., BORIGA, D. A., RUEBUSH, T. K., MCCORMICK, J. B., ROBERTS, J. M., OLOO, A. J., HAWLEY, W., LAL, A., NAHLEN, B. & CAMPBELL, C. C. 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. *American Journal of Tropical Medicine and Hygiene,* 60**,** 641-8.

BOWIE, C. 2007. The burden of disease in Malawi. *Malawi Medical Journal,* 18**,** 104-110.

BREMAN, J. G. 2001. The ears of the hippopotamus: manifestations, determinats and estimates of the malaria burden. *Am J Trop Med Hyg,* 64**,** 1-11.

BREMAN, J. G., ALILIO, M. S. & MILLS, A. 2004. Conquering the intolerable burden of malaria: what's new, what's needed: a summary. *The American journal of tropical medicine and hygiene,* 71**,** 1-15.

BROOKER, S., CLARKE, S., SNOW, R. W. & BUNDY, D. A. 2008. Malaria in African schoolchildren: options for control. *Trans R Soc Trop Med Hyg,* 102**,** 304-5.

CALIENDO, M. & KOPEINIG, S. 2008. Some practical guidance for the implementation of propensity score matching. *Journal of economic surveys,* 22**,** 31-72.

CAMERON, A. C. & TRIVEDI, P. K. 2013. *Regression analysis of count data*, Cambridge university press.

CARLIN, B. P. & LOUIS, T. A. 2000. *Bayes and empirical Bayes methods for data analysis*, CRC Press.

CARNEIRO, I. A., SMITH, T., LUSINGU, J. P., MALIMA, R., UTZINGER, J. & DRAKELEY, C. J. 2006. Modeling the relationship between the population prevalence of Plasmodium falciparum malaria and anemia. *The American journal of tropical medicine and hygiene,* 75**,** 82-89.

CASELLA, G. & GEORGE, E. I. 1992. Explaining the Gibbs sampler. *The American Statistician,* 46**,** 167-174.

CAULFIELD, L. E., RICHARD, S. A. & BLACK, R. E. 2004. Undernutrition as an underlying cause of malaria morbidity and mortality in children less than five years old. *The American journal of tropical medicine and hygiene,* 71**,** 55-63.

CDC. *Impact of malaria* [Online]. Available: http://www.cdc.gov/malaria/malaria_worldwide/impact.html [Accessed April 30 2013].

CHIB, S. & GREENBERG, E. 1995. Understanding the metropolis-hastings algorithm. *The American Statistician,* 49**,** 327-335.

CHIROMBO, J., LOWE, R. & KAZEMBE, L. 2014. Using Structured Additive Regression Models to Estimate Risk Factors of Malaria: Analysis of 2010 Malawi Malaria Indicator Survey Data. *PloS one,* 9**,** e101116.

CIBULSKIS, R. E., AREGAWI, M., WILLIAMS, R., OTTEN, M. & DYE, C. 2011. Worldwide incidence of malaria in 2009: estimates, time trends, and a critique of methods. *PLoS medicine,* 8**,** e1001142.

CLEMENTS, A. C., LWAMBO, N. J., BLAIR, L., NYANDINDI, U., KAATANO, G., KINUNG'HI, S., WEBSTER, J. P., FENWICK, A. & BROOKER, S. 2006. Bayesian spatial analysis and disease mapping: tools to enhance planning and implementation of a schistosomiasis control programme in Tanzania. *Tropical medicine & international health,* 11**,** 490-503.

CONNOR, S. J., CECCATO, P. N., DINKU, T., OMUMBO, J. A., GROVER-KOPEC, E. K. & THOMSON, M. C. 2006. Using climate information for improved health in Africa: relevance, constraints and opportunities. *Geospatial health,* 1**,** 17-31.

COX, J., HAY, S. I., ABEKU, T. A., CHECCHI, F. & SNOW, R. W. 2007. The uncertain burden of Plasmodium falciparum epidemics in Africa. *Trends Parasitol,* 23**,** 142-8.

CROMWELL, E. & KYEGOMBE, N. 2005. Food security options in Malawi: good neighbours make good friends. *Country Food Security Options Paper*, 2.

DERESSA, W., ALI, A. & BERHANE, Y. 2007. Household and socioeconomic factors associated with childhood febrile illnesses and treatment seeking behaviour in an area of epidemic malaria in rural Ethiopia. *Transactions of the Royal Society of Tropical Medicine and Hygiene,* 101**,** 939-947.

DRAKELEY, C., CORRAN, P., COLEMAN, P., TONGREN, J., MCDONALD, S., CARNEIRO, I., MALIMA, R., LUSINGU, J., MANJURANO, A. & NKYA, W. 2005a. Estimating medium-and long-term trends in malaria transmission by using serological markers of malaria exposure. *Proceedings of the National Academy of Sciences of the United States of America,* 102**,** 5108-5113.

DRAKELEY, C. J., CARNEIRO, I., REYBURN, H., MALIMA, R., LUSINGU, J. P., COX, J., THEANDER, T. G., NKYA, W. M., LEMNGE, M. M. & RILEY, E. M. 2005b. Altitude-dependent and-independent variations in Plasmodium falciparum prevalence in northeastern Tanzania. *Journal of Infectious Diseases,* 191**,** 1589-1598.

DZINJALAMALA, F. 2009. Epidemiology of malaria in Malawi. *In:* GUEBBELS, E. & BOWIE, C. (eds.) *Epidemiology of Malawi.* Division of Community Health: University of Malawi College of Medicine.

EARNEST, A., MORGAN, G., MENGERSEN, K., RYAN, L., SUMMERHAYES, R. & BEARD, J. 2007. Evaluating the effect of neighbourhood weight matrices on smoothing properties of Conditional Autoregressive (CAR) models. *International journal of health geographics,* 6**,** 54.

ELLIOTT, P., MARTUZZI, M. & SHADDICK, G. 1995. Spatial statistical methods in environmental epidemiology: a critique. *Statistical Methods in Medical Research,* 4**,** 137-159.

FEACHEM, R. G., PHILLIPS, A. A., HWANG, J., COTTER, C., WIELGOSZ, B., GREENWOOD, B. M., SABOT, O., RODRIGUEZ, M. H., ABEYASINGHE, R. R. & GHEBREYESUS, T. A. 2010. Shrinking the malaria map: progress and prospects. *The Lancet,* 376**,** 1566-1578.

FRUHWIRTH-SCHNATTER, S. 2013. Bayesian computing without tears-Try your luck with Monte Carlo algorithms. *In:* INSTITUTE FOR STATISTICS AND MATHEMATICS, D. O. F., ACCOUNTING AND STATISTICS, VIENNA UNIVERSITY OF ECONOMICS AND BUSINESS (ed.).

GALLUP, J. L. & SACHS, J. D. 2001. The economic burden of malaria. *The American journal of tropical medicine and hygiene,* 64**,** 85-96.

GEMAN, S. & GEMAN, D. 1993. Stochastic relaxation, Gibbs distributions and the Bayesian restoration of images*. *Journal of Applied Statistics,* 20**,** 25-62.

GETHING, P. W., PATIL, A. P., SMITH, D. L., GUERRA, C. A., ELYAZAR, I., JOHNSTON, G. L., TATEM, A. J. & HAY, S. I. 2011. A new world malaria map: Plasmodium falciparum endemicity in 2010. *Malar J,* 10**,** 1475-2875.

GOOVAERTS, P. 2006. Geostatistical analysis of disease data: accounting for spatial support and population density in the isopleth mapping of cancer mortality risk using area-to-point Poisson kriging. *International Journal of Health Geographics,* 5**,** 52.

GOSONIU, L., MSENGWA, A., LENGELER, C. & VOUNATSOU, P. 2012. Spatially explicit burden estimates of malaria in Tanzania: Bayesian geostatistical modeling of the malaria indicator survey data. *PloS one,* 7**,** e23966.

GOSONIU, L., VOUNATSOU, P., SOGOBA, N. & SMITH, T. 2006. Bayesian modelling of geostatistical malaria risk data. *Geospatial Health,* 1**,** 127-139.

GUERRA, C. A., GIKANDI, P. W., TATEM, A. J., NOOR, A. M., SMITH, D. L., HAY, S. I. & SNOW, R. W. 2008. The limits and intensity of Plasmodium falciparum transmission: implications for malaria control and elimination worldwide. *PLoS medicine,* 5**,** e38.

GUIKEMA, S. D. & GOFFELT, J. P. 2008. A flexible count data regression model for risk analysis. *Risk analysis,* 28**,** 213-223.

HAY, S. I., GUERRA, C. A., GETHING, P. W., PATIL, A. P., TATEM, A. J., NOOR, A. M., KABARIA, C. W., MANH, B. H., ELYAZAR, I. R., BROOKER, S., SMITH, D. L., MOYEED, R. A. & SNOW, R. W. 2009. A world malaria map: Plasmodium falciparum endemicity in 2007. *PLoS Med,* 6**,** e1000048.

HAY, S. I., GUERRA, C. A., TATEM, A. J., NOOR, A. M. & SNOW, R. W. 2004. The global distribution and population at risk of malaria: past, present, and future. *Lancet Infect Dis,* 4**,** 327-36.

HEILIG, G. K. 2012. World urbanization prospects the 2011 revision. *United Nations, Department of Economic and Social Affairs (DESA), Population Division, Population Estimates and Projections Section, New York*.

HERRERO, M. D., RIVAS, P., RALLÓN, N. I., RAMÍREZ-OLIVENCIA, G. & PUENTE, S. 2007. HIV and malaria. *Aids Rev,* 9**,** 88-98.

HESS, F. I., NUKURO, E., JUDSON, L., RODGERS, J., NOTHDURFT, H. D. & RIECKMANN, K. H. 1997. Anti-malarial drug resistance, malnutrition and socio-economic status. *Trop Med Int Health,* 2**,** 721-28.

HUFFMAN, G. J. & BOLVIN, D. T. 2013. GPCP Version 2.2 SG Combined Precipitation Data Set Documentation.

IMBAHALE, S., FILLINGER, U., GITHEKO, A., MUKABANA, W. & TAKKEN, W. 2010. An exploratory survey of malaria prevalence and people's knowledge, attitudes and practices of mosquito larval source management for malaria control in western Kenya. *Acta tropica,* 115**,** 248-256.

INGSTAD, B., MUNTHALI, A. C., BRAATHEN, S. H. & GRUT, L. 2012. The evil circle of poverty: a qualitative study of malaria and disability. *Malar. J,* 11**,** 15.

INSTITUTE FOR HEALTH METRICS AND EVALUATION. 2012. *GBD Profile:Malawi* [Online]. Health metrics and evaluation. Available: http://www.healthdata.org/sites/default/files/files/country_profiles/GBD/ihme_gbd_country_report_malawi.pdf [Accessed April 29 2013].

JUMBE, C. B. & ANGELSEN, A. 2011. Modeling choice of fuelwood source among rural households in Malawi: a multinomial probit analysis. *Energy Economics,* 33**,** 732-738.

KALU, K. M., OBASI, N. A., NDUKA, F. O. & OKO, M. O. 2012. Prevalence of Malaria Parasitaemia in Umuchieze and Uturu Communities of Abia State, Nigeria. *Asian Journal of Epidemiology,* 5.

KAZEMBE, L. N. 2007. Spatial modelling and risk factors of malaria incidence in northern Malawi. *Acta Tropica,* 102**,** 126-137.

KAZEMBE, L. N., KLEINSCHMIDT, I., HOLTZ, T. H. & SHARP, B. L. 2006a. Spatial analysis and mapping of malaria risk in Malawi using point-referenced prevalence of infection data. *International Journal of Health Geographics,* 5**,** 41.

KAZEMBE, L. N., KLEINSCHMIDT, I. & SHARP, B. L. 2006b. Patterns of malaria-related hospital admissions and mortality among Malawian children: an example of spatial modelling of hospital register data. *Malar J,* 5**,** 93.

KIANG, R., ADIMI, F. & SOEBIYANTO, R. 2009. *MALARIA MODELING & SURVEILLANCE* [Online]. Available: http://appliedsciences.nasa.gov/pdf/09Kiang_malaria_benchmark_report.pdf [Accessed April 30 2013].

LAW, D. G., SERRE, M., CHRISTAKOS, G., LEONE, P. & MILLER, W. 2004. Spatial analysis and mapping of sexually transmitted diseases to optimise intervention and prevention strategies. *Sexually Transmitted Infections,* 80**,** 294-299.

LAWSON, A., BIGGERI, A., BÖHNING, D., LESAFFRE, E., VIEL, J.-F. & BERTOLLINI, R. 1999. *Disease mapping and risk assessment for public health*, John Wiley & Sons.

LAWSON, A. B. 2013. *Bayesian disease mapping: hierarchical modeling in spatial epidemiology*, CRC Press.

LINDSAY, S. & MARTENS, W. 1998. Malaria in the African highlands: past, present and future. *Bulletin of the World Health Organization,* 76**,** 33.

LOWE, R., CHIROMBO, J. & TOMPKINS, A. M. 2013. Relative importance of climatic, geographic and socio-economic determinants of malaria in Malawi. *Malaria journal,* 12**,** 416.

LUKA, L. The case for improved governance as a tool for sustainable urban development in Malawi. 46th ISOCARP Conference, Nairobi, Kenya, September, 2010.

LUNN, D. J., THOMAS, A., BEST, N. & SPIEGELHALTER, D. 2000. WinBUGS-a Bayesian modelling framework: concepts, structure, and extensibility. *Statistics and computing,* 10**,** 325-337.

MALANEY, P., SPIELMAN, A. & SACHS, J. 2004. The malaria gap. *The American journal of tropical medicine and hygiene,* 71**,** 141-146.

MAPIRA, J. & MUNTHALI, A. 2011. Household energy demand: wood fuel consumption and peri-urban deforestation in the city of Masvingo (Zimbabwe). *Journal of Sustainable Development in Africa,* 13**,** 264-279.

MAWILI-MBOUMBA, D. P., AKOTET, M. K. B., KENDJO, E., NZAMBA, J., MEDANG, M. O., MBINA, J.-R. M. & KOMBILA, M. 2013. Increase in malaria prevalence and age of at risk population in different areas of Gabon. *Malaria journal,* 12.

MAXWELL, C. A., MSUYA, E., SUDI, M., NJUNWA, K., CARNEIRO, I. & CURTIS, C. 2002. Effect of community-wide use of insecticide-treated nets for 3–4 years on malarial morbidity in Tanzania. *Tropical Medicine & International Health,* 7**,** 1003-1008.

MENDIS, K. N. & CARTER, R. 1995. Clinical disease and pathogenesis in malaria. *Parasitology Today,* 11**,** PTI1-PTI16.

MESSINA, J. P., TAYLOR, S. M., MESHNICK, S. R., LINKE, A. M., TSHEFU, A. K., ATUA, B., MWANDAGALIRWA, K. & EMCH, M. 2011. Population, behavioural and environmental drivers of malaria prevalence in the Democratic Republic of Congo. *Malar J,* 10**,** 10.1186.

MHALU, F. S. 2005. Burden of diseases in poor resource countries: meeting the challenges of combating HIV/AIDS, tuberculosis and malaria. *Tanzan Health Res Bull,* 2005**,** 179-84.

MINISTRY OF HEALTH, NATIONAL MALARIA CONTROL PROGRAMME , MEASURE DHS & ICF INTERNATIONAL. 2012. *Malawi Malaria Indicator Survey (MIS) 2012* [Online]. Available: http://dhsprogram.com/publications/publication-MIS13-MIS-Final-Reports.cfm#sthash.BY2v7tMf.dpuf [Accessed June 01 2013].

MMBANDO, B. P., KAMUGISHA, M. L., LUSINGU, J. P., FRANCIS, F., ISHENGOMA, D. S., THEANDER, T. G., LEMNGE, M. M. & SCHEIKE, T. H. 2011. Spatial variation and socio-economic determinants of Plasmodium falciparum infection in northeastern Tanzania. *Malaria journal,* 10**,** 145.

MODIS. 2011. *EVI data archives* [Online]. Available: http://n4ft101u.ecs.nasa.gov/SAN/MOST/MOD10A2.005 [Accessed May 01 2013].

MUSENGE, E., CHIRWA, T. F., KAHN, K. & VOUNATSOU, P. 2013a. Bayesian analysis of zero inflated spatiotemporal HIV/TB child mortality data through the INLA and SPDE approaches: Applied to data observed between

1992 and 2010 in rural North East South Africa. *International Journal of Applied Earth Observation and Geoinformation,* 22**,** 86-98.

MUSENGE, E., VOUNATSOU, P., COLLINSON, M., TOLLMAN, S. & KHAN, K. 2013b. The contribution of spatial analysis to understsanding HIV/TB mortality in children:a structural equation modelling approach. *Global Health Action,* 6.

MUSENGE, E., VOUNATSOU, P. & KAHN, K. 2011. Space-time confounding adjusted determinants of child HIV/TB mortality for large zero-inflated data in rural South Africa. *Spatial and spatio-temporal epidemiology,* 2**,** 205-217.

NET ODA. 2011. *Millennium Development Goals* [Online]. Available: http://www1.eis.gov.bw/EIS/Web%20Page/MDG.aspx [Accessed July 01 2013].

NOBRE, A. A., SCHMIDT, A. M. & LOPES, H. F. 2005. Spatio-temporal models for mapping the incidence of malaria in Pará. *Environmetrics,* 16**,** 291-304.

NOON, C. E. & HANKINS, C. Spatial data visualization in healthcare: supporting a facility location decision via GIS-based market analysis. System Sciences, 2001. Proceedings of the 34th Annual Hawaii International Conference on, 2001. IEEE, 10 pp.

NOOR, A. M., ALEGANA, V. A., PATIL, A. P., MOLONEY, G., BORLE, M., YUSUF, F., AMRAN, J. & SNOW, R. W. 2012. Mapping the receptivity of malaria risk to plan the future of control in Somalia. *BMJ Open,* 2.

NOOR, A. M., GETHING, P. W., ALEGANA, V. A., PATIL, A. P., HAY, S. I., MUCHIRI, E., JUMA, E. & SNOW, R. W. 2009. The risks of malaria infection in Kenya in 2009. *BMC Infect Dis,* 9**,** 180.

NOOR, A. M., UUSIKU, P., KAMWI, R. N., KATOKELE, S., NTOMWA, B., ALEGANA, V. A. & SNOW, R. W. 2013. The receptive versus current risks of Plasmodium falciparum transmission in Northern Namibia: implications for elimination. *BMC infectious diseases,* 13**,** 184.

NTZOUFRAS, I. 2011. *Bayesian modeling using WinBUGS*, John Wiley & Sons.

O'MEARA, W. P., BEJON, P., MWANGI, T. W., OKIRO, E. A., PESHU, N., SNOW, R. W., NEWTON, C. R. & MARSH, K. 2008. Effect of a fall in malaria transmission on morbidity and mortality in Kilifi, Kenya. *The lancet,* 372**,** 1555-1562.

OKELLO, P. E., VAN BORTEL, W., BYARUHANGA, A. M., CORREWYN, A., ROELANTS, P., TALISUNA, A., D'ALESSANDRO, U. & COOSEMANS, M. 2006. Variation in malaria transmission intensity in

seven sites throughout Uganda. *The American journal of tropical medicine and hygiene,* 75**,** 219-225.

OKENU, D. M. 1999. An integrated approach for malaria control in Africa. *Malaria and Infectious Disease in Africa,* 10**,** 4-13.

OKIRO, E. A., NOOR, A. M., MALINGA, J., MITTO, B., MUNDIA, C. W., MATHANGA, D., MZILAHOWA, T. & SNOW, R. W. 2014. An epidemiological profile of malaria and its control in Malawi. A report prepared for the Ministry of Health, the Roll Back Malaria partnership and the Department for International Development. UK.

OLADEINDE, B., OMOREGIE, R., OLLEY, M., ANUNIBE, J., ONIFADE, A. & OLADEINDE, O. 2012. Malaria and Anemia among Children in a Low Resource Setting In Nigeria. *Iranian journal of parasitology,* 7**,** 31.

OMUMBO, J. A., HAY, S. I., SNOW, R. W., TATEM, A. J. & ROGERS, D. J. 2005. Modelling malaria risk in East Africa at high-spatial resolution. *Trop Med Int Health,* 10**,** 557-66.

PALMER, D. 2006. Tackling Malawi's human resources crisis. *Reproductive health matters,* 14**,** 27-39.

PATTANAYAK, S., DICKINSON, K., COREY, C., MURRAY, B., SILLS, E. & KRAMER, R. 2006. Deforestation, malaria, and poverty: a call for

transdisciplinary research to support the design of cross-sectoral policies. *Sustainability: Science Practice and Policy,* 2**,** 45-56.

PATZ, J. A. & OLSON, S. H. 2006. Malaria risk and temperature: Influences from global climate change and local land use practices. *Proceedings of the National Academy of Sciences,* 103**,** 5635-5636.

PEIKES, D. N., MORENO, L. & ORZOL, S. M. 2008. Propensity score matching. *The American Statistician,* 62.

PRICE, R. N., SIMPSON, J. A., NOSTEN, F., LUXEMBURGER, C., HKIRJAROEN, L., TER KUILE, F., CHONGSUPHAJAISIDDHI, T. & WHITE, N. J. 2001. Factors contributing to anemia after uncomplicated falciparum malaria. *The American Journal of Tropical Medicine and Hygiene,* 65**,** 614-622.

PROSPER, B. L. & DUKER, A. A. 2012. Spatio-temporal and statistical analysis of malaria in Amansie west district of Ghana. *Intenational Journal of Engineering Research & Technology***,** 6-20.

QUANTUM, G. 2011. *Development Team, 2012. Quantum GIS Geographic Information System. Open Source Geospatial Foundation Project* [Online]. Available: http://qgis.osgeo.org [Accessed March 01 2014].

REITER, P. 2001. Climate change and mosquito-borne disease. *Environmental health perspectives,* 109**,** 141.

REITER, P. 2008. Global warming and malaria: knowing the horse before hitching the cart. *Malaria Journal,* 7**,** S3.

RICCI, F. 2012. Social implications of malaria and their relationships with poverty. *Mediterranean journal of hematology and infectious diseases,* 4.

RIEDEL, N., VOUNATSOU, P., MILLER, J. M., GOSONIU, L., CHIZEMA-KAWESHA, E., MUKONKA, V. & STEKETEE, R. W. 2010. Geographical patterns and predictors of malaria risk in Zambia: Bayesian geostatistical modelling of the 2006 Zambia national malaria indicator survey (ZMIS). *Malar J,* 9**,** 37.

RUBIN, D. B. & THOMAS, N. 1996. Matching using estimated propensity scores: relating theory to practice. *Biometrics***,** 249-264.

SACHS, J. & MALANEY, P. 2002. The economic and social burden of malaria. *Nature,* 415**,** 680-685.

SARNA, A., LUCHTERS, S., MUSENGE, E., OKAL, J., CHERSICH, M., TUN, W., MALL, S., KINGOLA, N. & KALIBALA, S. 2013. Effectiveness of a community-based positive prevention intervention for people living with

HIV who are not receiving antiretroviral treatment: a prospective cohort study. *Global Health: Science and Practice,* 1**,** 52-67.

SNOW, R. W., AMRATIA, P., KABARIA, C. W., NOOR, A. M. & MARSH, K. 2012. The changing limits and incidence of malaria in Africa: 1939–2009. *Advances in parasitology,* 78**,** 169.

SNOW, R. W., 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**,** 624-40.

SNOW, R. W., CRAIG, M. H., NEWTON, C. & STEKETEE, R. W. 2003a. The public health burden of Plasmodium falciparum malaria in Africa. Working Paper 11. Disease Control Priorities Project, Bethesda, Maryland, USA: Fogarty International Center, National Institutes of Health.

SNOW, R. W., CRAIG, M. H., NEWTON, C. & STEKETEE, R. W. 2003b. *The public health burden of Plasmodium falciparum malaria in Africa* [Online]. Working Paper 11. Disease Control Priorities Project, Bethesda, Maryland, USA: Fogarty International Center, National Institutes of Health. Available: http://archives.who.int/prioritymeds/report/append/610snow_wp11.pdf [Accessed 08 April 2013].

SNOW, R. W., MARSH, K. & LE SUEUR, D. 1996. The need for maps of transmission intensity to guide malaria control in Africa. *Parasitology Today***,** 455-457.

SNOW, R. W. & OMUMBO, J. A. 2006. Malaria. *In:* JAMISON, D. T., FEACHEM, R. G., MAKGOBA, M. W., BOS, E. R., BAINGANA, F. K., HOFMAN, K. J. & ROGO, K. O. (eds.) *Disease and Mortality in Sub-Saharan Africa.* 2nd ed. Washington (DC).

SOMI, M. F., BUTLER, J. R., VAHID, F., NJAU, J., KACHUR, S. P. & ABDULLA, S. 2007. Is there evidence for dual causation between malaria and socioeconomic status? Findings from rural Tanzania. *The American journal of tropical medicine and hygiene,* 77**,** 1020-1027.

STRATTON, L., O'NEILL, M. S., KRUK, M. E. & BELL, M. L. 2008. The persistent problem of malaria: Addressing the fundamental causes of a global killer. *Social Science & Medicine,* 67**,** 854-862.

SUN, D., TSUTAKAWA, R. K., KIM, H. & HE, Z. 2000. Spatio-temporal interaction with disease mapping. *Statistics in Medicine,* 19**,** 2015-2035.

TAKEM, E. N., ACHIDI, E. A. & NDUMBE, P. M. 2010. An update of malaria infection and anaemia in adults in Buea, Cameroon. *BMC research notes,* 3**,** 121.

TARIMO, D. S., LWIHULA, G. K., MINJAS, J. N. & BYGBJERG, I. C. 2000. Mothers' perceptions and knowledge on childhood malaria in the holendemic Kibaha district, Tanzania: implications for malaria control and the IMCI strategy. *Tropical Medicine & International Health,* 5**,** 179-184.

TEAM, R. C. 2012. R: A language and environment for statistical computing.

TEKLEHAIMANOT & PAOLA MEJIA, A. 2008. Malaria and poverty. *Annals of the New York Academy of Sciences,* 1136**,** 32-37.

THE GLOBAL POVERTY PROJECT. *Malaria and extreme poverty* [Online]. Available: http://www.globalpovertyproject.com/infobank/malaria [Accessed July 10 2013].

THE GLOBAL POVERTY PROJECT Malaria and extreme poverty. http://www.globalpovertyproject.com/infobank/malaria

THE MALARIA ATLAS PROJECT. 2010. *The spatial distribution of Plasmodium falciparum malaria stratified by endemicity class map in 2010 in Africa+* [Online]. Available: http://www.map.ox.ac.uk/browse-resources/endemicity/Pf_class/africa-plus/ [Accessed September 09 2014].

ULLMAN, J. B. & BENTLER, P. M. 2003. *Structural equation modeling,* Wiley Online Library.

UNITED NATIONS UN National Accounts main aggregates database

http://unstats.un.org/unsd/snaama/introduction.asp

UNITED NATIONS. *UN National Accounts main aggregates database*

[Online]. Available: http://unstats.un.org/unsd/snaama/introduction.asp [Accessed July 21 2013].

UNITED NATIONS & HABITAT. 2011. *Malawi: Lilongwe Urban Profile* [Online]. United Nations Human Settlements Programm. Available: http://www.unhabitat.org [Accessed August 25 2014].

UNITED NATIONS DEVELOPMENT PROGRAMME. 2011. *Malawi: Human development indicators* [Online]. NY: United Nations Development Programme. Available: http://hdr.undp.org/en/countries/profiles/MWI [Accessed June 01 2013].

WAKEFIELD, J. 2007. Disease mapping and spatial regression with count data. *Biostatistics,* 8**,** 158-183.

WEBSTER, T., VIEIRA, V., WEINBERG, J. & ASCHENGRAU, A. 2006. Method for mapping population-based case-control studies: an application using generalized additive models. *International Journal of Health Geographics,* 5**,** 26.

WEISS, D. J., BHATT, S., MAPPIN, B., VAN BOECKEL, T. P., SMITH, D. L., HAY, S. I. & GETHING, P. W. 2014. Air temperature suitability for Plasmodium falciparum malaria transmission in Africa 2000-2012: a high-resolution spatiotemporal prediction. *Malaria Journal,* 13**,** 1-11.

WILSON, M. L., WALKER, E. D., MZILAHOWA, T., MATHANGA, D. P. & TAYLOR, T. E. 2012. Malaria elimination in Malawi: Research needs in highly endemic, poverty-stricken contexts. *Acta Tropica,* 121**,** 218-226.

WINSKILL, P., ROWLAND, M., MTOVE, G., MALIMA, R. C. & KIRBY, M. J. 2011. Malaria risk factors in north-east Tanzania. *Malar J,* 10**,** 98.

WORD BANK. 2013. *Country Brief: Malawi* [Online]. Available: http://www.worldbank.org/en/country/malawi/overview [Accessed October 10 2014].

WORLD BANK GROUP. *Malawi Country Data Profile* [Online]. Available: http://devdata.worldbank.org/external/CPProfile.asp?CCODE=MWI&PTYPE=CP [Accessed November 05 2013].

WORLD CLIMATE. 2012. *Gobal Climate Database* [Online]. Available: http://www.worldclim.org [Accessed May 01 2013].

WORLD HEALTH ORGANISATION. 2011. *Malaria factsheet* [Online]. Available: http://www.who.int/mediacentre/factsheets/fs094/en/ [Accessed May 04 2013].

WORLD HEALTH ORGANIZATION. *Malaria and HIV/AIDS interactions and implications: conclusions of a technical consultation convened by WHO, 23-25 June 2004* [Online]. Available: http://www.who.int/hiv/pub/malaria/en/malaria_hiv_aids.pdf [Accessed April 01 2013].

WORLD HEALTH ORGANIZATION. *Malaria in children under five* [Online]. Available: http://www.who.int/malaria/areas/high_risk_groups/children/en/ [Accessed September 05 2013].

WORLD HEALTH ORGANIZATION. *Millennium development goals* [Online]. Available: http://www.who.int/topics/millennium_development_goals/en/ [Accessed June 01 2013].

WORLD HEALTH ORGANIZATION. *What is malaria?* [Online]. Available: http://www.who.int/inf-fs/en/InformationSheet01.pdf. [Accessed April 30 2013].

WORLD HEALTH ORGANIZATION. 2012. *World malaria report* [Online]. Available:

http://www.who.int/malaria/publications/world_malaria_report_2012/wmr2012_no_profiles.pdf [Accessed April 29 2013].

WORRALL, E., BASU, S. & HANSON, K. 2005. Is malaria a disease of poverty? A review of the literature. *Tropical Medicine & International Health,* 10**,** 1047-1059.

YESHIWONDIM, A. K., GOPAL, S., HAILEMARIAM, A. T., DENGELA, D. O. & PATEL, H. P. 2009. Spatial analysis of malaria incidence at the village level in areas with unstable transmission in Ethiopia. *International Journal of Health Geographics,* 8**,** 5.

5.0 Appendices:

- **Published and in-press papers,**
- **ethics certificate**
- **code used in analysis**
- **Run-times**
- **Maps**

Appendix 1: WinBUGS code

Model without random effects

```
Model {
# Poisson Likelihood
        for (i in 1:N)
        { smear[i]~dpois(lambda[i] )
 log(lambda[i])<-log(total number of children[i]) + b[1] + b[2]*equals(stay in slum[i],1) +b[3]*equals(owns land for
agriculture[i],1) +b[4]*equals(child slept under net[i],1) +b[5]*equals(child slept under net[i],2)+b[6]*precipitation[i]
+b[7]*TSI[i] + b[8]*EVI[i] + b[9]*equals(type of place of residence[i],2)+b[10]*cluster altitude[i]
RR[i]<-exp(b[1]+b[2]*equals(stay in slum[i],1) +b[3]*equals(owns land for agriculture[i],1)
+b[4]*equals(child slept under net [i],1) +b[5]*equals(child slept under net [i],2) +b[6]*precipitation[i] +b[7]*TSI[i]
+b[8]*EVI[i] +b[9]*equals(type of place of residence[i],2)+ b[10]*cluster altitude[i])
        }
# Prior
        for (i in 1:10)
        {
            b[i]~dnorm(0.0,0.001)
        }
 }
```

Poisson regression model with both structured and unstructured random effect

```
model{
# Poisson Likelihood
        for (i in 1:N)
        { smear[i]~dpois(lambda[i] )
 log(lambda[i])<-log(total number of children[i]) + b[1] + b[2]*equals(stay in slum[i],1) +b[3]*equals(owns land for
agriculture[i],1) +b[4]*equals(child slept under net[i],1) +b[5]*equals(child slept under net[i],2)+b[6]*precipitation[i]
+b[7]*TSI[i] + b[8]*EVI[i] + b[9]*equals(type of place of residence[i],2)+b[10]*cluster altitude[i] +u[cluster[i]] + v[cluster[i]])
RR[i]<-exp(b[1]+b[2]*equals(stay in slum[i],1) +b[3]*equals(owns land for agriculture[i],1)
+b[4]*equals(child slept under net [i],1) +b[5]*equals(child slept under net [i],2) +b[6]*precipitation[i] +b[7]*TSI[i]
+b[8]*EVI[i] +b[9]*equals(type of place of residence[i],2)+ b[10]*cluster altitude[i]) + u[cluster[i]] + v[cluster[i]])
            }
# Prior
        for (i in 1:10)
            {
        b[i]~dnorm(0.0,0.001)
}
for (k in 1:140)
{
```

```
v[k]~dnorm(0.0,tauv)
}
tauv~dgamma(0.01,0.01)
u[1:140] ~car.normal(adj[], weights[], num[], tauu)
for (k in 1:sumNumNeigh)
        {
                weights[k] <- 1
        }
        tauu~dgamma(0.01,0.01)
        sigmau<-sqrt(1/tauu)
        sigmav<-sqrt(1/tauv)
}
```

Appendix 2: BayesX code

```
#BayesX

#importing libraries

library(spdep)

library(maptools)

library(foreign)

library(sp)

library(rgdal)

library(lattice)

library(R2BayesX)

library(shapefiles)

library(BayesX)
```

#model without random effect

```
Model1 <- bayesx(smear~as.factor(stay in slum)+as.factor(owns land for agriculture)+as.factor(children sleep under net)+precipitation+ TSI+ EVI+ cluster altitude+as.factor(type of place of residence), family=poisson, iter = 120000, burnin = 10000, step = 10,  data = data, weights=sampwt, offset=number_children)
```

#Convolution model random effect

```
Model2<-(smear~as.factor(stay in slum)+as.factor(owns land for agriculture)+as.factor(children sleep under net)+precipitation+ TSI+ EVI+ cluster altitude+as.factor(type of place of residence)+ sx(cluster,bs="mrf", map=malawibnd)+sx(cluster, bs="re") , family=poisson, iter = 120000, burnin = 10000, step = 10, data = data,  weights=sampwt, offset=number_children)
```

Appendix3: INLA code

#reading in the libraries

```
library(spdep)

library(INLA)

library(maptools)

library(foreign)

library(sp)

library(rgdal)

library(lattice)

library(shapefiles)
```

 # The shapefile of interest

```
malawiclust.shp<-readShapePoly("I:/paper2/GIS data/merge15.shp") proj4string(malawiclust.shp)=("+proj=longlat
+ellps=WGS84")

summary(malawiclust.shp)

str(malawiclust.shp, 2)

plot(malawiclust.shp,axes=T)
```

 # A nearest neighbour object

```
nbmala<-poly2nb(malawiclust.shp)

# Creating an INLA graph file

nb2INLA(file="malawi.graph",nbmala)

data=read.dta("I:/paper2/GIS data/mergeQGIS1.dta")

data<-cbind(data,region=as.numeric(data$DHSCLUST),region.struct=as.numeric(data$DHSCLUST))

attach(data)
```

#Model1-A generalized linear model (Full model)

```
Model1<- inla(smear~as.factor(stay in slum)+as.factor(owns land for agriculture)+as.factor(children sleep under net)+
precipitation+TSI+EVI+cluster altitude+as.factor(type of place of residence), family="poisson", data=data,
control.results=list(return.marginals.random=TRUE,  return.marginals.predictor=TRUE), control.compute=list(dic=1,mlik=1,
cpo=TRUE),offset=number_children)

summary(Model1)

plot(Model1)
```

#Model2-A convolution model

```
Model2<- inla(smear~as.factor(stay in slum)+as.factor(owns land for agriculture)+as.factor(children sleep under net)+
precipitation+TSI+EVI+cluster altitude+as.factor(type of place of residence)+f(region)+
f(region.struct,model="besag",graph="malawi.graph"),
family="poisson",data=data,control.results=list(return.marginals.random=TRUE,  return.marginals.predictor=TRUE),
control.compute=list(dic=1,mlik=1), offset=number_children)

summary(Model2)

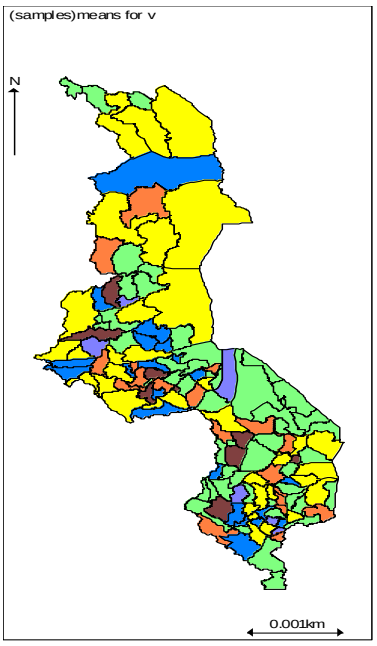
plot(Model2)
```

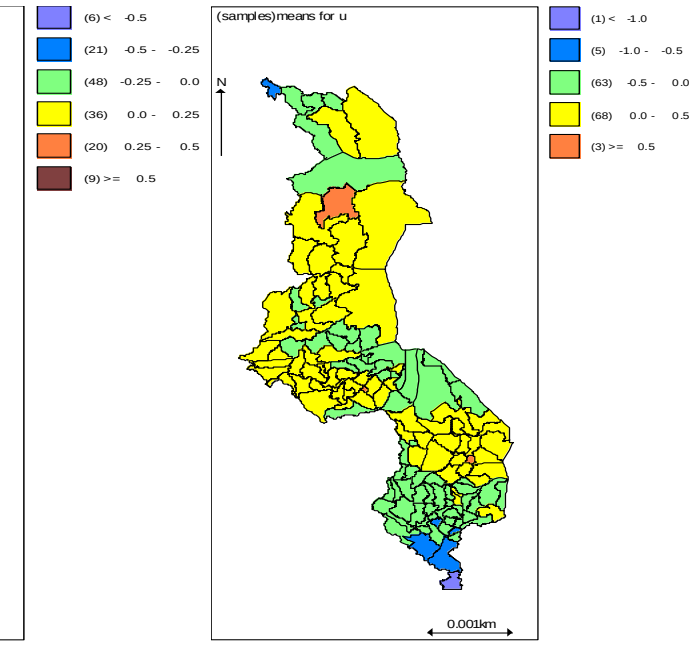
Appendix4: Run-times and number of iterations for the different methods used in analysis

Method	Structured model	Unstructured model	Convolution model
WinBUGS			
Run-time	15 890 seconds	14 976 seconds	5 857 seconds
Number of iterations	10 000	10 000	10 000
INLA			
Run-time	14.65 seconds	15.04 seconds	42.28 seconds
Number of iterations	Determined by method	Determined by method	Determined by method
BayesX			
Run-time	287.70 seconds	276.16 seconds	436.33 seconds
Number of iterations	120 000	120 000	120 000

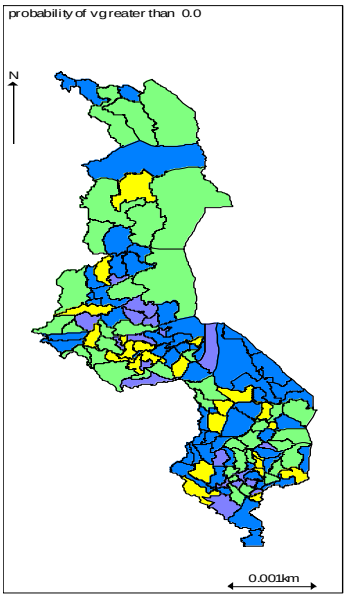
Appendix 5: WinBUGS maps

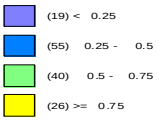
Unstructured effects

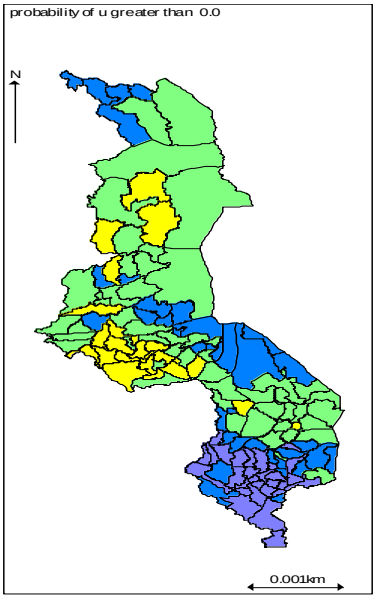


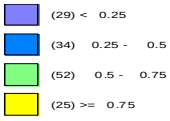


Structured effects









Appendix6: Human Research Ethics Clearance Certificate

R14/49 Ms Simangaliso Chitunhu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130962

NAME: (Principal Investigator)	Ms Simangaliso Chitunhu
DEPARTMENT:	Public Health Epidemiology and Biostatistics University of Witwatersrand
PROJECT TITLE:	Determinants of Malaria Episodes in Children under 5 in Malawi 2012
DATE CONSIDERED:	27/09/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Eustasius Musenge
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	30/09/2013

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**.

SChitunhu
Principal Investigator Signature

3/10/2013
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES