INSTITUTE OF TROPICAL AND INFECTIOUS DISEASES

UNIVERSITY OF NAIROBI

THE SPATIAL EPIDEMIOLOGY OF LEPROSY IN KENYA

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A Thesis Submitted in partial fulfillment of the requirements for the Degree of Master of Science
in Medical Statistics of University of Nairobi

2016
DECLARATION

This research is my original work and has not been presented to any other University for a degree award.

Signed ........................................... Date ...........................................

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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ARIMA</td>
<td>Autoregressive Integrated Moving Average</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guerin</td>
</tr>
<tr>
<td>BU</td>
<td>Buruli Ulcer</td>
</tr>
<tr>
<td>CAR</td>
<td>Conditional Autoregressive</td>
</tr>
<tr>
<td>CTLCs</td>
<td>County Tuberculosis and Leprosy Coordinators</td>
</tr>
<tr>
<td>DIC</td>
<td>Deviance Information Criteria</td>
</tr>
<tr>
<td>ENM</td>
<td>Ecological Niche Modeling</td>
</tr>
<tr>
<td>FBOs</td>
<td>Faith Based Organizations</td>
</tr>
<tr>
<td>G2D</td>
<td>Grade 2 Disability</td>
</tr>
<tr>
<td>GE</td>
<td>Google Earth</td>
</tr>
<tr>
<td>GIS</td>
<td>Geographic Information System</td>
</tr>
<tr>
<td>GLMM</td>
<td>Generalized Linear Mixed Models</td>
</tr>
<tr>
<td>GPS</td>
<td>Geographical Positioning System</td>
</tr>
<tr>
<td>HAT</td>
<td>Human African Trypanosomiasis</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immune deficiency Virus</td>
</tr>
<tr>
<td>INLA</td>
<td>Integrated Nested Laplace Approximation</td>
</tr>
<tr>
<td>Acronym</td>
<td>Full Form</td>
</tr>
<tr>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>KNBS</td>
<td>Kenya National Bureau of Statistics</td>
</tr>
<tr>
<td>LGCP</td>
<td>Log Gaussian Cox Process</td>
</tr>
<tr>
<td>LISA</td>
<td>Local Indicators of Spatial Association</td>
</tr>
<tr>
<td>MB</td>
<td>Multibacillary</td>
</tr>
<tr>
<td>MCMC</td>
<td>Markov Chain Monte Carlo</td>
</tr>
<tr>
<td>MDT</td>
<td>Multi Drug Therapy</td>
</tr>
<tr>
<td>NSP</td>
<td>National Strategic Plan</td>
</tr>
<tr>
<td>NTDs</td>
<td>Neglected Tropical Diseases</td>
</tr>
<tr>
<td>NTLD-P</td>
<td>National Tuberculosis, Leprosy and Lung Disease Program</td>
</tr>
<tr>
<td>PB</td>
<td>Paucibacillary</td>
</tr>
<tr>
<td>SCTLCs</td>
<td>Sub County Tuberculosis and Leprosy Coordinators</td>
</tr>
<tr>
<td>STHs</td>
<td>Soil Transmitted Helminths</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>UNITID</td>
<td>University of Nairobi Institute of Tropical and Infectious Diseases</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>ZIP</td>
<td>Zero-Inflated Poisson</td>
</tr>
</tbody>
</table>
ABSTRACT

Leprosy elimination is defined as a prevalence rate below 1 case per 10,000 population. This rate was attained in Kenya at the national level in 1989. However, there remain leprosy endemic counties where late diagnosis and physical disability persist. There is therefore need to define the populations at risk to enable the national program to plan leprosy control activities considering the County specific needs, as well as evidence based prioritization of resources within the respective counties. This is a retrospective ecological correlational study that aims to describe the spatial epidemiology of leprosy in Kenya for the period 2012 through to 2015. The study utilized secondary data sources; leprosy case based data was extracted from the National Leprosy Control Program database, whereas GIS and demographic data were obtained from KNBS. Exploratory analysis showed that there is active leprosy transmission in Kenya with children less than 15 years accounting for 7.5% of the total cases. Most notified cases were males (62%) whereas females accounted for the remaining 38%. 88% of all notified cases had MB leprosy and 52.9% had grade 1 or grade 2 disability. Two separate spatial Poisson Conditional Autoregressive (CAR) models were fitted; for all leprosy cases and for only new cases. The risk of leprosy incidence for all cases increased by about 5% for every 1 year increase in age, whereas a one percent increase in the proportion of MB cases increased the leprosy risk among new cases by approximately 4%. When all cases were considered, counties with the highest risks of leprosy include Kwale (RR of 15), Kilifi (8.9) and Homabay (4.1), whereas Turkana had the lowest relative risk of 0.005. A similar trend was observed with the new cases, with Kwale leading at a relative risk of 16, kilifi (8.6) and Homabay (3.7). Turkana remained the county with the lowest risk for new case incidence at a RR value of 0.003. The study concluded that leprosy
incidence exhibits geographical variation and there is therefore need to institute local control measures.
CHAPTER ONE: BACKGROUND

1.0 Introduction

This chapter provides an overview of leprosy history, its signs and symptoms, transmission, risk factors, diagnosis and treatment. It further outlines the leprosy surveillance system, highlighting the current global and local (Kenyan) trend of leprosy case notification. Finally it details the problem statement, justification and states the research hypothesis.

The causative agent of Leprosy (Hansen’s disease) is *Mycobacterium leprae*. It is a chronic infection mainly affecting the nerves and skin. This disease is named after its discoverer, Armauer Hansen and it is the first bacterium identified to infect humans (Hansen, 1874). It is thought to have spread from Egypt and parts of Middle East. This spread was fueled by lack of treatment/ a known cure (Irgens, 2002). It is this lack of knowledge about its treatment that facilitated its spread throughout the world.

1.1 Signs and Symptoms

Some of the key symptoms of leprosy include (WHO, 2012):

- Flat or raised skin patches usually with a decrease in or complete loss of sensation
- Numbness of the limbs
- Limb weakness. The eyelids may also be weak/ heavy
- Tenderness of the nerves
- Lumps, mostly in the face and/or ears.
- Leprosy reactions may cause neuritis leading to permanent deformities.
1.2 Transmission and Risk factors

The nasal mucosa is the major source of infection, followed by (injured) skin contact (Job et al., 2008). The incubation period of leprosy is controversial but generally ranges from three to ten years (Pinheiro et al., 2011) and seems to be shorter for Paucibacillary (PB) disease (2–5 years) than for Multibacillary (MB) disease (5–10 years and sometimes much longer) (Boon et al., 2006). A major risk factor of leprosy infection is contact with an infected person, specifically one with the MB form of the disease. As compared to individuals who do not get into contact with any leprosy cases, the probability of getting infected after contact with an MB case is 5 to 10 times higher whereas it is 2 to 3 times higher for PB disease. It has been shown that starting treatment reduces the infectiousness of patients and it is generally agreed that infectiousness is negligible after starting Multidrug treatment (WHO, 2009).

Genetics has also been shown to influence both acquiring the infection and its prognosis (Alter et al., 2008). It is however argued that infectivity among family members is largely by virtue of close contact and not genetics. In addition, leprosy incidence is higher among the poor for unclear reasons and in populations with a low coverage of BCG vaccination.

Leprosy occurs across all ages but mostly presents in adults, most probably due to the long incubation period. More male than female cases are usually reported and it is yet to be ascertained if gender is a risk factor or other sociocultural and/or health system factors influence the same. Nonetheless, more males than females present with MB disease in all populations (WHO, 2012).
It had been feared that HIV infected individuals were more prone to *Mycobacterium leprae* infection. This is however not the case; initiation of antiretroviral therapy may trigger an immune reaction causing leprosy lesions to worsen (Couppi’e et al., 2009).

### 1.3 Diagnosis

Clinical symptoms are the main guiding principles for the diagnosis of leprosy. Rarely, laboratory diagnosis is required for confirmation. The diagnostic symptoms include;

- Skin lesion(s) with sensory loss. This may or may not be accompanied by thickened nerves.
- Skin smears that reveal the bacteria (WHO, 2012).

The numbers of skin lesions are counted to enable classification of disease; PB disease (1 to 5 lesions) and MB disease (> 5 lesions). Whenever there is doubt, the patient is normally classified as MB (WHO, 2000). When the skin lesions are not characteristic of leprosy, the client should be informed about leprosy and may be referred to a higher level health facility (WHO, 2016). At the diagnosis stage, disability level is also assessed and graded as per the WHO guidelines:
Table 1: Disability Grading Scale

<table>
<thead>
<tr>
<th>Body Area</th>
<th>Signs / Symptoms</th>
<th>Disability Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands and Feet</td>
<td>No sensory loss, deformity not visible</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Sensory loss present, deformity not visible</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sensory loss present, deformity visible</td>
<td>2</td>
</tr>
<tr>
<td>Eyes</td>
<td>No leprosy related eye problems, no effect on vision</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Leprosy related eye problems present, vision mildly affected</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vision severely impaired</td>
<td>2</td>
</tr>
</tbody>
</table>

1.4 Treatment

Leprosy is currently treated using Multi Drug Therapy (MDT), which was recommended by a WHO study group in 1981, after resistance to a single drug therapy (dapsone) was observed. PB disease is treated using a combination of dapsone and rifampicin whereas combination for MB disease includes dapsone, rifampicin and clofazimin. The treatment duration is 6 months and 12 months for PB and MB cases respectively.

As the disease progresses into the chronic phase, leprosy reactions are common. The pain and fever is usually managed using paracetamol and aspirin. Severe inflammation may be managed using corticosteroids, specifically prednisolone. In addition any injuries/ wounds should be treated accordingly and the patient advised to rest (WHO, 2000).
1.5 Leprosy Surveillance System

Leprosy control is well integrated in the health care system in Kenya, involving most government health facilities as well as some FBOs, communities and private health care units. The health care workers in these facilities are responsible for case finding, infection control and treatment of leprosy patients. The County TB and leprosy coordinators (CTLCs) and their sub county counterparts, SCTLCs, are responsible for providing technical assistance and supervision to the health facilities. The SCTLCs are also responsible for aggregating data at the sub County level and updating case based information on the online database.

At the national level, the NTLD-P designs standard data collection and reporting tools for all the levels of reporting (national, county, sub-county and facility). The unit then facilitates information dissemination to relevant state departments as well as to WHO, as leprosy is a notifiable disease (Kenya NSP, 2015-2018).

1.6 Current leprosy situation

Since the introduction of MDT, the leprosy burden in the world has significantly reduced, from 5.2 million people in 1985 to 175,554 people in 2014. Leprosy elimination (below 1 case per 10,000 population) was achieved globally in the year 2000 (Global Leprosy Strategy, 2016-2020). The prevalence of leprosy has dropped drastically, from 21.1 per 10 000 in 1983 to 0.24 per 10 000 persons in 2014, with its elimination being achieved at national levels in all countries with a population of more than one million.

The number of new leprosy cases reported across 121 countries has stabilized over the past 8 years (WHO, 2014). This suggests that transmission of leprosy is still ongoing and Brazil, India
and Indonesia are the countries with the highest leprosy burden worldwide. The table below shows the leprosy prevalence at the end of 2014.

**Table 2: Leprosy prevalence and number of new cases detected in 2014**

<table>
<thead>
<tr>
<th>Region</th>
<th>Registered Prevalence</th>
<th>Number of New Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Rate per 10,000 pop.</td>
</tr>
<tr>
<td>African</td>
<td>19 968</td>
<td>0.26</td>
</tr>
<tr>
<td>Americas</td>
<td>29 967</td>
<td>0.33</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>2 212</td>
<td>0.04</td>
</tr>
<tr>
<td>European</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>South East Asia</td>
<td>119 478</td>
<td>0.63</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>3 929</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>174 554</strong></td>
<td><strong>0.25</strong></td>
</tr>
</tbody>
</table>

*Source: Global Leprosy Strategy, 2016-2020.*

The rate of Grade 2 Disability (G2D) among new cases has also remained relatively constant. In the year 2014, 14 110 (6.6%) new cases presented with G2D, corresponding to a rate of 2.0 cases per million. Children contributed 8.8% of all new cases indication active leprosy transmission. Most cases diagnosed were MB (61%) and males accounted for 64% of all new cases of leprosy (Global Leprosy Strategy, 2016-2020).

In Kenya, leprosy was eliminated at the national level in the year 1989. The number of new reported leprosy cases in the country has been on the decline, from 6,558 to 131 cases in 1986 and 2015 respectively (Kenya NTLD-P Annual Report, 2014). The trend in leprosy case
notification in Kenya is illustrated in figure 1 below. Most of the cases diagnosed suffer from MB disease and have visible deformity, with 60% of new cases notified in 2015 having grade 1 and 2 disability. In the same year, out of the total 131 Leprosy cases notified, majority (88%) were MB patients. Active case-finding carried out in some counties like Kwale, Kisumu and west Pokot yielded relatively high numbers of cases. In addition, the presence of childhood cases prove ongoing active transmission in the country and the large percentage of disability suggests late diagnosis.

**Figure 1: Trends in Leprosy case notification in Kenya, 1986-2012.**

![Image of chart showing trends in Leprosy case notification in Kenya, 1986-2012.](image)

**Source:** National Strategic Plan for TB, Leprosy and Lung Health (2015-2018).

**1.7 Problem Statement**

In Kenya, active leprosy transmission is ongoing and its effects are still being felt in specific counties, including but not limited to Kwale, Kilifi, Kisumu, Siaya, Homabay and Busia (Kenya NTLD-P Annual Report, 2014). Despite acknowledging that leprosy is still a problem at sub national level, there exist several challenges and constraints to its management:
• Late diagnosis largely contributed by a low suspicion index among health workers.

• Minimal funding of leprosy control activities since its elimination in the year 1989. In addition, there is low profiling of leprosy at all levels hence low prioritization in resource allocation even in counties with higher disease incidence.

• Communities are still ignorant about leprosy and social stigma results in delayed health seeking behavior.

• There is inadequate rehabilitation of the diagnosed leprosy and former leprosy cases.

• Lack of a clear understanding of the disease epidemiology.

Kenya strategizes to reduce the burden of leprosy. Part of the desired impact by the year 2018 is to half the cases with grade 2 disability by increasing to 90% the cases with grade 0 disability. (National Strategic Plan for TB, Leprosy and Lung Health, 2015-2018). Addressing the aforementioned challenges would go a long way in achieving these outcomes.

1.8 Justification

Leprosy has since shown geographical variations in many parts of the world. The factors influencing this distribution are not fully understood / remain unclear. In addition, regional patterns allow targeting of leprosy control activities e.g. active case finding which improves the cost–effectiveness of control programs, considering the reduced disease burden.

Not much is known about the transmission and risk of leprosy in Kenya. There is therefore need to define the populations at risk to enable the national program plan leprosy control activities considering the County specific needs, as well as evidence based prioritization of resources within the respective counties. Mapping the relative risks and potential risk factors will provide a framework for evaluating impact of the interventions.
1.9 Study Hypothesis

**Null Hypothesis**: There is no definitive spatial distribution of leprosy cases in Kenya.

1.10 General Objective

The study aims to determine the spatial distribution of leprosy cases in Kenya.

1.11 Specific Objectives

i) To describe the leprosy case notification trend in Kenya for the period 2012 through to 2015.

ii) To describe the spatial model for the distribution of leprosy cases and determine factors influencing leprosy incidence.

iii) To estimate and map the relative risk of leprosy incidence in the 47 counties in Kenya.
CHAPTER TWO: LITERATURE REVIEW

2.0 Introduction

This section provides a brief background on georeferenced data and statistical methods and tools that have been, and continue to be used for spatial and/or temporal studies (in public health). It further discusses applications of Geographic Information Systems (GIS) in the control of diseases, and specifically, leprosy, highlighting the methods used as well as the study outcomes.

2.1 Georeferenced Data

Generally georeferenced data can be classified into three:

- Geostatistical data; these are measurements that can be taken in any location, for example soil pH, temperature etc. The locations sampled form the basis of estimation of measurements at other unsampled locations (Wackernagel, 1995).
- Areal data; this consists of data aggregated across different regions which can be regular or irregular. Remote sensing can be used to display data in regular pixels (DeMers, 1997). However, irregular regions are the most common in health research and mostly includes administrative regions for example census tracts, districts and counties. Ecological studies are normally based on areal data and these may be purely descriptive or correlational (Elliot & Wartenberg, 2004).
- Point patterns; point patterns give event location by longitude and latitude. These patterns may be marked or unmarked; unmarked patterns only show event locations whereas marked ones give extra variables associated with each location (Schabenberger & Gotway, 2005).
2.2 Spatial and Spatial temporal Modeling

Spatial epidemiology describes and analyzes the geographical distribution of disease (Andrew, 2006), usually incorporating explanatory variables of interest. Mapping diseases begun in the 19th century and cholera and yellow fever were among the first diseases to be studied spatially (Walter, 2000). Over the years, improved statistical models have been employed to better illustrate and understand geographical distribution of disease.

Maps for different time periods are not comparable (Bernardinelli et al., 1995), necessitating the use of spatio-temporal models. A hierarchical Bayesian framework works well to incorporate the time factor as well as other random effects (Gomez-Rubio & Lopez, 2006).

2.2.1 Bayesian Spatial Modeling

Raw rates and standardized morbidity rates when presented in a choropleth map can be misleading and highly unstable for small regions. Bayesian analysis incorporates prior information and is thus better suited to handle few data as compared to the frequentist approach (Sylvain et al., 2015). Therefore, Bayesian methods are able to smoothen crude maps of disease risk, making estimates more stable. The BYM model (Besag et al., 1991) is commonly used but it does not factor in time. Other model extensions have been proposed to address this. For example, Bernardinelli et al. (1995) model the intercept and time as random effects. The time trend can also be assigned an autoregressive structure (Congdon & Southall, 2005).

2.3 Geographic Information Systems (GIS)

A GIS is used to manage and analyze all types of geographical data. The main areas of application of GIS in disease control are:
• Research to generate new knowledge; to understand and explain the spatial variation of diseases and its potential relationship with factors such as geographical, climatic, socio-cultural, and health system-related factors

• Public health; to design focused interventions

• Management; to plan and monitor control programs (Tanser & le Sueur, 2002).

There are three important functions of GIS in health research and policy analysis (Cromley & McLafferty, 2002):

• Spatial Database Management; integration of data from different sources, both qualitative and quantitative, with data from maps and other satellite images.

• Visualization and Mapping; this is the most basic application of GIS (Gauy et al., 2007) and according to Mason et al. (1975), it was initially used in the United States to study cancer distribution. GIS is also used in other fields such as archaeology and climatology.

• Spatial Analysis; involves simultaneous analysis of several risk/ environmental factors (Lapa et al., 2006).

2.4 Application of GIS in Disease Control

Globally, GIS is increasingly being applied in public health. It has been applied in the control of both infectious and non-infectious, macro and micro parasitic, as well as vector borne diseases. Dr. John Snow is famous for his work in London, Soho district which dates back to the year 1854, where he analyzed deaths due to cholera. He plotted the cholera deaths on a dot map and noted clustering around a water pump (McLeod, 2000). Narushige et al. (2015) reviewed historical documents to revisit Snow’s work using Scan statistic and Kernel density estimation to examine the mortality rate as well as the space time pattern of the disease outbreak. It was
confirmed that areas closest to the water pump had the highest mortality but no definite space-time pattern was noted. Other novel geospatial methods for example spatial video have been used to collect and map environmental covariates, exploring the epidemiology of cholera. In a coastal town of Haiti, Andrew et al. (2016) illustrated the potential of this new method, where water risks maps from a 2012 spatial video collection were used to guide a 2014 survey.

Influenza, viral hepatitis, diarrhea and Tuberculosis (TB) are among other infectious diseases for which GIS has been applied to facilitate control. Avian influenza A(H7N9) was first seen in humans in March 2013 in China. A study was conducted to investigate its spatial distribution and potential risk factors, using data as from March 2013 to December 2014. The Moran’s I was used to examine spatial distribution. In addition, logistic regression analysis was carried out which identified nine significant risk factors; relative humidity, migration route, railway, precipitation, spatial-temporal factor, river, temperature, lake and road. This study concluded that a significant spatial-temporal correlation existed (Wen et al., 2015). In Vellore, South India, a viral hepatitis outbreak in children below 10 years of age was investigated. This case control study mapped 965 children in total who were divided into groups with regard to age (less than 5 or more than 5 years) and sex. The Fisher’s exact was then used to assess symptoms of hepatitis between the groups, followed by a test for clustering (Thuppal et al., 2008). Other case control studies have incorporated the temporal effect as was the case in a northwestern Ecuador case control study on diarrhea. A Bayesian model was used in this study. All diarrhea cases from 21 out of 158 communities were collected from the year 2003 to 2008. The spatial clustering was modeled using log Gaussian Cox process (LGCP). A disease mapping model was then used for prediction in unsampled communities (Jaeil et al., 2014).
The spatial temporal distribution of TB has also been studied in various regions. An example from Beijing, China, utilized TB data for the period 2009 through to 2014. The study utilized lattice data aggregated at the district level. The TB incidence rate was measured and spatial autocorrelation analysis carried out; spatial, temporal and spatial temporal clusters were assessed. There was local spatial autocorrelation in individual districts but not across all Beijing districts (Lan et al., 2016).

In addition, GIS has been quite useful in the control of vector borne diseases worldwide, including but not limited to malaria, lyme disease, Barmah Forest Virus (BFV) and several Neglected Tropical Diseases (NTDs). In Tamil Nadu, India, an ecological study aimed to determine malarial incidence. The time scale was in months and environmental covariates included temperature, rainfall patterns and mosquito incidences. A multiple linear regression was used to investigate significance of these covariates which were in turn used to produce a risk map for malaria. Rainfall, temperature and forest cover were seen to influence malaria incidence (Devi et al., 2003). As malaria declined in India, Plasmodium falciparum (Pf) were on the increase. This necessitated generation of maps that highlighted high risk areas for malaria so as to inform efficient malaria control activities (Aruna et al., 2009). A relatively similar study by Elaine et al. (2013) in Brazil aimed to identify the environmental and social determinants of malaria infection in a rural settlement, using data for the year 2005. Proximity of residential area to mosquito breeding grounds and gold mines was measured using euclidian distance. Multiple logistic regression was used to model the malaria risk.

Lyme disease (LD) was recently (1990) recognized by CDC as a notifiable disease. Esra (2015) reviewed research on spatial temporal patterns of LD, with a focus on the reservoir hosts, vectors (ticks), humans and their interactions. He found that GIS-based studies helped pinpoint clusters
of interest thus improving the understanding of human transmission. Some studies quantified associations between LD incidence and the predictor variables.

Barmah Forest virus (BFV) is a common disease in Australia and is spread by mosquitoes. A study by Suchithra et al. (2011) investigated its spatial and temporal patterns, where incidence rates and standardized incidence rates of BFV disease were calculated. Moran’s I statistic and semi-vario-gram analysis were used for the assessment of spatial autocorrelation and spatial dynamics respectively. Mapping revealed substantial spatial temporal variation and a significant positive spatial autocorrelation of the disease incidence across all the time periods.

Neglected Tropical Diseases (NTDs) have lately been of interest and several studies have been carried out on the same. Spatial distribution of NTD-related mortality in Brazil was analyzed, including all deaths attributed to NTDs from the year 2000 to 2011. Several spatial and spatial-temporal clusters were identified. Join point regression was used to analyse the trend in time and Moran’s I used to check for spatial autocorrelation. It was concluded that socioeconomically disadvantaged regions faced higher NTD-related mortality (Francisco et al., 2016). Studies focusing on specific NTDs have also been done. For example, the incidence of Cutaneous leshmaniasis (CL) in northern Israel which began to rise in 2000, peaking in 2003 necessitated examination of the morbidity rate during the period 1999–2003, to find out whether new endemic areas were emerging and to identify suspicious hosts. Incidence rates were calculated by geographic area and mapped. Associations between age and gender and the place where the patient contracted the disease were examined using chi-square. The student's t-test was used for comparing groups regarding continuous variables, and the one-way ANOVA test was used for comparing differences among more than two groups (Olga et al., 2010). A more elaborate study in Central Iran assessed the risk of CL, using data for the period 2009 to 2013. Spatial analysis
and Moran’s I statistic were applied to detect hot spots and spatial autocorrelation respectively. The study concluded that there was potential for local transmission of CL (Fatemeh et al., 2016).

Despite the gains made through application of GIS, spatial analyses are still used relatively infrequently. A systematic review analyzed a total of 80 outbreak investigation reports between the years 1979 and 2013 worldwide. This review aimed at estimating the prevalence and utility of spatial analysis. Disease conditions that were most commonly investigated using spatial methods included waterborne infections, of which most reports came from United Kingdom. The techniques were applied throughout the investigations; from analysis, reporting and prediction (Smith et al., 2015).

Non-infectious chronic conditions have been no exception to this method of analysis. GIS and spatial temporal statistical methods have been used to study epidemiology and/or control of breast cancer (Basavegowda et al., 2016), chronic kidney disease (Jayasekara et al., 2013), diabetes (Laranjo et al., 2016), acromegaly (Naves et al., 2015), hypertension and ischemic heart disease (Qingyun et al., 2016), just to mention a few.

In Africa, GIS has been applied mainly in the control of infectious diseases, specifically malaria, cholera, polio and NTDs. Malaria is rampant in Africa, both in terms of mortality and morbidity. Tonnang et al. (2010) conducted a study to build models for prediction and mapping the distribution of Anopheles mosquitoes in the African continent. The variables analyzed included relative humidity, temperature and rainfall. These were used to calculate an ecoclimatic index (EI). Another continental level study sought to determine the trend in malaria transmission intensity from 2000 through to 2010 in Africa, and forty nine endemic countries were included in the study. A Bayesian space–time geostatistical framework was used for the prediction of
*Plasmodium falciparum* parasite rate and risk maps generated. It was concluded that despite reduction in malaria transmission, 57% of the population lived in areas with moderate to intense transmission (Noor et al., 2014).

Several country specific studies on malaria have been conducted. Examples include Mali, Namibia, Tanzania and Ghana. In Mali, the aim was to identify areas with a high risk for malaria, both in space and time. The expected cases were assumed to follow a poisson distribution. A global temporal analysis was carried out using classical Autoregressive Integrated Moving Average (ARIMA) time series analysis (Gaudart et al., 2006). In Namibia, Alegana et al. (2013) used a spatial temporal model to determine constituencies with high malaria incidence. In the preliminary analysis, a non-spatial Poisson regression model was used to test the univariate and multivariate associations of assembled environmental covariates and crude incidence. Environmental covariates selected via this preliminary analysis, the reported cases and catchment population per public sector health facility, were used to fit a Bayesian space-time zero inflated conditional-autoregressive (CAR) model using Integrated Nested Laplace Approximation (INLA). A Zero-Inflated Poisson (ZIP) model was used following the example of studies in low transmission settings, to handle count data with a lot of structural or excess zeros. In the United Republic of Tanzania, Hagenlocher & Castro (2015) used a logistic regression model to identify risk factors for malaria endemicity. A GIS was used to construct and visualize a malaria vulnerability index which was then integrated into a malaria risk map. The malaria risk pattern proved to be heterogeneous across the country. In Accra, Ghana, mortalities as a result of malaria and diarrhea between 1998 and 2002 were subjected to a spatial cluster analysis. This was done at the census tract level and visualized using ArcMap 9.3.1. Geostatistical methods, specifically frailty models were used to assess the spatial patterns of both observed and unobserved
mortalities as well as excess mortalities as influenced by environmental and socioeconomic factors. The distribution of risk factors for malaria and diarrhea were found to be uneven (Fobil et al., 2012).

There was a cholera outbreak in Lusaka, Zambia between November, 2003 and June, 2004. GIS was used to analyze the distribution of cases and transmission as well as the risk factors. A matched case-control study design was adopted. The spatial statistical methods to analyze distribution patterns were Moran’s I and average nearest neighbor. There was a significant association between poor sanitation and high cholera incidence (Sasaki et al., 2008).

According to Kamadjeu (2009), Google Earth (GE) can be used as a planning tool for disease control as was the case with polio eradication activities in the Democratic Republic of Congo. GE use improved field operations as well as allowing the creation of high quality maps that helped understand and monitor both the disease outbreak and response.

Some of the Neglected Tropical Diseases (NTDs) of major interest in Africa include Human African Trypanosomiasis (HAT), schistosomiasis, soil-transmitted helminthiasis, Buruli ulcer and mycetoma. An atlas initiative for Africa would allow major improvements in the understanding of the spatial distribution of HAT. Data collected by national sleeping sickness control programs, nongovernmental organizations and research institutes were collated over many years by the HAT Control and Surveillance Program of the World Health Organization. The number of new HAT cases and the number of people screened within a defined geographical entity were chosen as the key variables to map disease distribution in sub-Saharan Africa (Cecchi et al., 2009).
Prediction of the spatial distribution of schistosomiasis would assist in planning and implementing the mass distribution of praziquantel to control the disease. This was the case in Tanzania where data from 143 schools was used in Bayesian geostatistical models and binomial logistic regression models constructed. The environmental predictor variables were included as fixed effects and the models run in WinBUGS 14 (Clements et al., 2006).

*Mycobacterium ulcerans* causes a chronic skin disease known as Buruli ulcer (BU). To show its spatial distribution and hot spots in Ghana, a community case search (along the Densu river) was conducted in two districts. The E-trex Garmin Geographical Positioning System (GPS), marked the location of cases alongside community attributes. BU distribution and hot spots were visualized on a map generated using ArcGIS. Clustering of BU cases was associated with high levels of contamination in parts of the river (Kenu et al., 2014). In a separate study in Sudan, ecological niche modeling (ENM) was used to map the risk of mycetoma infection. This study revealed environments for mycetoma transmission (Samy et al., 2014).

In Kenya, application of GIS and spatial disease modeling is still limited with available studies focusing on infectious diseases. Of particular interest is malaria, TB, Schistosomiasis and soil-transmitted helminthiasis. Noor et al. (2009) presented a malaria risk map for Kenya. Cross sectional community surveys conducted from 1975 to 2009 were the source of *Plasmodium falciparum* rate data. Geo-positioning of every survey location was done using national digital settlement maps. To these locations, ecological and climate covariates were matched and examined for significance, after which the significant covariates were included in a Bayesian spatial-temporal model to predict maps of mean *Plasmodium falciparum* rate across the country for the year 2009.
The spatial and temporal distribution of TB in Kenya has been assessed by Kipruto et al. (2015), using small area estimation methodology. The spatial reference regions considered were the 47 Kenyan counties. The small area estimates were mapped to produce smear positive TB and favorable treatment outcomes maps. The covariates considered were gender, HIV positive proportion, directly observed Treatment (DOTs), average weight, average Body Mass Index (BMI) and average age. The significant covariates were used in the model to generate the relative risks, posterior probability means and the associated standard deviations which were then used to generate the spatial temporal maps. The spatial temporal maps generated showed distribution clustering of TB cases in a number of counties over the years (2012-2014).

To determine the geographical distribution and prevalence of schistosomiasis and soil transmitted helminthiasis (STHs) in south Nyanza, children from 95 schools were included in the cross sectional survey. Spearman correlation was used to estimate the correlation between schistosomiasis infection and the distance from a water body (lake), whereas the Mann-Whitney test compared infection intensities between males and females (Sang et al., 2014). In a separate study, Bayesian space-time geostatistical models for soil transmitted helminth species were developed and used to predict the probability that an infection prevalence exceeded the 20% threshold across the country for both 1989 and 2009 (Pullan et al., 2011).

2.4.1 Application of GIS in Leprosy Control

Globally, most of the relatively recent leprosy research has been conducted in parts of South America and South Asia, specifically Brazil and India where leprosy is still considered a public health concern.
In the State of Espírito Santo, Brazil, a descriptive study included leprosy cases identified from 2004 to 2009. A Bayesian approach was used for the analysis in order to smoothen anticipated fluctuations. The Global Moran’s I index was then calculated to check for spatial dependency (Poliane et al., 2012). In a similar study conducted in the state of Ceará, Northeast Brazil, the leprosy incidence rates was calculated for each municipality over a 9 year period i.e. 1991 to 1999. The Moran’s I statistic was also used as a measure of spatial autocorrelation in this study where spatial dependence was found to exist (Montenegro et al., 2004).

Several studies have analyzed leprosy incidence alongside epidemiological indicators and other risk factors. To describe the spatial patterns of leprosy in the Brazilian state of Tocantins, a study included all new leprosy cases in individuals residing in the state of Tocantins, between 2001 and 2012. In addition to the description of general disease indicators, a descriptive spatial analysis, empirical Bayesian analysis and spatial dependence analysis were performed by means of global and local Moran’s indexes. Clusters with high disease risk, late diagnosis and active transmission were detected in the south west and central north regions (Monteiro et al., 2015).

In India, linear mixed effects regression models were fit to analyze case detection trends at the district level. The state level predictors included in the model were; proportion of G2D at diagnosis, incidence of TB, coverage of the BCG vaccine, proportion of childhood cases and proportion of MB disease. TB incidence and BCG coverage did not show a statistically significant effect on the annual new case detection rate of leprosy. It was however shown that a higher proportion of childhood cases and MB disease were correlated with a higher annual case detection rate. The findings suggested declining disease rates with spatial heterogeneity both at state and district levels (West et al., 2014).
A separate study including 373 municipalities (as the observation units) in four states of Brazil, considered the following disease indicators; new case detection rates, childhood detection rates and new cases with G2D disability. Descriptive spatial analysis, spatial scan statistic and Bayesian analysis were carried out (Carlos et al., 2012).

In the municipality of Manaus in Brazil, 4,104 cases identified during the period 1998 to 2004 were georeferenced and local empirical Bayesian methods used to analyze the spatial distribution so as to estimate leprosy risk. Logistic regression was used to check for association between geographical distribution of leprosy cases and risk factors which included childhood incidence (severity index) and Social Need Index. The distribution of leprosy was found to be heterogeneous and it mostly affected vulnerable groups (Elsia et al., 2009). A separate study in the Amazon region utilized leprosy data during 2005 to 2007 to identify non-overlapping leprosy clusters. Ten such clusters were identified. The conclusion of this study was that leprosy was still endemic in the region, but could not be explained by socioeconomic factors (Penna et al., 2009). In addition, spatial scan statistics has been used to detect areas with increased case-detection rates in the Amazon region of Brazil. It has been shown that leprosy continues to be endemic despite the improving economic development (Maria et al).

Time factor can also be included to better understand the disease distribution. The use of spatial temporal models in leprosy research has however not been fully exploited. In North-East Brazil, several leprosy indicators were compared both in space and time. There was a reduction in the childhood cases and in the proportion of new cases with G2D, suggesting active leprosy detection activities and not expanding endemicity (Mastrangelo et al., 2009).
The spatial temporal distribution of leprosy cases in Bangladesh was studied over a 15 year period (1989–2003). This study revealed several spatio-temporal clusters of leprosy incidence where the cases within and without the clusters showed no significant difference in terms of age at detection, proportion of MB disease and sex ratio. The risk was highest near the town centers and decreased with increasing distance from the centers (Fischer et al., 2008).

In a study aimed to identify spatial patterns of leprosy occurrence for the period 1998 to 2006 in Rio de Janeiro, Brazil, analysis was done in three-year periods. Global Moran’s I and local (LISA) spatial autocorrelation statistics were calculated. With earlier diagnosis, there was marked improvement in the disease outcomes (Monica et al., 2012).

In the state of São Paulo, Southeastern Brazil, the spatial temporal epidemiology of leprosy was assessed as from January 2004 to December 2006. A positive correlation was found between the detection coefficients and “schooling” and “longevity”, whereas a negative correlation existed between “wealth” and leprosy detection. The time series analysis suggested declining endemicity while spatial analysis showed a higher leprosy risk in the northern part (Rodrigues et al., 2008).

In Africa, leprosy research is still very limited. In northern Malawi, GIS was employed to investigate relationship between leprosy incidence and socioeconomic, cultural factors and population density. Incidence rates could not be related to any of these covariates. There was however increased incidence with increasing distance from the main road (Sterne et al., 1995). In Kenya, leprosy research using GIS tools is lacking.
CHAPTER THREE: METHODOLOGY

3.0 Introduction

This chapter presents an overview of the materials and methods used in the study, detailing the study design and its limitations. It also specifies and elaborates the spatial model used and outlines how the data was managed.

3.1 Study Area

The study covered all the 47 administrative units (counties) in Kenya. Kenya covers an approximate area of 591,971 km² with an estimated population of 43 Million people in 2014 (KNBS, 2015).

3.2 Study Population

The study population included all notified cases of leprosy within a 4-year period (2012 to 2015), and who met the study criteria.

3.2.1 Inclusion Criteria

- All notified leprosy cases - Mapping the relative risk was done in two ways; (i) considering all the cases and (ii) only the new cases (excluding all cases of relapse, those resuming treatment and all those transferred in from another health facility)

- Observations having all the requisite variables

3.2.2 Exclusion Criteria

- Observations missing any one or more requisite variable(s) i.e. sex, age, type of leprosy, type of patient, and/or disability grade.
3.3 Study Design

An ecological correlational study design was adopted.

3.4 Bayesian Spatial Model

A generalized linear mixed model assuming a Poisson distribution of the outcome variable (leprosy notifications) was used i.e.

\[ y_i \sim \text{poisson}(\mu_i) \]

Where \( y_i \) is the number of leprosy cases reported in region (county) \( i \).

The relationship between leprosy cases notified and the covariates was characterized by spatial random effects. The GLMM is of the form:

\[
\log(\mu_i) = \log(E_i) + \beta_0 + \sum_{j=1}^{k} \beta_j X_{ij} + u_i + v_i
\]

Where:

\( u_i \) and \( v_i \) represent spatially unstructured and spatially structured random effects respectively.

\( X_{ij} \) represents the \( j^{th} \) covariate for county \( i \).

\( \beta_j \) represents the parameter vector of the covariates \( X_{ij} \), and \( \beta_0 \) is the model intercept which represents the risk of leprosy when all covariates are at zero.

\( E_i \) is the expected number of leprosy cases in county \( i \). In this model \( i \) ranges from 1 to 47. The \( E_i \) was calculated with indirect standardization of age and sex as follows:

\[
\text{Age specific } E_i = \left[ \frac{y_{sl}(m)}{P_{sl}(m)} \times p_{il}(m) \right] + \left[ \frac{y_{sl}(f)}{P_{sl}(f)} \times p_{il}(f) \right]
\]
\( y_{sl}(m) = \) number of male leprosy cases in age group \( l \) in the standard population (the whole country population was used as the standard population).

\( y_{sl}(f) = \) number of female leprosy cases in age group \( l \) in the standard population

\( P_{sl}(m) = \) total number of males in age group \( l \) in the standard population

\( P_{sl}(f) = \) total number of females in age group \( l \) in the standard population

\( p_{il}(m) = \) total number of males in age group \( l \) in county \( i \)

\( p_{il}(f) = \) total number of females in age group \( l \) in county \( i \)

Therefore;

\[
E_i = \sum \left( \left[ \frac{y_{sl}(m)}{P_{sl}(m)} \times p_{il}(m) \right] + \left[ \frac{y_{sl}(f)}{P_{sl}(f)} \times p_{il}(f) \right] \right)
\]

The county specific relative risks (RR) for mapping was calculated as follows;

\[
RR_i = \exp(\beta_0 + \sum_{j=1}^{k} \beta_j X_{ij} + u_i + v_i)
\]

Parameter estimation:

Considering the relatively few data points, Bayesian inference was used for parameter estimation and sampling done by Markov Chain Monte Carlo (MCMC) technique. Non-informative uniform and normally distributed priors were assigned for the model intercept and covariate parameter vector respectively i.e. \( \beta_0 \sim U(-\infty, +\infty) \)

\( \beta_j \sim Normal(0, \delta_{\beta}^2) \)
Spatially unstructured random effects were assumed to be normally distributed i.e. $u_i \sim Normal(0, \delta_u^2)$ whereas spatially structured random effects were assigned a conditional autoregressive prior i.e. $v_i \sim CAR(\delta_v^2)$, and the corresponding precision parameters given non-informative gamma distributed priors. Two counties were said to be neighbors if they shared a boarder implying that the conditional distribution of each $v_i$ given the rest, is;

$$v_i \sim N\left(\sum_{u_i \in N_i}^{\mu_i}, \delta^2\right)$$

Where $d_i$ is the number of neighbors of county $i$, and $N_i$ is the set of neighbors of county $i$.

The models were implemented using WinBUGS version 14 and MCMC convergence of all models parameters assessed by checking trace plots. The Deviance Information Criterion (DIC) was used to select best fitting model (smallest DIC).

### 3.5 Study Variables

The variables of interest are:

a) For the trend descriptive study:
   - Number of leprosy cases reported over the four year period
   - Annual new case detection rate (per 100,000 population)
   - Sex (Male/Female)
   - Age (Years)
   - Classification of patient (MB/PB)
   - Disability grade at diagnosis (0, 1, 2)

b) For the spatial model and disease risk mapping:
   - Number of leprosy cases per county
- Population density
- Proportion of < 15 year olds among newly diagnosed cases
- Proportion of newly diagnosed cases with G2D
- Proportion of MB cases among new cases
- Median age of leprosy cases (Years)
- County sex ratio

### 3.6 Data Management Plan

#### 3.6.1 Data Sources

The study utilized secondary data; leprosy case-based notification data extracted from the National Leprosy Control Program database and GIS and population based data were obtained from Kenya National Bureau of Statistics.

#### 3.6.2 Data Source Verification

Considering the few number of leprosy cases notified in the country, and the geographic distribution, counties with the highest number of notified cases were sampled (purposive) for data verification purposes. These included Kwale, Killifi, Malindi, Kisumu, Siaya, Homabay, Busia and Bungoma. Two health facilities from among those which reported any case of leprosy within the study period were randomly selected from each county and data in the facility register (considered to be the primary data source) matched to data available in the online TIBU system used to collect case based data from all the facilities notifying leprosy cases.
3.6.3 Data Analysis Plan

a) Exploratory Data Analysis

MS excel and STATA version 11.2 was used to organize/manage and describe emerging trends inherent in the data respectively. Data was summarized in graphs and frequency tables to illustrate changes in leprosy case detection over the years. Chi square tests were carried out to check for association between sociodemographic factors and disease indicators.

b) Model fitting and selection

Leprosy notification, GIS and demographic (2009 census) data was be used to calculate variables including population density and the various proportions as outlined in section 3.5. The spatial models were fit in WinBUGS 1.4 software. A null and full model were fit separately for all cases and only new cases. Better fitting models as evidenced by a lower Deviance Information Criteria (DIC) (Van der Linde, 2005) were selected for inferencing. The relative risks were then mapped.

3.6.4 Data Security and Confidentiality

The data extracted from the National Leprosy Control Program data base was anonymized and no reference made to the patient names, serial numbers or address/ immediate neighborhoods or any other person identifiable variable. All data were password protected hence only authorized persons had access to it.

3.6.5 Data Availability/Sharing

All the study findings will be publicly available through publication of the work in a reputable journal.
3.7 Ethical Considerations

Ethical approval was sought from Kenyatta National Hospital/University of Nairobi Ethics and Research Committee. Data confidentiality was given priority throughout the research process.
CHAPTER 4: RESULTS

4.0 Introduction

The study explored leprosy incidence categorized by disease type, age, gender, type of patient and other disease indicators. This chapter summarizes findings from both the exploratory data analysis and the spatial models fitted.

4.1 Description of Leprosy Case Notification Trend

A total of 467 leprosy cases were notified in Kenya over the four year period distributed across 28 counties. Out of these, 291 (62%) were males and 176 (38%) females. The annual case notification rates for males was persistently higher than that of females, with respective highs of 0.33 and 0.28 cases per 100,000 population in 2014.

Table 3: Annual leprosy case notification rates by sex

![Graph showing the annual leprosy case notification rates by sex from 2012 to 2015.]

The mean and median age of all leprosy cases was 43.4 and 43.5 respectively. The new cases had a mean age of 42.6 and a median of 40, with a range of between 2-89 years whereas the rest of the cases had a mean age of 46.9 and a median of 47, with a range of between 6-82 years. Most
of the leprosy patients were 65 years and older whereas the least number was recorded among the age group 0-14 years. A total of 35 cases (7.5% of all cases) were below the age of 15 years. Generally, the number of cases reported increased with increasing age.

Table 4: Age distribution of notified leprosy cases

The cases are categorized into patient type i.e. new cases and non-new who include all cases of relapse, those resuming treatment and all those transferred in from another health facility. The annual case notification rate was highest in the year 2014; 0.33 and 0.28 per 100,000 population for all cases and new cases respectively. There were 380 new cases representing about 81% of all notified cases.
Of the total number of cases, 409 were of the MB type whereas the remaining 58 were PB, accounting for 88% and 12% respectively. This pattern of reporting was relatively similar across time, with all years reporting over 80% MB cases. Excluding cases for which disability grading was not done at diagnosis, 34.5% presented with grade 1 disability whereas 18.4% had grade 2 disability. In total, 52.9% presented with either grade 1 or 2 disability.
The association between leprosy type and some demographic and disease indicators was assessed using the chi square test. These included the year of diagnosis, sex, age, type of patient and disability grade. None of these factors showed an association with the leprosy type; all p values >0.05.

Table 7: Chi square test results

<table>
<thead>
<tr>
<th>Variables</th>
<th>Type of Leprosy</th>
<th></th>
<th></th>
<th>Chi² (df)</th>
<th>Pr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year (of diagnosis)</td>
<td></td>
<td>MB cases (%)</td>
<td>PB cases (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>71 (89)</td>
<td>9 (11)</td>
<td></td>
<td>2.852 (3)</td>
<td>0.415</td>
</tr>
<tr>
<td>Year</td>
<td>Cases</td>
<td>New Cases</td>
<td>Not New Cases</td>
<td>Type of Patient</td>
<td>New Cases</td>
</tr>
<tr>
<td>-------</td>
<td>-------</td>
<td>-----------</td>
<td>---------------</td>
<td>----------------</td>
<td>-----------</td>
</tr>
<tr>
<td>2013</td>
<td>95 (83)</td>
<td>19 (17)</td>
<td></td>
<td></td>
<td>329 (87)</td>
</tr>
<tr>
<td>2014</td>
<td>128 (90)</td>
<td>14 (10)</td>
<td></td>
<td></td>
<td>80 (92)</td>
</tr>
<tr>
<td>2015</td>
<td>115 (88)</td>
<td>16 (12)</td>
<td></td>
<td></td>
<td>80 (90)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

### 4.2 Spatial Analysis

To better understand the distribution dynamics, two separate models were fit; the first included all leprosy cases and the other only new cases. In both cases, a null and a full model were fitted and their DIC compared.

#### 4.2.1 The Spatial Model

Demographic and disease related covariates informed by the extensive literature review were used to fit a spatial Poisson CAR model. The covariates included sex ratio, population density
per square kilometer, proportion of cases under 15 years of age among newly diagnosed cases, proportion of cases with G2D among new cases, proportion of new cases with MB disease and the median age.

The models were implemented using WinBUGS version 1.4. For each model, 500,000 MCMC iterations were ran, with the initial 50,000 discarded to cater for the burn-in period and there after keeping every tenth sample value. Convergence of models parameters was assessed by checking trace plots and autocorrelation plots. In both cases, the full model fit better (lower DIC) as compared to the null.

**Model 1: All Leprosy Cases**

When all cases were considered, age proved to be the significant predictor, with the risk of leprosy incidence increasing by about 5% for every 1 year increase in age. Table 8 below summarizes the model results.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Null model</th>
<th>Full model</th>
<th>Exponent Estimates (Full model)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>Mean (95% C.I)</td>
<td>Mean (95% C.I)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2.103 (-2.708, -1.62)</td>
<td>2.995 (-13.46, 18.04)</td>
<td></td>
</tr>
<tr>
<td>Sex ratio</td>
<td>-</td>
<td>-8.473 (-23.57, 7.406)</td>
<td>2.0E-4 (5.8E-11, 1.645)</td>
</tr>
<tr>
<td>Population density</td>
<td>-</td>
<td>1.113E-4 (-4.673E-4, 1.00)</td>
<td>1.00 (0.009, 1.00)</td>
</tr>
</tbody>
</table>
Model 2: New Leprosy Cases

Among newly diagnosed cases, only the proportion of MB cases was a significant predictor for leprosy incidence. A one percent increase in the proportion of MB cases increased the leprosy risk by approximately 4%.

Table 9: Spatial Poisson regression results for new leprosy cases

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Null model</th>
<th>Full model</th>
<th>Exponent Estimates (Full model)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean (95% C.I)</td>
<td>Mean (95% C.I)</td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-2.097 (-2.763,-1.57)</td>
<td>8.329 (-7.854,26.21)</td>
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<tr>
<td>Sex ratio</td>
<td>-</td>
<td>-14.84 (-33.75,1.566)</td>
<td>3.58E-7 (2.2E-15, 4.78)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Population density</td>
<td>7.785E-5</td>
<td>(-5.833E-4, 4.7532E-4)</td>
<td></td>
</tr>
<tr>
<td>Proportion &lt; 15 years</td>
<td>0.02 (-0.029, 0.071)</td>
<td>1.02 (0.97, 1.07)</td>
<td></td>
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<tr>
<td>Proportion G2D</td>
<td>0.004 (-0.023, 0.029)</td>
<td>1.004 (0.98, 1.03)</td>
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<tr>
<td>Proportion of MB</td>
<td>0.043 (0.003, 0.092)</td>
<td>1.04 (1.003, 1.096)</td>
<td></td>
</tr>
<tr>
<td>Median age</td>
<td>0.028 (-0.039, 0.092)</td>
<td>1.028 (0.96, 1.096)</td>
<td></td>
</tr>
<tr>
<td>Std.dev (u)</td>
<td>0.498</td>
<td>1.145</td>
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<tr>
<td>Std.dev (v)</td>
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<td>1.353</td>
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<td>DIC</td>
<td>191.36</td>
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</tr>
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</table>

### 4.2.2 Leprosy Distribution Maps

Maps for leprosy actual and expected counts as well as the relative risks were generated. The maps indicate that the western and south east regions have higher than expected counts given their age and sex distribution, as well as high relative risks. Counties with the highest risks of leprosy incidence include Kwale (RR of 15), Kilifi (8.9) and Homabay (4.1), whereas Turkana had the lowest relative risk of 0.005. A similar trend is observed when it comes to new cases with Kwale leading at a relative risk value of 16, Kilifi (8.6) and Homabay (3.7). Turkana remained the county with the lowest risk of new case incidence at a RR value of 0.003. Appendix 2 and 3 rank the county relative risks indicating their 95% credible intervals for all cases and new cases respectively. The figures below illustrate the variation of leprosy distribution in the country. **All leprosy cases**
Figure 2: Observed and expected leprosy counts respectively

Figure 3: Leprosy relative risks and 95% C.I; lower bound, mean, and upper bound respectively.
New leprosy cases

Figure 4: Observed and expected new cases respectively

2.5% for RR

(samples) means for RR

97.5% for RR

< 1  1.0-5.0  5.0-10.0  10.0-15.0  > 15.0
Figure 5: Leprosy relative risks (new cases) and 95% C.I; lower bound, mean, and upper bound respectively
CHAPTER 5: DISCUSSION

5.0 Introduction
This final chapter interprets the results from chapter 4, their implication and further gives
recommendations on leprosy control in Kenya. It also highlights the study limitations hence the
caveats when making reference to this work.

5.1 Interpretation of results
The leprosy case notification trend in Kenya is characterized by more male than female cases, a
high proportion of MB disease and G2D, presence of active transmission and higher counts with
increasing age. The annual case notification rates increased from 2012 and peaked in 2014
followed by a drop in 2015. Possible explanations might be increasing endemicity or improved
case detection activities that may include improved geographical coverage and awareness among
the population. In Kenya, leprosy control activities have not been a priority. In the year 2014,
funds were availed to conduct an active case finding in some counties like Kwale, Kisumu and
West Pokot, generating considerably high numbers of cases. This kind of financial support is not
consistent and the health system in Kenya largely relies on passive surveillance of leprosy. As
earlier discussed, a low suspicion index for leprosy among health workers is detrimental to the
process. The data suggests that there is under reporting of leprosy in the country.

Leprosy transmission remains active as evidenced by the 7.5% of the cases being below the age
of 15 years. Childhood cases are usually associated with recent active foci of transmission, given
leprosy’s long periods of incubation i.e. 2-5 years for PB disease and 5-10 years or sometimes
longer for MB disease. The mean and median ages of all leprosy cases (43.4 and 43.5) shows
that leprosy affects mostly adults. The general increase in cases as age increases might also be
explained by the long incubation period of disease. In support of this, 52.9% of the cases presented with either grade 1 or 2 disability, indicating late diagnosis.

Contact with a leprosy case, especially of the MB form is the major risk factor for leprosy transmission. Out of all diagnosed cases over the study period, 88% had MB disease and only 12% were classified as having PB disease. As much as the numbers of cases notified across the country are few, most of them being of MB type should be of great concern.

The results also indicate that more males than female cases were reported across the ages. From the results, it remains unclear whether there is a significantly higher risk in males or if it is merely due to a biased case ascertainment. Nonetheless, the Global Leprosy Strategy (2016-2020) advocates for special focus on women and children, a direction Kenya should take too.

A similar trend of leprosy case notification was exhibited in Msambweni, an endemic sub county in Kenya, between the period 2007-2012. Out of the 111 cases identified, the median age was 42 years (range: 5-80 years); 66% being males. Multibacillary leprosy was reported in 95% patients while 5% had paucibacillary leprosy. In terms of treatment, 78% were new patients. 41% and 29% had grade two and one disability at the start of treatment respectively. Majority of patients sought treatment after developing disabilities, and many were lost to follow-up (Kadivane et al., 2015).

The regression models revealed that significant risk factors for leprosy incidence in Kenya include the age (for all cases) and the proportion of MB disease among newly diagnosed cases (for new cases). These findings are consistent with existing literature; given MB contact is a high risk factor hence the higher the proportion, the higher the probability of contact. In addition, with increasing age, so does the probability of manifestation of an earlier infection. The other
predictor variables included in the model (sex ratio, population density, G2D proportion and childhood cases among new cases) were not statistically significant. Several studies both agree and conflict with these findings. For instance, in a study in India, there was a positive relationship between leprosy incidence and proportion of childhood cases. In addition, an increase in the proportion of MB cases was associated with increased case detection rates (West et al., 2014). Early diagnosis has been associated with marked improvement of epidemiological situation of leprosy in Rio de Janiero, Brazil (Monica et al., 2012). In addition, active detection of cases in North East Brazil as suggested by reduced cases among persons under the age of 15 years and reduced proportion of G2D, reinforced the positive role of stakeholders and other partners’ involvement in the control of leprosy.

The model in this study did not include a measure of socioeconomic status and other cultural factors. This was due to the difficulty in reliably obtaining these values. Some studies have proved that socioeconomic status influences leprosy incidence. In the state of Sao Paulo, South East Brazil, schooling and longevity was shown to have a positive relationship with leprosy incidence whereas increasing wealth decreased leprosy incidence (Rodrigues et al., 2008). In addition, vulnerable groups as measured by the social index were at a higher risk of leprosy in Manaus municipality in Northern Brazil (Elsia et al., 2009). Other studies have conflicted these findings as was the case in Malawi where socioeconomic, cultural factors and population density showed no statistical significance (Sterne et al., 1995). In the Brazil Amazon region, high endemicity could not be explained by socioeconomic conditions of the population (Penna et al., 2009). In addition, Maria et al showed that leprosy remains endemic in this area despite increasing economic development. Nonetheless, there is need to estimate the influence of socioeconomic status on leprosy incidence in Kenya.
As depicted by the spatial maps, counties with high relative risks tend to be close to each other; in western and south east regions. This suggests a geographic variation in either the risk factors, population based factors and/or health system. Also, leprosy awareness may have played a role in higher case detection in these regions. Several studies have proved that leprosy incidence and prevalence shows spatial autocorrelation. In Bangladesh, several spatial temporal clusters were observed for voluntarily reported cases. However, the cases within and without the clusters did not differ in age at detection, % with MB disease or sex ratio (Fischer et al., 2008). In the Brazilian state of Espirito Santos, leprosy showed spatial autocorrelation (Poliane et al., 2012), and so was the case in the state of Ceara (Montenegro et al., 2004) and Tocantus (Monteiro et al., 2015). In the latter, there was clustering of increased disease risk, ongoing transmission and late diagnosis.

5.2 Recommendations for leprosy control

The recommendations outlined in this section are informed by the research findings and are aligned with the National Strategic Plan for Leprosy (2015-2018). There is need to drastically but steadily improve the leprosy surveillance system in the country. One of the fundamental strategies towards improving the surveillance system proposed by the NSP is mapping of leprosy cases to identify the hot spots, an objective achieved by this study.

To effectively implement leprosy control activities given the constrained resources, focus should initially be on the high risk counties herein defined as counties with a relative risk of more than one. These include 8 counties namely; Kwale, Kilifi, Homa Bay, Siaya, Busia, Mombasa, Kisumu and Lamu. In these counties, the following approaches should be implemented:
• Training of health care workers and community health volunteers on leprosy, specifically early symptoms of the disease to increase the index of suspicion. Further, leprosy data ought to be shared during routine data review sessions; awareness is better created through persistence rather than one-off training sessions.

• All contacts of children (0-14 years) diagnosed with leprosy should be traced and screened.

• Carefully planning and conducting active case finding ensuring no biased case ascertainment; women, children and other vulnerable populations to be included. The respective county health departments should be proactive and allocate resources for leprosy control instead of relying on the national government and ad hoc donor support.

• Improving rehabilitation services access for all patients with physical disability.

A well planned surveillance system will not only improve treatment outcomes, but also strengthen monitoring and evaluation by generating data that is comparable over time.

5.3 Study limitations

Some of the study assumptions and limitations include:

• The leprosy case notification rate is used as a proxy for disease incidence. This does not capture the true incidence of disease as not all leprosy cases may be registered at a health facility. In addition, the health seeking behavior, access to and utilization of health services is beyond the scope of this study.

• Ecological fallacy; the findings of this study will only be valid at the county level and cannot be extended to the individual level.
• The modifiable area unit problem; available data will be analyzed with respect to the 47 county boundaries hence study findings are only valid for these specific boundaries.
• This study assumed a Poisson distribution for the leprosy counts, and does not in any way imply that it is the model that best fits the data. There is room to explore other statistical models and their DIC values compared.

5.4 Conclusion

Leprosy has been neglected for a long time in the public health arena after the declaration of its elimination as a public health problem. This study proves that leprosy is still affecting people adversely and causing disability in certain parts of Kenya and emphasizes the importance of local strategies to address localized disease states.
REFERENCES


Maria, L.F. Penna, Maria, L., Wand-del-Rey de Oliveira, and Gerson Penna. *Spatial Distribution of Leprosy in the Amazon Region of Brazil.*


WHO Expert Committee on Leprosy; eighth report (2012).


APPENDICES

Appendix 1: WinBUGS code for fitting the spatial Poisson CAR full model

model
{
# Likelihood
for(i in 1:N)
{
  Y[i]~dpois(mu[i])
  log(mu[i])<-log(Eall[i])+beta0+beta1*sexratio[i]+beta2*density[i]+beta3*propunder15[i]+beta4*propG2D[i]+beta5*propMB[i]+beta6*medianage[i]+u[i]+v[i]
  RR[i]<-
  exp(beta0+beta1*sexratio[i]+beta2*density[i]+beta3*propunder15[i]+beta4*propG2D[i]+beta5*propMB[i]+beta6*medianage[i]+u[i]+v[i]) # County specific relative risk
  # Prior on unstructured random effects
  u[i]~dnorm(0,precu)
}
# CAR prior for spatial random effects
v[1:N]~car.normal(adj[],weights[],num[],precv)
for(k in 1:sumNumNeigh)
{
  weights[k]<-1
}
# Other priors

\[ \beta_0 \sim \text{dflat()} \]

\[ \beta_1 \sim \text{dnorm}(0, 0.00001) \]

\[ \beta_2 \sim \text{dnorm}(0, 0.00001) \]

\[ \beta_3 \sim \text{dnorm}(0, 0.00001) \]

\[ \beta_4 \sim \text{dnorm}(0, 0.00001) \]

\[ \beta_5 \sim \text{dnorm}(0, 0.00001) \]

\[ \beta_6 \sim \text{dnorm}(0, 0.00001) \]

\[ \text{prec}_u \sim \text{dgamma}(0.01, 0.01) \] # priors on precision

\[ \text{prec}_v \sim \text{dgamma}(0.5, 0.0005) \]

\[ \text{sigma}_v < - \sqrt{1/\text{prec}_v} \] # Standard deviation of \( v \)

\[ \text{sigma}_u < - \sqrt{1/\text{prec}_u} \] # Standard deviation of \( u \)

}

# Initial values

\[ \text{list(} \text{prec}_u=1, \text{prec}_v=1, \beta_0=0, \beta_1=0, \beta_2=0, \beta_3=0, \beta_4=0, \beta_5=0, \beta_6=0, u=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0), v=c(0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)) \]
### Appendix 2: Ranked leprosy relative risks per County; all cases

<table>
<thead>
<tr>
<th>No.</th>
<th>County Name</th>
<th>Mean RR</th>
<th>95% Credible Interval</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2.5%</td>
</tr>
<tr>
<td>1</td>
<td>Kwale</td>
<td>14.96</td>
<td>10.03</td>
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<td>Siaya</td>
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Appendix 3: Ranked leprosy relative risks per County; new cases

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<th>County Name</th>
<th>Mean RR</th>
<th>95% Credible Interval</th>
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Appendix 4: Map of Kenya; Administrative boundaries