# SPATIAL MODELLING OF PERINATAL MORTALITY IN MCHINJI, MALAWI

MSC. (BIOSTATISTICS) THESIS

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UNIVERSITY OF MALAWI
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# SPATIAL MODELLING OF PERINATAL MORTALITY IN MCHINJI, MALAWI

## MSc (Biostatistics) Thesis

By

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# Declaration

I the undersigned hereby declare that this thesis/dissertation is my own original work which has not been submitted to any other institution for similar purposes. Where other people's work has been used acknowledgements have been made.

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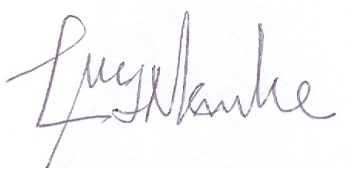
Signature:  Date:. . . .....

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# Dedication

To my parents and fiancée for their care and love. God has been so good to bless me with a family and fiancée who did all they could. It takes a lot of time to know what love is. It is not the big things, but little things that mean enough. I know a lot of prayers have been done by you to get me through thick and thin.

You are always there for me, pushing me and guiding me always to succeed. You have been showing me how to love, care and that you will always be there for me. I thank you all for your time and I am proud to say that you are mine.

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Above all else I give my thanks and praise to Jehovah for wonderful gift of life and the golden chance given to me to study at Chancellor College, University of Malawi.

# Abstract

The main aim of the study was to quantify small-scale geographical variations in perinatal mortality and estimate risk factors associated with perinatal mortality in Mchinji, Malawi.

The study modelled infant mortality in the first 7 days of life, hence logistic regression approach was appropriate to investigate risk factors for the mortality. The Bayesian STAR modelling approach was applied to account for the influence of both individual and contextual factors on perinatal mortality. Socio-demographic and delivery factors were considered in the study. Modelling and inference used the fully and empirical Bayesian approaches. The methodology was applied to analyze the prevalence and risk factors of perinatal mortality, using data from 2005 to 2010 collected by MaiMwana project in Mchinji district in Malawi. The number of subjects considered for analysis is 7, 627, representing 92 percent of the total number of subjects.

The factors that were associated with perinatal mortality are as follows: previous pregnancy compared to none (OR = 0.70, CI: 0.51, 0.99); first ANC visit in first trimester with at least 4 visits (OR = 0.29, CI: 0.10, 0.84), second trimester with less than 4 visits (OR = 0.28, CI: 0.10, 0.79), second trimester with at least 4 visits (OR = 0.22, CI: 0.08, 0.61), third trimester with less than 4 visits (OR = 0.18, CI: 0.06, 0.55) and third trimester with at least 4 visits (OR = 0.05, CI: 0.01, 0.23) compared to none; blood sample test compared to none (OR = 1.92, CI: 1.44, 2.62); syphilis test compared to none (OR = 0.60, CI: 0.41, 0.85); abdominal examination compared to none (OR = 0.32, CI: 0.21, 0.49); pregnancy danger signs advice compared to none (OR = 0.28, CI: 0.21, 0.37); skilled birth attendant compared to non-skilled birth attendant (OR = 0.73, CI: 0.58, 0.94); normal labour duration compared

to prolonged labour duration (OR = 0.37, CI: 0.28, 0.49); gestation period of at least 9 months compared to that of 7 to 8 months (OR = 0.11, CI: 0.08, 0.14); and normal delivery compared to other modes (OR = 0.18, CI: 0.12, 0.28). Perinatals from mothers with the age range of 16 to 40 years had reduced prevalence of dying whereas those from mothers with the age of less than 16 years and greater than 40 years were associated with higher prevalence of dying. After accounting for all significant covariates, high perinatal mortality (OR $\geq$ 1) was observed in zones located on the eastern part whereas low perinatal mortality was observed in zones found on the western part of the district.

The findings of the study have shown that perinatal mortality was high on the eastern part and low on the western part of Mchinji district. In the study area, the eastern part should be given first priority in the provision of targeted interventions. Targeting health interventions to poorer or higher risk areas and ensuring universal coverage are promising approaches for promoting equity and reducing perinatal mortality.

**Keywords**: STAR models, MCMC, Full Bayesian, REML and Empirical Bayesian.

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# List of Abbreviations and Acronyms

| | |
|---|---|
| AIC | Akaike Information Criterion |
| ANC | Antenatal Care |
| BIC | Bayesian Information Criteria |
| CAR | Conditional Autoregressive |
| DIC | Deviance Information Criterion |
| EmONC | Emergency Obstetric and Neonatal Care |
| FANC | Focused Antenatal Care |
| GAM | Generalized Additive Model |
| GAMM | Generalized Additive Mixed Model |
| GLM | Generalized Linear Model |
| GLMM | Generalized Linear Mixed Model |
| GRF | Gaussian Random Field |
| ITNs | Insecticide Treated Nets |
| MCMC | Markov Chain Monte Carlo |
| MDHS | Malawi Demographic and Health Survey |
| MiP | Malaria infection in Pregnancy |
| MRF | Markov Random Field |
| PNC | Postnatal Care |
| RDTs | Rapid Diagnostic Tests |
| REML | Restricted (Residual) Maximum Likelihood |
| SBA | Skilled Birth Attendance |
| SP | Sulphadoxine-Pyrimethamine |
| STAR | Structured Additive Regression |
| TBA | Traditional Birth Attendant |
| TTV | Tetanus Toxoid Vaccination |
| WHO | World Health Organisation |

March 10, 2013

# Chapter 1

# Introduction

## 1.1 Background

There has been an increasing awareness, in recent years, that perinatal period is a neglected public health problem (Martines et al., 2005). This has been underscored by the fact that about 4 million newborns are dying every year during the first four weeks of life and the rate of perinatal mortality has remained unchanged in the past decades (Lawn et al., 2005). To address the problem, interventions targeting mothers and newborns have been encouraged (Martines et al., 2005). Some improvements can be seen, but still the pace is slow, especially in the intra-partum and early neonatal periods (Lawn et al., 2009). Most of these neonatal deaths occur during the first day of life and complications related to delivery care contribute to a large proportion of the overall neonatal mortality (Målqvist et al., 2010). Several studies have been conducted using different methodologies in trying to identify the potential risk factors and causes of perinatal mortality in many countries including Malawi (Ishaque et al., 2011; Lawn et al., 2010; Muula and Metaferia, 2009). However, more infants are still dying every day (Gabrysch and Campbell, 2009; Majeed et al., 2007). The purpose of this study is to quantify the principal risk factors that influence stillbirths and early neonatal mortality, and to produce a map of all-cause perinatal mortality spatial patterns in Mchinji district using Bayesian statistical models.

## 1.2 Defining Perinatal Mortality

Perinatal mortality is the sum of stillbirths and ENDs (Diallo et al., 2010; Lee et al., 2011). ENDs are deaths within the first 7 days of life after delivery (WHO, 2006). Stillbirth is a late fetal death weighing more than 1000 grams prior to the complete expulsion, and it usually occurs after 28 weeks of pregnancy (Lawn et al., 2010). The death is usually indicated by failure of the fetus to breathe after such separation or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles (Jehan et al., 2009). Stillbirths are categorized into ante-partum and intra-partum. Ante-partum stillbirths are stillbirths that occur during antenatal period and before onset of labour, whereas intra-partum stillbirths are stillbirths occurring after the onset of labour, or as "fresh stillbirths" (Lawn et al., 2005).

The rates of stillbirths and ENDs may be considered as indicators of quality of ante-partum, intra-partum and neonatal care (Johnston and Coory, 2005; Shrestha et al., 2006). However, Garne (2001) has argued that perinatal and neonatal mortality rates are not good indicators for comparing quality of perinatal health services between countries because definitions of these outcomes still vary across the developed world. As such the wide variations seen in neonatal outcomes may be attributable to external influences. For example, differences in definition, ascertainment levels and registration as well as hospital policies regarding delivery and neonatal unit admission, particularly around the limits of viability. Nevertheless, both ante-partum and intra-partum fetal deaths are major contributors to perinatal mortality as a consequence of prematurity or sudden infant death syndrome (Khashoggi, 2005; Majeed et al., 2007).

## 1.3 Burden of Perinatal Mortality

The annual global number of perinatal deaths as estimated by WHO in 2004, stood at 5.8 million with 3 million stillbirths and 2.8 ENDs. Sub-Saharan Africa (SSA) had the highest

perinatal mortality rate, estimated to be 56 per 1, 000 births in 2004, followed by the Asian region with 47 per 1, 000 births (Diallo et al., 2010). In 1995, the WHO estimated the overall perinatal mortality rate in low-income countries to be 57 per 1, 000 births compared with 11 per 1, 000 births in high-income countries. Of the estimated 7 million perinatal deaths in 1995, more than 4 million occurred in Asia and over 2 million in Africa (Majeed et al., 2007). Within the African region there is considerable variation, with the Central and West African regions having the highest perinatal mortality rates in the world, at 74 and 69 per 1, 000 births respectively (WHO, 2007). An earlier report from Malawi showed a perinatal death rate of 68.3 per 1, 000 births in 1996; 56% were stillbirths and the remaining 44%, ENDs (McDermott et al., 1996). The MDHS conducted in 2004 reported perinatal mortality rate of 34 per 1, 000 births whereas that of 2010 reported perinatal death rate of 40. In Kenya, Weiner et al. (2003) reported a perinatal mortality rate of 118 per 1, 000 births in 2003. In a Nigerian teaching hospital Kuti et al. (2003) reported a perinatal mortality rate of 77.03 per 1, 000 total births. In South Africa, however, a much lower perinatal mortality rate of 59 per 1, 000 births has been reported, but still much higher than what is reported from similar high income countries (Muula and Metaferia, 2009). The estimated incidences of stillbirths and ENDs vary worldwide based on socio-economic, demographic and clinical profiles. Although sophisticated perinatal diagnostics and better intra-partum monitoring have reduced the global incidence, unfortunately the problem remains predominantly high in developing countries (Gabriela, 2003). Perinatal mortality is more difficult to prevent than infant mortality, hence it has received global attention as a proxy indicator of maternal and child health care of a country (Khashoggi, 2005). In low-income countries a significant proportion of stillbirths occur in the intra-partum period and these deaths are commonly attributed to avoidable factors related to inadequate maternity care (Muula and Metaferia, 2009).

## 1.4 Causes and Risk Factors of Perinatal Mortality

Numerous studies have been carried out with the aim of identifying the potential risk factors and causes of perinatal mortality. There are many risk factors and causes of perinatal mortality. Stillbirths are often associated with the following factors: major congenital anomalies; multiple systemic anomalies; central nervous system anomalies; renal agenesis; skeletal anomalies; umbilical cord complications; vaginal bleeding; anaemia; hypertension; oedema; prolonged rupture of membranes; non-cephalic presentation; severe intrauterine growth retardation; maternal shock; pre-eclampsia; and extreme prematurity and uncontrolled diabetes mellitus with resultant macrosomia (Majeed et al., 2007). Maternal smoking, advanced maternal age, high parity and obesity are widely recognized maternal contributing factors, whereas congenital anomalies, intrauterine growth retardation, cord complications and infections are the common fetal causes of antepartum stillbirths (Gabriela, 2003). Intra-partum fetal death is usually the result of fetal distress or obstructed labour and reflects poor quality of clinical care. In their study Fretts et al. (1995) found that older women had a higher prevalence of conditions that could increase the risk of fetal death. Globally, the more perinatal deaths are caused by infections, preterm birth and birth asphyxia. These main causes account for 87% of neonatal deaths worldwide, with infection (36%), preterm birth (28%) and birth asphyxia (23%) (Jehan et al., 2009).

In their study Bill and Melinda Gates Foundation (2009) reported that preterm birth, severe infections (sepsis, pneumonia and meningitis), and birth asphyxia account for 76% of neonatal deaths. Fetal sepsis at term has been associated with deterioration in the fetal acid-base status and a prolongation of labour while in their study Nelson and Ellenberg (1984) have shown that prolonged rupture of membranes and chorioamnitis are major predictors of cerebral palsy (Majeed et al., 2007). In several studies, twins have been found to be at high risk of perinatal death (Engmann et al., 2009; Habib et al., 2008). Preterm birth and intrauterine growth restriction are two factors suggested to increase the vulnerability of multiple births to perinatal death (Diallo et al., 2010). In their study Jehan et al. (2009) found out that the

infection, including sepsis, pneumonia and meningitis, which is an important contributor to neonatal deaths occurs after 3 days postpartum among hospital-born neonates.

Birth asphyxia is a serious clinical problem worldwide. Each year approximately 4 million babies are born asphyxiated, which results in one million deaths and an equal number of serious neurological squelae, such as cerebral palsy, mental retardation, and epilepsy (Majeed et al., 2007; WHO, 2005). Asphyxia is failure of the fetus or newborn to get oxygen or lack of perfusion to various organs (Lee et al., 2011). Perinatal asphyxia is a leading factor contributing in perinatal and neonatal mortality which reflects social, educational and economical standards of the community. Its incidence is very high in developing countries. Poverty, illiteracy, low status of women, poor hygiene, lack of clean water and sanitation, family inability to recognize danger signs, and inadequate access to medical care all increase the risk for morbidity following birth asphyxia in developing countries (Halloran et al., 2009). An estimated 1 million children who survive birth asphyxia live with chronic neuro-developmental morbidities, including cerebral palsy, mental retardation, blindness, long term intellectual impairment and behavioral problems, and learning disabilities (Lee et al., 2011, 2008). One of the interventions of reducing neonatal deaths due to asphyxia is neonatal resuscitation. Neonatal resuscitation is the set of interventions that are provided at the time of birth to support the establishment of breathing and circulation (Lee et al., 2011).

With regards to infectious diseases, malaria contributes significantly to perinatal disease burden in terms of pregnancy losses, prematurity due to preterm labour and intra-uterine growth retardation (Mwaniki et al., 2010).The pregnant woman has a higher risk of contracting malaria than her non-pregnant counterpart due to immune-complacence. *Plasmodium falciparum* infection in pregnancy is associated with an increased risk of maternal and fetal complications including maternal anaemia and low birth weight (Smith et al., 2010). *Plasmodium falciparum* has also been associated with stillbirth especially in primigravidas owing to its high prevalence and extensive placental damage (Ishaque et al., 2011). WHO has recommended a package of interventions for preventing and controlling MiP in endemic areas, which includes the early diagnosis and treatment of malaria, intermittent preventive treat-

ment during pregnancy (IPT) using SP and the use of ITNs. Currently, SP-IPT has been rated as having the most favourable cost-benefit profile because of its relatively low cost, high compliance and efficacy in reducing maternal anaemia and low birth weight. However, implementation of IPT in pregnancy in most settings is limited by social, cultural, economic and operational challenges despite good coverage of antenatal services. In addition, resistance to SP has been spreading across SSA and thus the effectiveness of SP-IPT has been questioned (Newman et al., 2003). Screening for malaria using RDTs during FANC visits and treating those women who are positive for malaria with an effective combination of drugs (termed intermittent screening and treatment (IST)) appears to be an alternative approach to control MiP in areas with high SP resistance (Smith et al., 2010).

Although maternal anaemia is multifactorial, malaria is known to contribute significantly to its occurrence in pregnancy. Anaemia affects 41.8% of pregnant women globally, with the highest prevalence in Africa (WHO, 2006). In the study conducted by Ali et al. (2011), the prevalence of preeclampsia and eclampsia was significantly higher in women with severe anaemia (8.2% and 3.3%, respectively). Preeclampsia is a pregnancy condition in which high blood pressure and protein in the urine develop after the 20th week of pregnancy. It is a pregnancy-specific condition and is associated with high maternal mortality and morbidity as well as risk of perinatal death, preterm birth, and intrauterine growth restriction. It occurs in 4 - 7% of pregnant women worldwide (Landau and Irion, 2005). The risk factors of preeclampsia are first pregnancy and multiple pregnancy. The multiple pregnancy includes nulliparity; family or own history of preeclampsia; pre-existing diabetes or increased body many mass index; multiple pregnancy; maternal age; renal disease; hypertension or raised blood pressure at booking; and chronic autoimmune disease (Shamsi et al., 2010).

Syphilis remains a major cause of avoidable perinatal death in many countries despite being treatable, and despite the WHO recommendation that all pregnant women be tested as part of routine antenatal care. Most studies report syphilis to have a relative risk of stillbirth in the range of 2 to 5. However, a Tanzanian study reported a relative risk of 18 for women with active syphilis (Ishaque et al., 2011).

Approximately 370,000 children were newly infected with HIV during 2009 through mother to child transmission (UNAIDS:, 2010). SSA, the region most affected by HIV, accounts for 67% of HIV infections worldwide and 91% of new infections among children (Byamugisha et al., 2010). Children born to mothers with HIV are at increased risk of dying, even when they themselves are uninfected. However, in the absence of any intervention, 30-45% of children born to mothers with HIV will become infected through in-utero, peripartum or breast milk exposure, and, without treatment, 35% of these will die before they are one year old. Studies have shown that short-course, easy-to-use, and affordable antiretroviral regimens can significantly reduce mother-to-child transmission (MTCT) of HIV (Lewycka et al., 2010).

## 1.5 Health Systems and Community Correlates of Perinatal Mortality

Although unexplained perinatal deaths will continue to occur, perinatal mortality can be reduced if its causes and risk factors in a community are given priority in antenatal and intra-partum care programmes (McDermott et al., 1996). Early identification of high risk cases with improved antenatal and perinatal care can decrease such high mortality. Antenatal, delivery and postnatal care services are amongst the recommended interventions aimed at preventing maternal and newborn death worldwide (Mrisho et al., 2009; Titaley et al., 2010b). Through ANC, women benefit from various interventions, including counselling about healthy lifestyles, the provision of iron/folic acid supplements, and TTV reported four ANC checks, one in the first trimester, one in the second and two in the last trimester, and control of nutritional deficiencies (Titaley et al., 2010b).

ANC is defined as health care services related to pregnancy provided by skilled health personnel before delivery (Graner et al., 2010; Titaley et al., 2010b). This includes the provision of therapeutic interventions that would benefit the woman and her infant, as well as education about the importance of planning for a safe birth. A review on interventions for neonatal survival demonstrated that up to 12% of neonatal deaths could be averted by the

provision of ANC services at 90% coverage. ANC enables health professionals to identify potential risks for the pregnancy or for the delivery and to provide prompt treatment for women experiencing health problems during pregnancy (WHO, 2005). Observational studies from both developed and developing countries have shown a protective effect of ANC services on neonatal deaths, and inadequate ANC has been associated with adverse pregnancy outcomes (Titaley et al., 2010a). WHO considers it essential that all women are offered TTV, screening and treatment of anaemia and syphilis, and are examined for pregnancy related complications such as hypertensive disorders and mal-presentations (Graner et al., 2010).

Most obstetric complications occur around the time of delivery and cannot be predicted. Therefore, it is vital that all pregnant women have access to a skilled birth attendant. Access to skilled delivery care is also crucial to prevent stillbirths and to improve newborn survival (Gabrysch and Campbell, 2009). EmONC requires SBA with the ability to provide parenteral medications; carry out procedures like manual removal of the placenta, forceps or vacuum deliveries; perform blood transfusions, cesarean sections and provide newborn care/resuscitation. Current efforts to reduce peripartum deaths focus on skilled delivery attendance for every birth backed up by emergency obstetric care and facility-based delivery. However, 60 million births currently occur outside facilities, 52 million without skilled attendance (UNICEF, 2009). The information provided during ANC visits enables women and their family members to recognize and act on danger signs or complications, and adopt health promoting behaviours such as adhering to prescribed treatments and referral advice. The scope of health education and counselling on pregnancy and related complications provided to women during ANC visits in most Sub-Saharan African countries is often inadequate or nonexistent. This may be a contributing factor to the discrepant pattern of high ANC but low SBA uptake in many of these settings (Magona et al., 2011).

The evidence from recent research suggests that information on the importance of immediate PNC on maternal and early neonatal health is rarely provided during antenatal consultations. PNC is defined as health services provided to mothers and newborns within the first 42 days after childbirth. It includes early detection and treatment of complications and diseases

as well as education about breastfeeding, immunization and nutrition (Mrisho et al., 2009; Titaley et al., 2010b). The postnatal period, just after delivery and through the first 6 weeks of life is recognized as a critical time for both mothers and newborns. PNC services enable health professionals to identify post-delivery problems, including potential complications, and to provide treatments promptly (Titaley et al., 2010b). In most countries including Malawi, neonates are recommended to receive at least 2 adequate health care checks within the period of 0 to 7 days and 8 to 28 days after birth. In postnatal services, women usually receive services such as BCG, Hepatitis B and Polio immunization, as well as counselling about breastfeeding and infant health care (NSO, 2011; Titaley et al., 2010b).

The ANC policy in Malawi follows the newest WHO FANC approach to promote safe pregnancies and at least four ANC visits are recommended for women without complications. The new schedule of visits is as follows: first visit should occur by the end of 16 weeks of pregnancy; second visit between 24 and 28 weeks of pregnancy; third visit at 32 weeks; and fourth visit at 36 weeks. However, women with complications, special needs, or conditions beyond the scope of basic care may require additional visits (NSO, 2011). Over 90% of women have at least one ANC visit during pregnancy in Malawi, but perinatal and neonatal mortality are still high (Lewycka et al., 2010). This may partly have to do with poor quality services, but also making the first visit late, or not all of the recommended visits. Much less is known about the utilization of PNC services, the importance of which has recently been emphasized. In their study Gabrysch and Campbell (2009) found out that women with an unwanted pregnancy are more likely to underutilize ANC services, and that unwanted pregnancies are associated with late start or less frequent ANC visits compared to wanted pregnancies.

Studies from developing countries have reported the influence of demographic and socio-economic factors on the utilization of maternal and child health care services. Women with higher economic status, higher educational levels, and who live in urban areas with adequate health care services are more likely to utilize health care services (Titaley et al., 2010b). Therefore, efforts to improve ANC and PNC should focus on addressing geographical and

economic access while striving to make services more culturally sensitive (Mrisho et al., 2009). Geography and culture can both lead to failure to access health care, and therefore inequity in infant survival. Another factor is the impact of dysfunctional health services; communities may have geographic access to adequate health services but fail to derive any benefit from them (Mulholland et al., 2008; Penchansky and Thomas, 1981). Gaps between mortality of infants from wealthier and poorer families within most countries are unacceptably wide and in some areas the gap is increasing (Wagstaff, 2000). Availability of ANC and PNC services as well as differences in ethnic norms and practices are some of the factors influencing disparities in child mortality at community level. Evidently, the combined effects of all these factors are likely to cause geographical disparities in childhood mortality, including perinatal mortality (Kazembe and Mpeketula, 2010).

## 1.6 Problem Statement

In recent years, the impact of stillbirths and early neonatal mortality has attracted considerable attention in Malawi, as there is still a good number of perinatal deaths despite an increased amount of funds to the Ministry of Health by the government and non-governmental organizations. There have been formal attempts to come up with the main risk factors and causes of the same, but, little consensus has emerged. Due to the increased costs on health services being rendered to achieve Millennium Developmental Goal number 4 of targeting a two-thirds reduction of under-five deaths between 1990 and 2015, there is still a need for methods that will help to understand the influencing factors and causes of perinatal mortality.

Several studies have been carried out on the subject yielding different results as to what factors and causes are most responsible for the increased perinatal mortality. For example, (Muula and Metaferia, 2009) determined the prevalence of stillbirths, early hospital neonatal death and associated factors in Blantyre, Malawi using a prospective observational study of pregnant and post-natal women that was conducted at the Queen Elizabeth Central Hospital using descriptive statistics. In addition, McDermott et al. (1996) assessed the prevalence and

risk factors for perinatal death among pregnant women in Mangochi, Malawi over the period 1987-1990 using logistic regression analysis. Recently, Lewycka (2011) evaluated the impact of a community based women's group intervention where among other methods logistic regression was used. All these studies were carried out with little regards to spatial distribution of perinatal mortality, hence the need for this study.

With high perinatal mortality burden and considering the scarce resources in Malawi, targeted interventions are required to reduce this mortality. The study of spatial variation in perinatal mortality can assist in highlighting hot spots and cold spots for the targeted interventions. However, despite the increase in the use of Bayesian spatial models in risk mapping and prediction of health outcomes (Diggle et al., 2002; Gemperli et al., 2006; Riedel et al., 2010; Schur et al., 2011), few studies have analysed spatial variations in population dynamics including all-cause perinatal mortality using these models.

## 1.7 Study Objectives:

### 1.7.1 Main Objective

To quantify small-scale geographical variations in perinatal mortality and estimate risk factors associated with perinatal mortality in Mchinji, Malawi, by applying Bayesian STAR modelling approach.

### 1.7.2 Specific Objectives

1. To investigate the geographical pattern associated with perinatal mortality prevalence in specific zones in Mchinji, Malawi.

2. To determine the potential risk factors associated with perinatal mortality, including evaluating the effect of birth attendant on perinatal mortality in Mchinji.

3. To compare results from the Generalized Linear Models and the flexible approaches

(STAR Models) in determining risk factors of perinatal mortality.

## 1.8 Significance of the Study

Results of the study will provide necessary information to policy makers, which will help in decision making as regards to the addressing of the health inequalities in the study area as well as improvement of the access to quality health services. In particular, the information will provide guidance on how best to allocate the limited resources in the study area to reduce perinatal mortality. The information will also help in making a decision on whether there is still a need to conduct more awareness campaigns on importance of health care-seeking practices during pregnancy and infant bearing period in trying to promote safe motherhood in Malawi.

Bayesian statistical models allow one to accurately quantify inequalities in health, identifying risk factors for mortality within a population and predicting mortality at unsampled locations, and, ultimately, generating smoothed maps of mortality risk (Beale et al., 2008). These models relax the assumption of independence by, for example, incorporating random effects to measure spatial correlation as a function of distance between locations (Sartorius et al., 2011).

## 1.9 Structure of the Thesis

The rest of this thesis is structured as follows: Chapter 2 gives the statistical theory of spatial epidemiology, while Chapter 3 gives the application of Bayesian spatial models in perinatal mortality. Chapter 4 presents the results and summary of the analysis. Lastly, Chapter 5 provides a discussion of results, conclusion, recommendations and limitations of the study.

# Chapter 2

# Statistical Theory

## 2.1 Spatial Epidemiology

Many individual and household level factors have been identified as key determinants of perinatal mortality using various epidemiological studies (Sartorius et al., 2011). The integration of spatial dimension into epidemiological investigations provides an opportunity for conducting more informative descriptive analyses and gaining additional insights into the causal processes under investigation (Pfeiffer et al., 2008). Therefore, spatial epidemiology should be encouraged to understand better the key determinants of perinatal mortality. Spatial epidemiology is the study of the spatial or geographical distribution of disease incidences and its relationship to potential risk factors. Knowledge of the spatial and temporal variations of diseases and characterization of its spatial structure is essential for the epidemiologist to better understand the population's interaction with its environment. Advances in technology now allow not only disease mapping but also the application of spatial statistical methods, such as cluster analysis (Kulldorff et al., 1997; Rosenberg et al., 1999) and ecological analysis (Ali et al., 002a,b, 2001) in epidemiological research. Geographic Information System (GIS) methods and modern statistical methods like Bayesian models allow an integrated approach to address both tasks; that is, inference on the geographical distribution of the health outcome and its prediction at new locations. Bayesian spatial modelling has increasingly been applied in epidemiological research, especially with regards to malaria risk and transmission.

For example, Gemperli et al. (2004) carried out a Bayesian spatial analysis of infant mortality in Bali that confirmed well-known risk factors and found a spatial pattern of infant mortality that showed a clear relationship with established foci of malaria transmission. The binary logistic linear geo-statistical model was also applied by (Diggle et al., 2002)to quantify risk factors for childhood malaria in Gambia, in which the presence of malarial parasites in blood sample was parameterized in terms of child-level covariates, village-level covariates, and separate components for residual spatial and non-spatial extra-binomial variation.

Although Bayesian spatial models help in risk mapping and predicting health outcomes, no previous studies have used these methods to analyse the spatial distribution of perinatal mortality in Malawi. More studies on perinatal mortality in Malawi have used classical and Generalized Linear Models, which fail to quantify the effect of covariates on the response variable effectively.

### 2.1.1 Spatial data types

Spatial data can be collected at different levels and in different ways. For example, they can be collected at district, Traditional Authority (TA), zone, village, household and individual levels, and as count or binary. The type and intended use of spatial data determines the choice of the appropriate statistical modelling approach (Pfeiffer et al., 2008). Usually, data are collected at particular locations. In many cases, the location may provide additional insight into circumstances associated with the data item. The field of spatial statistics involves methods utilizing location and distance in inference. Some methods are extensions of familiar techniques such as regression, GLMs, and time series, while others drive from particular models of stochastic processes in space (Waller, 2005). Much of the recent increase in the use of spatial statistics can be tied to the relatively simultaneous increases in both spatial data availability, including accurate location measurements via Global Positioning System (GPS) technology, and rapid improvements in computational power allowing advances in both spatial data structures and in the fitting of extraordinary complex models via sophisticated algorithms.

Spatial statistical methods may be classified by the inferential questions of interest, which are motivated by application and often fall into categories based on the type of data available. Three useful categories of spatial data are provided by Cressie (1993) that also serve to categorize both inferential questions and approaches. These categories include: spatial point data; geostatistical data; continuous; and lattice or regional data.

#### 2.1.1.1 Spatial point data

These data consist of a set of observed locations in a defined study area. The locations themselves are considered as realization of some random process and seek inference regarding the properties of this process. The questions of interest try to find the following: whether the observations are equally likely at all locations. If not, where are observations more or less likely; whether there are (spatially- referenced) covariates that drive the probability of observations occurring at particular locations; whether the presence of an observation at a particular location either encourages or inhibits further observations nearby. If the observations do impact the probability of nearby observations, the questions try to find the range of influence of observations (Stevenson, 2003).

#### 2.1.1.2 Geo-statistical data

These types of data consist of a set of measurements taken at fixed set of locations. In this case, the locations are set by design and not random. An inferential question of interest is prediction of the same outcome at locations where no measurements were taken (Gemperli et al., 2004; Diggle et al., 2002; Kneib, 2005). The literature on spatial prediction builds from a fairly simple concept: spatial correlation suggests that one should give more weight to observations near the prediction location than to those far away. Spatial prediction theory explores how to optionally set these weights based on estimates of the underlying spatial autocorrelation structure (Waller, 2005).

Point and geo-statistical spatial data can be visualized by plotting the locations of study subjects using their Cartesian coordinates. In addition to this, these data types can be explored using different techniques in order to identify patterns, unusual or interesting features and to develop hypotheses. Some of the techniques employed include: kernel smoothing; spatial fil-

ters; and K-function, (see (Stevenson et al., 2005)). With point data, a variogram computed from the residuals can also be used in identifying the presence of residual spatial autocorrelation. When the variogram for the observed data lies within the 95% limits throughout the plotted region, it shows that there is no evidence of unaccounted-for second-order structure in the data at 5% significance level (Pfeiffer et al., 2008).

#### 2.1.1.3 Continuous data

When dealing with continuous spatial variables, the aim in most cases is to collect data at series of fixed sampling points and to use that data to predict the value of the variable of interest at other unsampled locations (Stevenson et al., 2005). These data can be visualized by plotting values recorded at each sampled location onto a map. While proportional symbol maps are useful for preliminary visualization of data, they give no appreciation of spatial continuity. In this case, the mean of the variable of interest across the entire area under investigation is predicted to achieve the continuity. There are two ways for estimating the mean of variable of interest across space, and these are: tessellation and kernel estimation techniques.

#### 2.1.1.4 Lattice data

Finally, data may be observed from a set of regions partitioning the study area, referred to as lattice data by (Cressie, 1993) and regional data by (Waller and Gotway, 2004). With lattice (area) data, the geographical space under investigation is comprised of a set of sampling units, typically made by portioning the region into fixed areas that are regularly or irregularly defined in space (Stevenson, 2003). Regional data generally involve summary measures for each region, for example, number of residents in an enumeration district, average income for residents of the region, or number of perinatal deaths within a study area. Inferential questions often involve accurate estimation of summaries from regions with small sample sizes ("small area estimation"), or regression or generalized linear modelling linking outcomes and covariates measured on the same set of regions (Pfeiffer et al., 2008).

These data can be explored using different ways, which include: standardized mortality ratios; Bayesian smoothing; and autocorrelation statistics. However, if the areal units where

the data are collected are small relative to the overall size of the study region, the exploratory methods for point data such as kernel smoothing can be used by applying values for each areal unit to a specific point (Stevenson, 2003). In the following subsection of cluster analysis autocorrelation statistics, more especially Moran's $I$ and LISA, will be discussed.

### 2.1.2 Cluster analysis

Fundamental to the spatial epidemiologist is the investigation of possible disease clustering. Cluster analysis provides opportunities for the epidemiologist to understand the spatial distribution of diseases and the possible association between demographic and environmental exposures (Besag and Newell, 1991); (Kulldorff et al., 2006, 1997; Kulldorff and Nagarwalla, 1995; Kulldorff et al., 2005). Cluster analysis is categorized into two and these are global and local cluster analysis. Global cluster analysis can obscure local effects since the assumption of stationarity is rarely met whereas the local cluster analysis delineates the characteristics of the clusters, such as size, location and intensity. The most widely used measure of global clustering in spatial statistics is the method proposed by (Moran, 1950). Moran's Index is a weighted correlation coefficient that is used to measure deviation from spatial randomness.

Testing for (global) spatial autocorrelation using the Moran $I$ statistic is a useful starting point for such analyses. The term spatial autocorrelation and, in particular, the term positive spatial autocorrelation refers to the property of attributes measured at nearby or adjacent geographical locations having similar values whereas negative spatial autocorrelation refers to the property of attributes measured at nearby geographical locations having dissimilar values (Haining et al., 2009). Statistically, spatial autocorrelation is a second order (covariance) property of a random variable defined over an area. There are numerous quantitative measures for spatial autocorrelation such as the Moran and Geary coefficients, which can be evaluated for any length of distance separation when sufficient data are available (Haining, 2003). A spatial weights matrix, $W$, is required in order to generate the Moran $I$ statistic, which has the form:

$$I = \frac{n}{\sum\sum w_{ij}} \frac{\sum\sum w_{ij}(y_i - \bar{y})(y_j - \bar{y})}{\sum (y_i - \bar{y})^2}. \tag{2.1}$$

This measure is a spatial equivalent of the standard product moment correlation coefficient. The weighting terms, $w_{ij}$, are defined either from patterns of zone adjacency or using some form of distance-decay function. A value of Moran's $I = 1$ indicates perfect positive spatial autocorrelation, whilst a value of $I$ very close to 0 indicates no spatial autocorrelation. Moran's $I$ provides a global summary of the degree of linear association between a vector of observed values and a weighted average of the neighboring values (Anselin, 1995).

To provide further insight into the composition of this statistic, local indicators of spatial association (LISA) may be determined for each area such that the sum of the LISA statistics for all zones is proportional to the global Moran's $I$. The LISA statistic for each area is calculated as:

$$I_i = Z_i \sum_{j,j \neq i}^{n} w_{ij} Z_j \tag{2.2}$$

where $Z_i$ and $Z_j$ are the observed values in standardized form, and $w_{ij}$ is a spatial weights matrix in row-standardized form. LISA statistics are used as indicators of local autocorrelation or as tests for outliers in global spatial patterns in the form of a Moran scatterplot (Anselin, 1996, 1995). More recently tests for GLM residuals to test for spatial autocorrelation have been suggested (Lin and Zhang, 2007).

There are different techniques of modelling spatial data depending on their categories and types. In the subsequent subsection the general overview of spatial regression will be discussed.

### 2.1.3 Modelling spatial data

The broad principles of regression analysis and modelling also apply to spatial datasets. In spatial context, the main aim is to model the variation in some spatially distributed dependent variables, for example, perinatal mortality, from a set of independent variables. A general framework to perform spatial data analyses is provided by regression models which have been developed for a variety of response types (Kneib, 2005). The most outstanding method is the classical linear regression model, where the response variable $y$ is assumed to be independent

normal or Gaussian distributed and covariates, say $x_1, \ldots, x_p$, act linearly on the response. By assumption, the conditional expectation of $y$ is:

$$\eta = E(y|x_1, \ldots, x_p) = \gamma_0 + x_1\gamma_1 + \cdots + x_p\gamma_p \tag{2.3}$$

where the unknown parameters $\gamma_1, \ldots, \gamma_p$ are regression coefficients and determine the strength and direction of the corresponding covariate's influence. In equation 2.3, each observation has an underlying mean of $\sum_i x_i\gamma_i$ and normally distributed random error term $\varepsilon$, with zero mean and uncorrelated variance-covariance matrix $\sum\sigma$, i.e., $\varepsilon_i \sim N(0, \sum\sigma)$, where $\sum\sigma = Var(y) = Var(\varepsilon) = \sigma^2 I$, and $I$ is $p \times p$ identity matrix. The assumption of independent observations also implies that $E(\varepsilon_i\varepsilon_i) = E(\varepsilon_i)E(\varepsilon_i) = 0$ (Osei, 2010). When using standard statistical methods, which assume independence of observations to analyze spatially correlated data the standard error of the covariate parameters is underestimated and thus the statistical significance is overestimated (Cressie, 1993).

For health outcome spatial data of small areas with relatively small populations at risk and few observed cases, rates may not follow the assumptions of the linear model. In such cases, a direct connection between the expectation of $y$ and the linear predictor $\eta$ is not possible. GLMs can be employed, which extend the classical linear model for Gaussian responses to more general situations such as binary or count data (Fahrmeir and Tutz, 2001; McCulloch and Searle, 2001; McCullagh and Nelder, 1989; Nelder and Wedderburn, 1972) to ensure the appropriate domain of $E(y|x_1 \ldots, x_p)$. When the more general transformation or response function $h$, is introduced equation 2.3 can be rewritten as:

$$h(\eta) = E(y|x_1, \ldots, x_p) = h(\gamma_0 + x_1\gamma_1 + \cdots + x_p\gamma_p). \tag{2.4}$$

GLMs assume that the distribution of the response variable $y$ belongs to an exponential family when covariates $u$ and unknown parameters $\gamma$ are given, that is,

$$f(y|u) = exp\left(\frac{y\theta - b(\theta)}{\phi}\right) c(y, \phi), \tag{2.5}$$

where b(.), c(.), $\theta$ and $\phi$ determine the respective distributions (Fahrmeir and Tutz, 2001). The mean $\mu = E(y|u, \gamma)$ is linked to a linear predictor $\eta$ by $\mu = h(\eta)$, where $\eta = u'\gamma$. Here

$h$ is a known response function, and $\gamma$ are unknown regression parameters (Fahrmeir et al., 2003; Fahrmeir and Tutz, 2001; Kneib, 2005).

In most practical regression situations, however, classical models and GLMs fail to quantify the effect of covariates on the response variable effectively because of the following reasons: the assumption of a strictly linear effect on the predictor may not be appropriate as some effects may be of unknown nonlinear form; some observations may be spatially temporally correlated; heterogeneity among individuals or units may not be sufficiently described by the covariates; and the interaction between covariates may be of complex, nonlinear form (Kandala et al., 2007; Kneib, 2005). To overcome these difficulties STAR models are used. The following section will give a review on STAR models.

## 2.2 Structured Additive Regression (STAR) Models

STAR models are more flexible as they incorporate nonlinear and the usual fixed effects of risk factors, while accounting for both structured and unstructured spatial effects in the joint model. Mostly regression models involving spatial random effects are handled through STAR models. In this case, the strictly linear predictor is replaced by a semi-parametric structured additive predictor

$$\eta_i = f_1(\nu_{i1}) + \ldots + f_p(\nu_{ip}) + u_i'\gamma, \tag{2.6}$$

where $i$ is a generic observation index, the $\nu_i$ are generic covariates of different type and dimension, and the $f_i$ are (not necessarily smooth) functions of the covariates (Fahrmeir et al., 2003). These functions are comprised of nonlinear effects of continuous covariates, time trends and seasonal effects, two-dimensional surfaces, varying coefficient models, *i.i.d.* random intercepts and slopes, and temporally or spatially correlated effects. Covariates with parametric effects are subsumed in the term $u_i'\gamma$.

The following subsection will discuss GLMs for both binary and count data followed by the subsections of Generalized additive models, Generalized additive mixed models, Geo-additive models and Varying coefficient models.

### 2.2.1 Generalized Linear Models (GLMs)

#### 2.2.1.1 Models for binary data

For binary responses $y_i \in \{0, 1\}$ the expectation is given by the probability $p = P(y = 1)$, which requires appropriate response functions to ensure $p \in [0, 1]$. The binary data typically are transformed using the logit function. The central assumption of this model is that the probability, $p$, of the dependent variable, $y$, taking the value 1 (rather than 0) follows the logistic curve. Obviously, any cumulative distribution function satisfies this condition and different model formulations are obtained for different choices of the distribution function. In any case, the scale parameter is fixed at $\phi = 1$ (Kneib, 2005). In subsequent paragraphs logit and probit models will be discussed.

When choosing the natural link function,

$$q = log\left(\frac{p}{1-p}\right), \tag{2.7}$$

the logit model is obtained and it corresponds to the logistic distribution function as response function. In this study, the logistic modelling was carried out for all the models by letting the response variable, $y_i$, be the survival status of the infant $i$ at location $s_i$, $s = 1, \ldots, S$, and defining $y_i = 1$ if the infant died within the 7 days of life and the same $y_i = 0$ otherwise. Then the response, $y_i$ is distributed as a binary (Bernoulli) random variable with expected probability of dying being equal to $p_i$ which can be modelled through logistic regression as

$$Y_i|x_i \sim Ber(pi), \tag{2.8}$$

$$p_i = P(y_i = 1|xi) = \frac{exp(\beta_i x_i)}{1 + exp(\beta_i x_i)} \tag{2.9}$$

where $x_i$ are predictors. The logistic model is linearised by the logit transform. The regression model then becomes

$$q = log\left(\frac{p}{1-p}\right) = \beta_0 + x_1\beta_1 + \ldots + x_p\beta_p + \varepsilon. \tag{2.10}$$

where errors are assumed to be *i.i.d* and the predictor variables not to be co-linear. Due to the intuitive interpretation of the regression coefficients based on odds and odds ratios,

the logit model is most commonly used when analyzing binary data, especially in medical applications.

In probit models, the logistic distribution function is replaced by the standard normal distribution. Since for the probit models the evaluation of the likelihood is computationally more demanding and parameter estimates are not interpretable in terms of odds or odds ratios, the logit model is often preferred in practice. However, probit models are used in fully Bayesian generalized linear models, where estimation of the likelihood is based on MCMC simulations (Osei, 2010).

#### 2.2.1.2 Models for count data

With count or rate data, Poisson and Negative Binomial regression models may be applicable. These models are similar in form to the binary logit model, but in this case the response variable, $y$, is count (integer) data (hence non-continuous). Poisson models assume that the mean and variance of the data is the same. In the case of mean being equal to the variance, the Poisson log linear model is often used to model counts of rare events (Griffith and Haining, 2006). However, if the marginal mean and variance are of the form:

$$E(Y) = \lambda \tag{2.11}$$

and

$$Var(Y) = \phi\lambda = E(Y) \tag{2.12}$$

where $E(Y)$ denotes the expected value of $Y$, and $\phi > 1$, then this is an example of overdispersion or "extra-Poisson" variation and in the case of $\phi < 1$ denotes underdispersion. The negative binomial log linear models in this case are used in trying to overcome the overdispersion (Haining et al., 2009).

In Generalized linear modelling, and in particular the Poisson log linear modelling of counts using the log link function, the particular attention is paid jointly to the problems of overdispersion and spatial autocorrelation (Haining et al., 2009). Overdispersion has been recognized as a problem for GLMs with grouped data for many years (Cameron and Trivedi, 1998; McCullagh and Nelder, 1983). The models of Poisson log linear and Negative Binomial log linear

are represented by:

$$Ln[E(Y(i))] = Ln[\lambda(i)] = E[Y(i)] + \beta_0 + \beta_1 x_1(i) + \ldots + \beta_k x_k(i) \tag{2.13}$$

where, $Y(i)$ are counts of infant deaths for area $i$, $E[Y(i)]$ is the expected value of $Y$ for area (or location) $i$, $\lambda(i)$ is the intensity parameter, $E(i)$ are expected counts (number of deaths) in area $i$, $Ln[E(i)]$ is the offset variable or population-based value (e.g. the underlying population at risk in each modelled zone), which controls for size differences across the set of areal units, and $\beta_0, \beta_1, \ldots, \beta_k$ are regression parameters (McCullagh and Nelder, 1983).

### 2.2.2 Generalized additive model (GAM)

The predictor of the GAM (Hastie and Tibshirani, 1990) for observation $i$, where $i = 1, \ldots, n$ is given by

$$\eta_i = f_1(x_{i1}) + \ldots + f_k(x_{ik}) + u_i'\gamma. \tag{2.14}$$

In the model above, $f_k$ are smooth functions of continuous covariates $x_i$ and can be modelled by using the random walk priors and Bayesian P(enalized)-splines, see (Brezger and Lang, 2003; Fahrmeir and Lang, 001a; Lang and Brezger, 2003).

### 2.2.3 Generalized additive mixed model (GAMM)

The GAMM extends the GAM by introducing cluster specific random effects as illustrated in the expression below:

$$\eta_{ic} = f_1(x_{ic1}) + \ldots + f_k(x_{ick}) + b_{1c}w_{ic1} + \ldots + b_{qc}w_{icj} + u_{ic}'\gamma \tag{2.15}$$

where $b_c = (b_{1c}, \ldots, b_{qc})$ is a vector of *i.i.d.* random intercepts (if $w_{icj} = 1$) or random slopes with respect to the cluster indicator $c \in 1, \ldots, C$. These random effects components are modelled by *i.i.d.* Gaussian priors for $b_{jc}$ (Clayton, 1996).

### 2.2.4 Geo-additive models

These models are used when additional geographic information for the observations in the dataset is available. For example, in the study of perinatal mortality the sub-districts where mothers of new born babies live are given and may be used as an indicator for regional differences in the survival of new born babies. A reasonable predictor for such data is given by

$$\eta_i = f_1(x_{i1}) + \ldots + f_k(x_{ik}) + f_{spat}(s_i) + u_i'\gamma \tag{2.16}$$

where $f_{spat}$ is an additional spatially correlated (random) effect of the location $s_i$ an observation pertains to. Models with a predictor that contains a spatial effect are also known as geo-additive models (Kammann and Wand, 2003). The spatial effect in these models may be modelled using MRFs (Besag et al., 1991) or two dimensional P-splines (Brezger and Lang, 2003).

### 2.2.5 Varying coefficient model (VCM)

The Varying Coefficient Models also known as geographically weighted regression models, when the spatially varying regression coefficients are included, are proposed by (Hastie and Tibshirani, 1993) and are defined by

$$\eta_i = g_1(x_{i1})z_{i1} + \ldots + g_k(x_{ik})z_{ik} \tag{2.17}$$

where the modifiers $x_{ik}$ are continuous covariates or time scales and the interacting variables $z_{ik}$ are either continuous or categorical. In these models, the effect modifiers are not necessarily restricted to be continuous as in (Hastie and Tibshirani, 1993). For example, the geographical location may be used as effect modifiers (Fahrmeir et al., 2003).

STAR models are highly parameterized; therefore they are computationally more demanding than other methods (Pfeiffer et al., 2008). To overcome this problem Bayesian approaches are usually used. The following section will discuss how Bayesian approaches are structured.

## 2.3 Bayesian inference in STAR models

Bayesian statistics is considered as an alternative to the classical theory. The main difference between the classical statistical theory and the Bayesian approach is that the latter considers parameters as random variables, just like the data, that are characterized by a prior distribution. The prior distribution expresses the information available to the researcher before any data are involved in the statistical analysis. The Bayesian framework allows for the inclusion of prior knowledge about the parameters along with the information contained in the data to produce robust results. The additional (prior) information is used to strengthen the modelling process and reduce bias in local estimates. The prior guesses for these parameters (possibly 'borrowed' from spatially adjacent and/or regional or national information) are then combined with the likelihood of the observed data to obtain posterior distributions for the parameters, from which inferential analysis proceeds.

Bayesian estimation and inference in statistical modelling provides a number of advantages over the classical approaches. This includes a more natural interpretation of parameter intervals, and the ease with which the true parameter density may be obtained. Bayesian approach has recently been given much focus due to the widespread adoption of MCMC methods. In the past, Bayesian estimation and inference was often scary due to the requirement of numerical integration. The MCMC estimation method decomposes complicated estimation problems into simpler problems that rely on conditional distributions for each parameter in the model (Gelfand and Smith, 1990). In classical approaches such as maximum likelihood estimation, inference is based on the likelihood of the data alone.

Generally, in Bayesian approach, the likelihood of the observed data $y$ given a $d$ dimensional parameter set $\theta$, denoted as $p(y|\theta)$, is used to modify the prior beliefs $p(\theta)$ with the updated knowledge summarized in a posterior density $p(\theta|y)$. Applying Bayes theorem, $p(\theta|y) = p(y|\theta)p(\theta)/p(y)$ is found, where the marginal likelihood $p(y)$ is obtained by integrating the likelihood over the prior densities, i.e., $p(y) = \int p(y|\theta)p(\theta)d(\theta)$. Since $p(y)$ can be regarded as a normalizing constant, the posterior density can be simplified as $p(\theta|y) \propto p(y|\theta)p(\theta)$ (Osei,

2010).

Inference for STAR models can be performed either with full Bayesian (FB) or an empirical Bayesian (EB) approach. With FB inference, unknown variance or smoothing parameters are considered as random variables with suitable hyper-priors and can be estimated jointly with unknown functions and covariate effects, using computationally efficient extensions of MCMC techniques. For EB inference, variance or smoothing parameters are considered as unknown constants, and are estimated by using REML (Augustin et al., 2006, 2004; Fahrmeir et al., 2004).

In Bayesian inference, the unknown functions $f_1, \ldots, f_p$, the vectors of function evaluations, and the fixed effects parameter $\gamma$ in 2.6 are supplemented by appropriate prior assumptions (Fahrmeir et al., 2004). In the absence of any prior knowledge diffuse priors are the appropriate choice for fixed effects parameters, i.e., $\gamma_j \propto const.$

Priors for the unknown functions $f_1, \ldots, f_p$ depend on specific type of the corresponding covariates and prior beliefs about the smoothness of $f_j$ (Augustin et al., 2006); (Brezger and Lang, 2006). In this case, the function evaluations $f_j = (f_j(\nu_{1j}), \ldots, f_j(\nu_{nj}))'$ of the unknown function, $f_j$ are expressed as the product of the matrix product of the design matrix $V_{ij}$ and a vector of unknown parameters $\beta_j$, i.e., $f_j = V_j\beta_j$. Therefore, the structured additive predictor 2.6 is written in matrix notation as

$$\eta = V_1\beta_1 + \ldots + V_p\beta_p + U\gamma, \tag{2.18}$$

where $U$ corresponds to the usual design matrix for fixed effects (Augustin et al., 2006; Brezger and Lang, 2003; Fahrmeir et al., 2004).

A prior for a function $f_j$ is now defined by specifying suitable design matrix $V_{ij}$ and prior distribution for the vector $\beta_j$ of the unknown parameters. The general form of the prior for $\beta_j$ is a multivariate Gaussian distribution with density

$$p(\beta_j|\tau_j^2) \propto exp\left(-\frac{1}{2\tau_j^2}\beta_j' K_j \beta_j\right) \tag{2.19}$$

where the precision matrix $K_j$ acts as a penalty matrix that shrinks parameters towards zero,

or penalizes too abrupt jumps between neighboring parameters (Fahrmeir et al., 2004, 2003; Kneib, 2005). In most cases $K_j$ is rank deficient, i.e., $k_j = rank(K_j) < dim(\beta_j) = d_j$. Hence, the prior for $\beta_j$ is partially improper. The variance parameter $\tau_j^2$ is equivalent to the inverse smoothing parameter in a frequentist approach and controls the tradeoff between flexibility and smoothness (Kneib, 2005; Rue and Held, 2005).

### 2.3.1 Priors for continuous covariates and time scales

There are several alternatives that are used for modelling effects of continuous covariates or time trends. These are random walk priors, see (Fahrmeir and Lang, 001a,b), Bayesian P-splines (Lang and Brezger, 2003) and Bayesian smoothing splines (Hastie and Tibshirani, 2000).

#### 2.3.1.1 Random walk priors

A common approach in dynamic or state space models is to find the estimate of the parameter, $\beta_{jm}$ for each distinct $x_j^{(m)}$, i.e., $f(x_j^{(m)}) = \beta_{jm}$, and penalize too abrupt jumps between successive parameters using random walk priors (Fahrmeir and Lang, 001a). There are several random walks but the most commonly used are first or second order random walk models, which are defined by

$$\beta_{jm} = \beta_{j,m-1} + u_{jm} \tag{2.20}$$

or

$$\beta_{jm} = 2\beta_{j,m-1} - \beta_{j,m-2} + u_{jm} \tag{2.21}$$

with Gaussian errors $u_{jm} \sim N(0, \tau_j^2)$ and diffuse priors $\beta_{j1} \sim const$, or $\beta_{j1}$ and $\beta_{j2} \sim const$, for initials values, respectively (Fahrmeir et al., 2004, 2003; Kneib, 2005).

Both specifications act as smoothness priors that penalize too rough functions $f_j$. A first order random walk penalizes too abrupt jumps $\beta_{jm} - \beta_{j,m-1}$ between successive states whereas the second order random walk penalizes deviations from the linear trend $2\beta_{j,m-1} - \beta_{j,m-2}$ (Fahrmeir and Lang, 001a).

#### 2.3.1.2 Penalized splines (P-splines)

One increasing popular idea to estimate smooth effects of continuous covariates are penalized splines, introduced by (Eilers and Marx, 1996). The continuous and time varying effects are often assumed to vary smoothly and are modelled using the Bayesian P-splines. This approach assumes that the unknown smooth function $f_j$ of the covariate $x_j$ can be approximated by the polynomial spline of degree $l$ defined on a set of equally spaced knots $x_j^{min} = \varsigma_{j,0} < \varsigma_{j,1} < \ldots < \varsigma_{j,s-1} < \varsigma_{j,s} = x_j^{max}$ within the domain of $x_j$ (Osei, 2010; Lang and Brezger, 2004).

The space of the polynomial splines can be shown to be $(M+l)$-dimensional subspace of the space of $(l-1)$ times continuous differentiable functions. Assuming that $f_j(x_j)$ is approximated by polynomial spline leads to the representation that can be written in terms of a linear combination of $d = M + l$ B-spline basis functions $B_m$, i.e.,

$$f_j(x_j) = \sum_{m=1}^{d} \beta_{j,m} B_m(x_j) \tag{2.22}$$

where $\beta_j = (\beta_{j1}, \ldots, \beta_{jd})'$ corresponds to the vector of unknown regression coefficients from the data (Osei, 2010; Kazembe, 2009; Augustin et al., 2006; Kneib, 2005).

The B-splines form a local basis since the basis functions $B_m$ are only positive within an area covered by $l + 2$ knots. This property is important for the construction of the smoothness penalty for the Penalized-splines. In the case of equidistant knots, all basis functions are of the same functional form and they can only be shifted along the $x$-axis. In the contrary case of non-equidistant knots, the smoothness of the basis functions increases with increasing degree (Kneib, 2005).

The crucial point in this type of estimation procedure is the choice of number of knots. For a small number of knots, the resulting spline may not be flexible enough to capture the variability of the data. For a large number of knots, however, the estimated curves tend to over-fit the data, resulting into obtaining too rough functions (Augustin et al., 2006; Fahrmeir et al., 2004; Kneib, 2005; Osei, 2010). As a remedy to these problems an adaptive knot selection approaches can be employed, which use specific criteria and strategies to choose optimal set

of basis functions (Biller and Fahrmeir, 2001; Biller, 2000; Hansen and Kooperberg, 2002). In this point of view, Eilers and Marx (1996) suggests the use of moderately large number of equally spaced knots (usually between 20 and 40) to ensure enough flexibility, and to define a roughness penalty based on first or second order differences of adjacent B-Spline coefficients to guarantee sufficient smoothness of fitted curves (Augustin et al., 2006; Fahrmeir et al., 2004, 2003). This leads to penalized likelihood estimation with penalty terms

$$pen(\lambda_j) = \frac{1}{2}\lambda_j \sum_{m=k+1}^{d} (\Delta^k \beta_m)^2, \tag{2.23}$$

where $\lambda_j$ is a smoothing parameter. As a consequence, large values of the smoothing parameter $\lambda_j$ lead to estimates close to a horizontal line (first order differences) or a linear effect (second order differences). In general, when the smoothing parameter goes to infinity the limiting polynomial is of the order $k-1$ and is, therefore, independent from the degree of the spline basis (Fahrmeir et al., 2004; Kneib, 2005; Waller, 2005).

### 2.3.2 Priors for spatial covariates

Spatial statistical methods incorporate spatial correlation according to the way geographical proximity is defined. Proximity further depends on the geographical information, which can be available at areal or point-location level. Nearness in space introduces correlations between the observations rendering the independence assumption of standard statistical methods invalid. Ignoring spatial correlation will result in underestimation of the standard error of the parameter estimates. Proximity in areal unit data is defined by their neighboring structure whereas in point-referenced or geostatistical data is determined by the distance between sample locations (Gemperli, 2003). Bayesian methods have been applied extensively in recent years for modelling both areal unit and geo-statistical data as they allow flexible modelling and inference, and provide computational advantages via the implementation of MCMC methods (Gelfand and Smith, 1990). The spatial structure is commonly introduced in a hierarchical fashion via the prior distribution of area of site-specific random effects, although spatial dependence can be built directly on Gaussian response data (Gemperli, 2003). The

choice of prior distributions depends on the type of spatial data. In the following paragraphs priors for areal and geostatistical data will be discussed.

Spatial effects are introduced into regression models to account for the spatial relation that is often encouraged by unobserved, spatially varying covariates. It is useful to split spatial effects into correlated (structured) part $f_{str}$ and a spatially uncorrelated (unstructured) part $f_{unstr}$, that is,

$$f_{spat}(s) = f_{str}(s) + f_{unstr}(s). \tag{2.24}$$

The main reason for splitting is that spatial effects are surrogate of many unobserved influential factors, some of them obey a strong spatial structure and others may be present only locally. These structured and unstructured spatial effects are estimated separately with the aim of distinguishing between the two kinds of the influential factors (Besag et al., 1991). There are different models or prior distributions for structured spatial effects but the most popular spatially structured prior distribution for the structured component is a special case of the conditional intrinsic Gaussian autoregressive (CAR) model (Besag and Kooperberg, 1995; Besag et al., 1991). The unstructured heterogeneity component is typically parameterized as being normally distributed with mean zero and variance $\tau^2$. The strength of the 'mix' of structured and unstructured heterogeneity components depends on the priors specified for $\sigma^2$ and $\tau^2$. Large values of $\sigma^2$ allow structured random effects to show wide variation (resulting in little spatial smoothing) whereas small values of $\sigma^2$ forces all the spatial heterogeneity terms to be similar (resulting in greater spatial smoothing) (Stevenson, 2003).

Usually unobserved covariates bring the problem of heterogeneity among clusters of observations. Neglecting the unobserved heterogeneity may lead to considerably biased estimates for the remaining effects. If $c \in 1, \ldots, C$ is a cluster variable indicating the cluster a particular observation belongs to, then the common approach to overcome the problem of the unobserved heterogeneity is by introducing an additional Gaussian $i.i.d$ effects $f_j(c) = \beta_{jc}$ with $\beta_{jc} \sim N(0, \tau_j^2), c = 1, \ldots, C$. In this case, the design matrix $\Psi$ is a $C$- dimensional 0/1 incidence matrix and the penalty matrix is the identity matrix, i.e., $K = I$ (Fahrmeir et al., 2004). Therefore, the prior of the joint vector of regression coefficients $\beta_c = (\beta_1, \ldots, \beta_C)'$ is

proper. In this case, MRF priors or two dimensional surface smoothers are assumed for the smooth spatial part whereas GRF priors are assumed for the uncorrelated part.

#### 2.3.2.1 Markov random fields (MRF) priors

The MRF prior introduces a structure based on neighborhood (Besag et al., 1991; Besag, 1974). The mean effect of a phenomenon under this consideration is taken as the mean of the effects of the neighboring areas as illustrated in equation:

$$f_{str}(s)|f_{str}(s'), s' \neq s, \tau^2_{str} \sim N\left(\frac{1}{N_s}\sum_{s'\sim s} f_{str}(s'), \frac{\tau^2_{str}}{N_s}\right), \tag{2.25}$$

where $N_s$ is the number of adjacent spatial units and $s' \sim s$ denotes that the spatial unit $s'$ is a neighbour of spatial unit $s$. The conditional mean of $f_{str}(s)$ is the unweighted average of the function evaluations of neighboring spatial units. The $N$ x $S$ design matrix $\Psi$ is a 0/1 incidence matrix. The number of columns is equal to the number of spatial units since only one parameter is estimated for each spatial unit. Its value in the $i$-th row and the $s$-th column is 1 if the $i$-th observation is located in the $s$-th spatial unit and 0 otherwise (Fahrmeir et al., 2003; Kandala et al., 2011, 2007; Osei, 2010; Salau, 2010). The $S \times S$ penalty matrix $K$ has the form of an adjacency matrix (Fahrmeir et al., 2003).

#### 2.3.2.2 Stationary Gaussian random fields (Kriging)

If exact locations $s = (s_x, s_y)$ are available, GRF priors, originating from the field of geostatistics, can be used to model spatial effects (Diggle et al., 1998; Kammann and Wand, 2003). The estimation of GRFs is also referred to as Kriging. This technique involves predicting a zero mean spatially correlated process at each location in a study area using an optimal weighted linear combination of neighboring observed values of the spatial process under investigation (Matheron, 1971, 1965). Two variations of this technique are ordinary kriging and universal kriging. Ordinary kriging is applied in the situation where the first order component of the spatial process has a constant mean and does not vary geographically. Universal kriging is applied in the more general situation where a first order trend exists (Stevenson, 2003).

In GRFs the spatial component $f_{spat}(s) = \beta_s$ is assumed to follow a zero mean station-

ary Gaussian random field $\{\beta_s :\in R^2\}$ with variance $\tau^2$ and isotropic correlation function $\rho(\beta_s, \beta_{s+h}) = \rho(\parallel h \parallel)$. This means that correlations between sites that are $\parallel h \parallel$ units apart are the same, regardless of direction and location of the sites. Choosing an appropriate correlation function $\rho(r)$, $r = \alpha \parallel h \parallel$, is important since the resulting estimates for spatial effect inherit properties like continuity and differentiability from the correlation function (Stein, 1999). Several proposals of correlation functions have been made in geostatistics literature, among which the Matérn family is recommended due to its flexibility (Stein, 1999). In its general form, the Matérn correlation function is given by

$$\rho(r; \alpha, \nu) = \frac{1}{2^{\nu-1}\Gamma(\nu)} \left(\frac{r}{\alpha}\right)^{\nu} \kappa_{\nu} \left(\frac{r}{\alpha}\right), \alpha > 0, \nu > 0. \tag{2.26}$$

where $\Gamma$ is the Gamma function and $K_{\nu}$ is the modified Bessel function of the order $\nu$ (Abramowitz and Stegun, 1974).

Spatial estimates are usually much more sensitive to the choice of the variance $\tau^2$ and other parameters of the Matérn family (Nychka, 2000). For a finite set of observed spatial locations $s \in \{s_1, \ldots, s_S\}$ the prior for $\beta = (\beta_1 \ldots, \beta_S)'$ can be cast into the general form 2.19 since the corresponding random field is assumed to be Gaussian. Similar to the MRFs, the design vector $\nu$ for a GRF is given by a 0/1- incidence vector.

#### 2.3.2.3 Low-rank Kriging

The main difference between GRFs and MRFs with respect to their numerical properties under mixed model based inference is the dimension of the penalty matrix, $K$. The dimension of $K$ for the MRFs is equal to the number of different regions and is therefore independent from the sample size whereas that of GRFs is determined by the number of distinct locations which is usually close to or equal to the sample size. So the number of regression coefficients used to describe MRF is usually much smaller than for a GRF and therefore the estimation of GRFs is computationally much expensive (Fahrmeir et al., 2003). To overcome this difficulty, low-rank Kriging has been introduced by (Nychka et al., 1998) and formulated in a geo-additive setting by (Kammann and Wand, 2003). The low-rank Kriging imposes less computational burden compared to the full-rank Kriging since it does not invert the spatial covariance matrix at each MCMC iteration as the full-rank Kriging does. The goal is to

approximate GRFs using only a compact set of parameters, which is achieved by using only a subset $D = \{k_1, \ldots, k_d\} \subset C = \{s_s, \ldots, s_S\}$ of the set of all distinct observation points $C$ as knots of a Matérn spline. These knots can be chosen to be "representative" for the set of distinct locations $C$ based on a space filling algorithm (Nychka and Saltzman, 1998).

#### 2.3.2.4 Interaction surfaces

A common approach for modelling interactions between covariates is based on varying coefficient models introduced by (Hastie and Tibshirani, 1993) in the context of smoothing splines. When both interacting covariates are continuous the more flexible approach when the exact locations, $s_i$ are available can be based on (non-parametric) two-dimensional surface fitting as suggested by (Brezger et al., 2005) and (Lang and Brezger, 2004). Here, it is assumed that the unknown surface $\beta_{str}(s_i) = f(x_i, y_i)$ can be approximated by the tensor product of two univariate B-splines, i.e.,

$$f(x_i, y_i) = \sum_{p=1}^{m_1} \sum_{\nu=1}^{m_2} \beta_{p\nu} B_{1p}(x_i) B_{2\nu}(y_i) \tag{2.27}$$

where $B_{11}, \ldots, B_{1m1}$ are the basis functions in $x_i$ direction and $B_{21}, \ldots, B_{2m2}$ in $y_i$ direction. The design matrix $X_1$ now becomes $n \times m_1.m_2$ dimensional and consists of products of basis functions (Fahrmeir et al., 2003; Kazembe and Mpeketula, 2010). Priors for $\beta_{pv}$ are based on spatial smoothness priors as specified in (Besag and Kooperberg, 1995). The vector of regression coefficients $\beta = (\beta_{11}, \ldots, \beta_{m1m2})'$ can be arranged corresponding to the two-dimensional regular array of basis functions in the $(x_i, y_i)$-plane. Following the idea of one-dimensional P-splines, the two-dimensional random walk priors can be assigned in trying to enforce smoothness of the estimated surface.

The most commonly used prior specification based on the four nearest neighbors can be defined by

$$\beta_{p\nu}| \sim N\left(\frac{1}{4}(\beta_{p-1,\nu} + \beta_{p+1,\nu} + \beta_{p,\nu-1} + \beta_{p,\nu+1}), \frac{\tau^2_{p\nu}}{4}\right) \tag{2.28}$$

for $p, \nu = 2, \ldots, m-1$ and appropriate changes for corners and edges (Besag and Kooperberg, 1995).

### 2.3.3 Mixed model based inference

The preceding section uses FB approach whereas mixed model based inference uses EB approach. This approach is based on generalized linear mixed model (GLMM) representations developed in (Lin and Zhang, 1999) for longitudinal data analysis using smoothing splines, or in (Kammann and Wand, 2003) for geo-additive models using stationary Gaussian random fields. Using computationally efficient REML algorithms, the GLMM methodology for EB inference in STAR models and even for fairly large data sets can be applied.

The EB approach is achieved by recasting the predictor model 2.18 as a GLMM after approximate reparameterization (Green, 1987; Lin and Zhang, 1999). This provides the key for simultaneous estimation of the function evaluations $f_j$ and the variance parameters $\tau_j^2$ in the empirical Bayes approach. The model 2.18 can be rewritten as a mixed model by assuming that $\beta_j$ has dimension $d_j$ and the corresponding penalty matrix has the rank $r_j < d_j = dim(\beta_j)$ (Brezger et al., 2005; Elliot et al., 2000; Kazembe, 2009). Each parameter vector $\beta_j$ is partitioned into a penalized ($\beta_j^{pen}$) and unpenalized ($\beta_j^{unp}$) part yielding a variance component model (Brezger et al., 2005; Fahrmeir et al., 2004),

$$\beta_j = \Psi_j^{unp}\beta_j^{unp} + \Psi_j^{pen}\beta_j^{pen} \tag{2.29}$$

for some well defined $d_j$ x $(d_j - r_j)$ matrix $\Psi_j^{unp}$ and a $d_j$ x $r_j$ matrix $\Psi_j^{pen}$. When decomposition 2.29 is applied to all the components of the predictor model 2.18, it yields

$$\eta = X^{unp}\beta^{unp} + X^{pen}\beta^{pen}. \tag{2.30}$$

The GLMM with fixed effects and random effects can be obtained in 2.30. The posterior in terms of this GLMM representation can be given by the expression

$$p(\beta^{unp}, \beta^{pen}|y) \propto L(y, \beta^{unp}, \beta^{pen}) \prod_{j=1}^{p} p(\beta_j^{pen}|\tau_j^2), \tag{2.31}$$

where $p(\beta_j^{pen}|\tau_j^2) \sim N(0, \tau_j^2 I)$ and $p(\beta_j^{unp}) \propto const.$ Estimation of regression coefficients and variance parameters is carried out using iterative weighted least squares and approximated REML (Fahrmeir et al., 2004, 2003). At the first iteration the default (starting) values are

assumed for the penalized, unpenalized and variance parameters. Then updates for $\beta_j^{unp}$ and $\beta_j^{pen}$ are obtained in the first step by solving a system of linear equations given estimates for the variance parameters. In the second step, updates of the variance parameters are obtained by maximizing the approximate restricted log-likelihood. The restricted log-likelihood is maximized through a Fisher scoring technique. The two steps are iterated until convergence (Fahrmeir et al., 2004).

Generalization of the REML technique to non-normal data is not straightforward, since the definition of error contrasts is not possible for more general responses due to the nonlinear dependency of $y$ on $\beta$ in GLMMs. An alternative approach by Harville (1974) to the estimation of variances in Gaussian mixed models that leads to exactly the same restricted log-likelihood for $\tau^2$ and $\sigma^2$ and that can additionally be extended to more general responses is possible.

### 2.3.4 Inference based on MCMC

Inference for the posterior distribution of the model parameters in FB is based on the MCMC simulation technique. The simulation basically involves generating samples from the posterior distribution of the unknown parameters. The fully Bayesian inference is based on the analysis of the posterior distribution of the model parameters. In general, the posterior is highly dimensional and analytically intractable, which makes direct inference almost impossible. This problem is avoided by using MCMC simulation techniques, whereby samples are drawn from the full conditional of parameters given the rest of the data. As indicated by (Fahrmeir et al., 2004), when the original parameterization is chosen, the posterior is given by

$$p(\beta, \tau^2, \gamma|y) \propto L(y, \beta, \gamma) \prod_{j=1}^{p} \Big\{ p(\beta_j|\tau_j^2) p(\tau_j^2) \Big\}, \tag{2.32}$$

where the quantity $p(\beta, \tau^2, \gamma)$ is the prior density function and $L(.)$ denotes the likelihood which is the product of individual likelihood contributions.

Two major algorithms used for producing FB estimates are the Gibbs Sampler and the Metropolis-Hastings (M-H) algorithm. The Gibbs Sampler simulates new values for a pa-

rameter based on the conditional distribution of that parameter. After each iteration step, new values are used to replace the old ones. This process is then repeated until the estimates converge. Using the M-H approach on the other hand involves generating estimate values from a proposed distribution and then comparing the values to those from the previous iteration step using posterior probabilities. A decision is then made to either accept or reject the values basing on the acceptance probability (Ntzoufras, 2009).

### 2.3.5 Hybrid Bayesian inference

With a hybrid Bayesian (HB) approach, the variance parameters $\tau^2$ are first estimated by REML. Then, instead of drawing from inverse gamma full conditionals, full Bayesian inference is performed by plugging in the REML estimates for $\tau^2$. This strategy aims at combining advantages of EB and FB inference: stable estimation of the variance components, and the full posterior analysis for regression functions and parameters of primary interest (Fahrmeir et al., 2004; Kneib, 2005). For example, this type of inference allows for computation of posteriors of any nonlinear functionals, simultaneous credible intervals and probability statements (Knorr-Held, 2004).

In FB and HB approaches, M-H algorithm based on IWLS proposals can be used if general responses from an exponential family are given. The idea of IWLS updates has been introduced by Gamerman (1997) for the estimation of GLMMs and adapted to the present situation of STAR models in (Brezger et al., 2005).

### 2.3.6 Testing for Convergence

Testing for convergence of the algorithm is done to know whether the algorithm has reached its equilibrium distribution or not. There are many ways to monitor convergence. The simplest way is to monitor the Monte Carlo error since small values of this error indicate that the quantity of interest being calculated is done with precision (Kneib, 2005). Monitoring autocorrelation is also very useful since low or high values indicate fast or slow convergence,

respectively. Another way is to monitor the trace plots: the plots of the iterations versus the generated values. If all values are within a zone without strong periodicities and (especially) tendencies, then convergence can be assumed. Convergence of the Markov chains to their stationary distributions is usually assessed by inspecting sampling paths and autocorrelation functions of sampled parameters. In majority of cases, however, the IWLS updating scheme has excellent mixing properties and convergence problems do not occur (Fahrmeir et al., 2004; Kneib, 2005). The term convergence of an MCMC algorithm refers to situations where the algorithm has reached its equilibrium and is generating values from the desired target distribution and iteration refers to a cycle of the algorithm that generates a full set of parameter values from the posterior distribution (Ntzoufras, 2009).

Although a theoretical comparison of EB and FB inference reveals several differences between both inferential concepts, it should be noted that in many applications the differences are comparably small. If larger differences are observed, it may be an indicator for a weakly identified model or other problems caused by the model formulation. Therefore, it is advisable to compare the results of both approaches, if possible (Kneib, 2005).

## 2.4 Model Comparison and Selection

In data analysis, comparison and selection are used to find model or subset of models that describe the data as well as studying sensitivity of the results to prior specification (Vaida et al., 2008). Choosing between alternative models presents a particular challenge. Each additional parameter may improve the fit of the model to the sample dataset, but at the cost of increasing model complexity (Smith, 2011). The foremost goal of model comparison is achieving good generalizability by striking the right balance between two opposing pressures, goodness of fit and complexity. There are different representative measures of generalizability that achieve this balance. Some of these measures are: Akaike Information Criterion (AIC); Bayesian Information Criterion (BIC); Deviance Information Criterion (DIC); and correlation coefficient squared ($R^2$).

The most common statistic now used in model comparison is the AIC. AIC is given by $AIC = -2log_e(L(\theta|data)) + 2K$, where $2log_e(L(\theta|data))$ is the value of the maximized log-likelihood over the unknown parameters ($\theta$), given the data and the model, and $K$ is the number of estimable parameters in that approximating model. When the value of $K$ is large relative to sample size $n$, a small-sample (second-order) corrected version called $AIC_c$ is used, which is given as $AIC_c = -2log_e(L(\theta)) + 2K(n/(n-K-1))$ (Hurvich and Tsai, 1989). The corrected version is often computed since it is asymptotic to the standard version. It is recommended that the corrected version be used unless $n/k > 40$ (Burnham and Anderson, 2002). Both AIC and $AIC_c$ are estimates of expected, relative Kullback-Leibler information and are useful in the analysis of real data in the 'noisy' sciences. Assuming independence, AIC-based model selection is equivalent to certain cross-validation methods (Stone, 1977, 1974).

A second information theoretic measure, which places greater weight on the number of parameters used, is often also provided. This is known as the BIC, or sometimes as the Swartz Criterion. The BIC is based, in part, on the likelihood, and it is closely related to the AIC. It has the simpler form: $BIC = -2ln(L) + Kln(n)$, where $n$ is the sample size, $k$ is the number of free parameters to be estimated and $L$ is the maximized value of the likelihood function for the estimated model (Liddle, 2008).

The AIC and BIC are defined as sum of the log-likelihood and the degrees of freedom ($df$). The log-likelihood measures the goodness of fit whereas the $df$ measures model complexity. The smaller values of AIC or BIC indicate better fitting model (Kazembe, 2009). The penalty term is larger in BIC than in AIC.

The third information theoretic measure is DIC, which is used to compare the fit and complexity of hierarchical models in Bayesian data analysis (Spiegelhalter et al., 2002). The DIC is given by $DIC = \bar{D} + p_D$ , where $\bar{D}$ is the posterior mean of the deviance, which is a measure of goodness of fit, and $p_D$ is the effective number of parameters, which is a measure of model complexity and penalizes over-fitting.

Models with small values of DIC are considered for the interpretation of results as they indicate better fitting to the data and lower complexity (Spiegelhalter et al., 2002). The DIC is an extension of the AIC and is based on the posterior distribution of the deviance statistic. It has been proposed as a rule of thumb that AIC differences within 1 to 2 units of the best model suggest similar support for both models, models with AIC differences of between 3 to 7 from the best model are weakly differentiated and the differences of more than 7 units is regarded as strong evidence in favor of the model with the smaller DIC (Burnham and Anderson, 2002). The major advantage of the DIC over AIC is that it can easily be calculated from the output of the MCMC simulation (Spiegelhalter et al., 2002). AIC and BIC require calculating the likelihood at its maximum over $\theta$, which is not readily available from the MCMC simulation.

In the derivation of DIC, it assumed that the specified parametric family of probability distributions that generate future observations encompasses the true model. This assumption does not always hold, and it is desirable to consider model assessment procedures in that scenario. Also, the observed data are used both to construct the posterior distribution and to evaluate the estimated models. Therefore, DIC tends to select over-fitted models. Recently, these issues are resolved by Ando (2007), Bayesian predictive information criterion, BPIC. The criterion is calculated as $IC = -2E^{\theta}[log(p(y|\theta))] + 2p_D$, where the first term is a measure of how well the model fits the data and the second term is a penalty on the model complexity.

Another good-of-fit measure based on the DIC is the $R^2_{DIC}$ which Miaou et al. (2003) defined as: $R^2_{DIC} = 1 - (DIC_{model} - DIC_{ref})/(DIC_{max} - DICref)$. The $R^2_{DIC}$ attempts to standardize the DIC in the same way as the traditional $R^2$ (Miaou et al., 2003). In this expression $DIC_{model}$ is the DIC value for the model under evaluation, $DIC_{max}$ is the DIC value under a fixed one-parameter model and $DIC_{ref}$ is a DIC value from a reference model (the best model) which can also be approximated as $DIC_{ref} = n$ (Miaou et al., 2003).

In this study, the Generalised Linear Models, Generalised Additive Models and Geo-additive Models of binary outcomes were fitted using EB and FB approaches.

# Chapter 3

# Application of Bayesian spatial models in Perinatal Mortality

## 3.1 Study Setting

The project was carried out in Mchinji district in the Central Region of Malawi. It has a population of about 456,558 as of 2011, of whom about 80% live in rural areas and make a living through subsistence farming (Machingura et al., 2011). The main ethnic group is the Chewa (90%), and the predominant religion is Christianity (97%). In 2006, it was reported that 99% of women in the district attended antenatal care at least once during their pregnancy, but only 58% delivered at a health facility (Lewycka et al., 2010). Maternal and perinatal health care is provided by personnel from one district hospital (a first referral and secondary health facility), four rural community hospitals (one government and three mission hospitals), one maternity unit, six health centres that provide maternity care, two dispensaries and two private clinics that offer ANC services. Quality is compromised by the severe shortage of personnel, low morale of the health providers, and irregular drug supplies. TBAs were available in all localities. There has been little research in rural Africa on sustainable community-based interventions to reduce maternal and perinatal mortality, although this is changing. Mchinji district was considered for the project as one of the districts with high HIV cases, and with a good number of the population living in rural areas.

## 3.2 Study Design

The study was a retrospective design of 5 years using data that was collected by MaiMwana project from 2005 to 2010. The project used controlled cluster-randomized trial design, as the allocation and loci of the interventions were groups rather than individuals. The project had 48 clusters in total. Out of the total number of clusters, 24 were allocated to women's group intervention and the other 24 were taken as controls. Using a factorial design, each of the arms of the women's group trial was randomized a second time, with 12 clusters to receiving the volunteer counselling intervention and 12 acting as controls. An independent surveillance system for outcomes was designed and implemented in all the 48 clusters and 7 sub- regions, covering a population of 144,000.

## 3.3 Data Collection

Data were collected as follows. Women with the age range of 10 to 52 years were identified and enrolled into the study after seeking informed consent. All participants were visited monthly to identify pregnancies and births, as well as neonatal, infant and maternal deaths by trained enumerators. All events were recorded in a register holding an up-to-date list of all women in the cluster (generated from the baseline survey, plus new residents). One enumerator was visiting all participants in one cluster. The qualitative data were collected through semi-structured interviews and focus groups. After delivery, the mothers were interviewed for one-month to find more about behaviours and events during pregnancy, delivery and postpartum. All deaths of infants were followed up by a supervisor who was verifying the death and conduct a verbal autopsy interview between two and six weeks after the death to elicit the causes and contributing factors of the deaths. There were five supervisors, each based at a nodal office.

The survival time of each newborn baby was computed in days. All stillbirths and newborn babies whose survival time was at most 7 days were classified as perinatal deaths. The

response, $y_i$, was therefore binary that takes the value $y_i = 0$ if the infant $i$ survived the first 7 days and $y_i = 1$ if the infant died.

The covariates considered in the study were socio-demographic factors including area of residence (presence of trading centre), use of mosquito net by the mother, maternal age at a time of delivery, parity, and timing of first and number of ANC visit, depending on trimesters (first, second and third). Lastly, clinical or obstetric variables that were considered for the analysis were blood sample test, blood pressure test, urine sample test, syphilis test, vaginal examination, abdominal examination, advice on danger signs of pregnancy, malaria prophylaxis at ANC, birth attendant, labour duration, gestation period, mode of delivery and baby outcome. To overcome any potential problems with the analysis, data relating to twins was excluded. The geo-coordinates of the villages were sourced from National Statistical Office captured in 2010 census. All the variables considered in the analysis were modelled as categorical variables, except maternal age at time of delivery which was modelled as continuous variable. The exact geo-coordinates of villages (sub-districts) were used as spatial covariates.

## 3.4 Data Management

All quantitative data collected were delivered to the main office for data entry in a relational database management system in Microsoft Access run on a dedicated server and workstations. Each participant was given a unique ID number generated from the TA, cluster, and village and household she was coming from. All quantitative data from the mortality surveillance, morbidity, care practice and behaviour questionnaires and process evaluation were linked to the participants through this unique ID. After checking and entering, all questionnaires were archived in a locked room for future reference. Qualitative information was audio recorded after receiving verbal consent from respondents. Data in Chichewa was translated into English by a bilingual speaker. To ensure conceptual, grammatical, and syntactical equivalence, translations were reviewed collaboratively by the researcher who obtained the

data and the translator (both bilingual Chichewa-English speakers), and the lead researcher (English speaker). All data were subsequently transcribed and imported into a database in MAXqda 2 (VERBI Software version 2).

## 3.5 Quality control

To ensure quality of the data, one enumerator per cluster was identifying births and deaths, and each event was cross-checked by one interviewer. Supervisors were making regular field visits to check the quality of work done by enumerators and interviewers and observe some interviews. Each supervisor was responsible for between six and ten clusters. Interviewers were meeting with enumerators weekly in order to check on their work and receive updates on births and deaths in their area. Supervisors were meeting with interviewers and enumerators fortnightly to check on their work, discuss problems and provide quality control feedback. A sample of 200 one-month interviews was selected to be independently re-done by the supervisor, in order to be able to estimate recall and interviewer error rates.

Quantitative data was checked in three stages. The first check was performed after completion of the questionnaire, by the MEO *in full* and a Nodal Data Checker based at one of the five nodal offices. The second check was done by a team of two Data Checkers based at the main office. The last stage of data checking was done at the point of data entry by the four Data Entry Clerks. Further checks were carried out internally within the electronic data-handling environment. Data entered into the study databases were regularly reviewed for inconsistencies and missing information. Lists of women interviewed and key fields to be verified were produced.

## 3.6 Dealing with loss to follow-up

Minimizing loss to follow-up is an important aspect of trial conduct. For residents or respondents who were temporarily unavailable, the main strategy was to keep following them

up until the outcome was ascertained. All women who were living in the study areas permanently were maintained in the database, and were appearing every month in the register. Any events (such as pregnancy or birth) that were reported but no further details were known, were selected and lists were produced to remind field-workers of the need for follow-up. For residents or respondents who were permanently unavailable, basic information about dates and timings of events was sought from other community members such as friends or neighbours.

## 3.7 Reducing contamination

Contamination may occur when people from one cluster have come into contact with people from another. In the rural villages of Mchinji, there are many opportunities for social mixing. In order to reduce the possibility of contamination, the project team opted to use clusters of villages rather than individual villages as the unit of randomization, thus reducing rates of travel across cluster boundaries. Furthermore, each zone had a defined 'buffer area' around the perimeter. A population of 3,000 in each zone was required to achieve the desired sample size, but rather than selecting villages at random from each zone, only villages at the centre of the zonal area were eligible for inclusion in surveillance and intervention activities. This reduced the possibility of communication between neighbouring study villages in intervention and control areas. In addition, women's group facilitators and volunteer counsellors were residents of the zone in which they were working. This reduced the possibility of transferring intervention benefits to neighbouring communities. There were also no any records of non-governmental organisations working on interventions undertaken by the main study.

## 3.8 Ethical Considerations

All protocols were observed and permission was granted by the directors of MaiMwana project to use their dataset. The data were used basing on the main study ethics approval. The main study was registered by Malawi National Health Sciences Research committee and

ethics committee of University College London Institute of Child Health. The data were collected after verbal and written consent were received from community leaders after full consultation and discussions. The regional, district and village leaders, and local health and development professionals had ongoing access to the research programme and were to be the first to be briefed on study findings and outcomes through written and verbal reports. Before each instance of data collection, verbal consent was obtained from the participants after explaining the process and advantages and disadvantages of taking part in the study. Participation in intervention activities was voluntary, and participants were free to start or stop as they wished.

The study team considered it unethical to strengthen services only in intervention and not control areas. Control communities were benefiting from low-cost improvements in equipment, supplies and training at all primary level facilities in the district in intervention and control areas. The training was for the Field Interviewers. The Field Interviewers were trained in interviewer skills, methods of data collection, negotiation skills and team building.

## 3.9 Statistical Data Analysis

Data from control groups were used for the analysis in order to have a true picture of perinatal mortality in the study area. The number of subjects that took part in the study for the control groups was 8, 320 but after data cleaning depending on the variables that were of interest in the analysis only 7, 627 subjects with complete data were considered for the analysis. The analysis focused on the occurrence of perinatal deaths.

### 3.9.1 Descriptive Data Analysis

The variables of interest were assessed for any statistical significance of apparent associations with the response variable, perinatal mortality using the chi-square test, and between quantitative variables using one-way analysis of variance (ANOVA) test. The following covariates that showed significant bivariate association with perinatal mortality at $p$-value of 0.05 were

selected for subsequent multivariate analysis: use of mosquito net by the mother, maternal age at time of delivery, parity, ANC visits, blood sample test, blood pressure test, syphilis test, abdominal examination, advice on danger signs of pregnancy, birth attendant, labour duration, gestation period and mode of delivery. For more details on significant variables refer to tables 4.1 and 4.2. The table 3.1 gives the summary of these covariates.

Table 3.1: Description of covariates

| *Variable* | *Type* | *Description* |
|---|---|---|
| | | **Response Variable** |
| perinatal | binary | baby outcome: 1 = dead and 0 = survived |
| | | **Specific covariates** |
| m_age | continuous | maternal age |
| mothernet | binary | mother slept under net: 0 = No; 1 = Yes |
| prev_preg | binary | previous pregnancy: 0 = No; 1 = at least 1 pregnancy |
| ancfvisit | categorical | timing of first and number of ANC visits: 0 = None; 1 = $1^{st}$ trimester, <4 visits; 2 = $1^{st}$ trimester, ≥4 visits; 3 = $2^{nd}$ trimester, <4 visits; 4 = $2^{nd}$ trimester, ≥4 visits; 5 = $3^{rd}$ trimester, <4 visits; 6 = $3^{rd}$ trimester, ≥ 4 visits |
| ancblood | binary | blood sample test: 0 = No; 1 = Yes |
| ancbp | binary | blood pressure test: 0 = No; 1 = Yes |
| ancfta | binary | syphilis test: 0 = No; 1 = Yes |
| ancexam | binary | abdominal examination: 0 = No; 1 = Yes |
| ancidanger | binary | danger signs advice: 0 = Not received; 1 = Received |
| skilled | binary | birth attendant: 0 = Non-skilled; 1 = Skilled |
| labourduration | binary | labour duration: 0 = Prolonged; 1 = Normal |
| gest_period | binary | gestation period: 0 = 7 to 8 months; 1 = at least 9 months |
| delmode | binary | mode of delivery: 0 = Other; 1 = Normal |

In addition to bivariate analysis, exploratory spatial data analysis was carried out to assess the clustering of the perinatal mortality in the study area. Chi- square and one-way ANOVA tests were done using STATA 10 whereas the cluster analysis was done using GeoDa 0.9.5-(Beta). Multivariate data analysis was done in BayesX, version 2.0.1 and maps were created in R 2.14 using the outputs from BayesX.

### 3.9.2 Model Building

Bayesian hierarchical models were fitted to estimate the amount of spatial heterogeneity in perinatal mortality as well as associations between risk factors and perinatal mortality in the presence of spatial correlation. Ignoring this correlation would result in underestimating the variance of the effects of the risk factors (Cressie, 1993). Logistic models were used to assess geographic heterogeneity and the effects of different covariates. A total of nine logistic models were developed to determine the relationship between perinatal mortality and the potential risk factors. The table 3.2 gives a summary of the models that were considered.

Table 3.2: Models considered to assess the factors that are associated with probability of perinatal mortality

| Model | Variables |
|---|---|
| M0 | Fixed effects |
| M1 | Fixed effects + Nonlinear effects |
| M2 | M1 + Unstructured Spatial effects at zone level |
| M3 | M1 + Structured Spatial effects at zone level |
| M4 | M1 + Spatial effects (Structured + Unstructured) at zone level |
| M5 | M1 + Spatial effects (Structured + Unstructured) at TA level |
| M6 | Similar to model M4 but with maternal age as a categorical variable |
| M7 | Similar to model M4 but without birth attendant variable |
| M8 | Spatial effects (Structured + Unstructured) only at zone level |

The first model, M0 in this study was the logistic regression model of the form: $y_i = u_i\gamma + \varepsilon_i$ where $\varepsilon_i \sim N(0, \sigma^2)$, for observations $(y_i, u_i), i = 1, \ldots, n$, on the response variable $y$ and the vector $u$ of the covariates, which assumes that the mean $E(y_i|u_i)$ can be modelled through a linear predictor $u_i'\gamma$ (Kandala et al., 2011). This model was fitted by modelling the binary response variable with a binomial probit link function of the form: $P(y_i = 1/\eta_i) = \Phi(\eta_i)$, where $\Phi$ is the probit link function modelled with the linear predictor: $\eta_i = u_i'\gamma$. Having in mind that the assumption of a strictly linear effect on the response variable $y$ may not be appropriate with the continuous covariates, the additive model, M1 that account for nonlinear effects in continuous variables was fitted.

Considering that the above models M0 and M1 do not account for spatial effects, and the

hierarchical structure of the data, geo-additive models that simultaneously account for the spatial dependence in the variables were fitted. The third model, M2 was an improvement of the second model and was fitted by introducing uncorrelated spatial effects to model M1 in trying to account for nonlinear smooth functions of the continuous covariates and for the effect of unobserved spatially unstructured covariates. The fourth model, M3 was fitted by introducing structured or correlated spatial effects to model M2 in trying to account for the effect of unobserved spatially structured covariates. Model M4 was fitted by introducing structured and unstructured spatial effects to model M1, that is, at zone level. Model M5 was implemented by modelling model M4 at large area level (TA - level) in trying to assess the effects of size of the area-level at which the analysis was done. Model M6 was developed by modelling Model M4 which had the lowest DIC value with maternal age as a categorical variable in trying to evaluate the bias arising from modelling it as a fixed effect. Model M7 was arrived at by modelling the same best model M4 without the birth attendant variable in trying to assess the effect of not having this variable in the model on perinatal mortality. Model M8 was developed by considering the spatial effects only. Lastly, models M4, M7 and M8 were estimated using EB approach for comparison with FB model.

### 3.9.3 Fully Bayesian approach

In this study, FB inference was used basing on the analysis of the posterior distribution of the model parameters by drawing random samples via MCMC simulation techniques to all the nine models. This type of inference stems from the posterior distribution, that is, the conditional distribution of the parameters given the observed data, $p(\theta|data)$. Gibbs sampler algorithm was used for MCMC simulations, which was drawing samples successively from the full conditionals for $\beta_1, \ldots, \beta_p$, $f_{str}(s)$, $f_{unstr}(s)$, $\tau_j^2$, $j = 1, \ldots, p$, $str$, $unstr$ and $\sigma^2$.

#### 3.9.3.1 Assigning priors to different covariates

As in FB approach there is a need of assigning prior assumptions to all unknown functions $f_1(x)$, $f_{unstr}(s)$, $f_{str}(s)$ and for the fixed effect regression parameter $\gamma$, various priors were assigned. Independent diffuse prior, $p(\gamma) \propto constant$ was assumed for the fixed regression

parameters, $\gamma$ due to the absence of any prior knowledge. Bayesian P-splines with second order random walk prior and number of knots of 20 was chosen for the continuous variable. MRF and GRF priors were used for the structured spatial components, $f_{str}(s)$. MRF was used basing on the conditional distribution of the spatial neighbourhood relationship for the lattice data (Besag et al., 1991; Besag, 1974) whereas GRF was used basing on point-location data. With the help of geo-coordinates, P-splines with 2 dimensional first order random walk priors and number of knots of 20 were also assigned to the spatial components.

Inverse gamma priors for variance component with known hyper-parameters were assigned to the unstructured spatial effects. Since the regression parameters depend on the choice of hyper-parameters being used, other choices of hyper-parameters have been used in this study to investigate the sensitivity of the models. Four alternatives of priors were used in the sensitivity analysis and these include: $IG$(a = 1, b = 0.005); $IG$(a = 0.5, b = 0.0005); $IG$(a = 0.001, b = 0.001); and $IG$(a = 0.01, b = 0.01). The first and second choices are suggested by (Besag and Kooperberg, 1995; Kelsall and Wakefield, 1999), respectively. The third has often been used as choice for the variances of random effects.

### 3.9.4 Empirical Bayesian approach

In addition to the FB approach, empirical Bayesian of structured additive regression model M4 was also carried out using two-dimensional first order random walk prior for spatial effects, which is based on the four nearest neighbours. Model M4 was further modelled without the birth attendant variable in trying to assess the effects of not having this variable in the model on perinatal mortality. The best model, M4 was also modelled with spatial effects only. The results were compared using AIC or BIC. These information criteria are defined as sum of the log-likelihood and the degrees of freedom (df). The smaller the AIC or BIC value the better the model (Kazembe and Mpeketula, 2010).

### 3.9.5 Model Implementation and Comparison

All models were estimated using BayesX version 2.0.1 (Belitz et al., 2009). In all the fitted models the probit link function was used because sampling was relatively fast since all conditionals for the regression parameters $\beta$ and $\gamma$ are again Gaussian. In addition, the convergence of the algorithm for all models was assessed using trace plots.

For FB approach, a total number of 12, 000 MCMC iterations were used with the first 2, 000 samples as burn-in and every 20th sampled parameter of the Markov chain was stored. This yielded 500 samples for parameter estimation. Only main effects were considered for all covariates and interaction effects were not considered because of the number of the covariates used. Means, standard deviations and quantiles estimated from the posterior distributions were used to assess the model fit for all models. The credible intervals (CI) were used to assess the significance of the parameters. The strictly linear models were compared with the additive models and the geo-additive models using DIC values (Spiegelhalter et al., 2002). The model with smallest DIC was preferred.

For EB approach, the regression coefficients are estimated iteratively. For each model fitted, convergence was achieved when the change in regression parameters was 0.00001 and terminated at 400 iterations if convergence was not achieved. However, under 20 iterations all models converged. The $p$-values were used to assess the significance of the parameters.

## 3.10 Limitations of the study

The study was a population-based as all births and deaths in the study areas were eligible for inclusion, and thus strictly speaking sampling error does not arise. However, selection forces may have acted at any of four main stages; selection of villages, selection and enumeration of households and women of childbearing age, identification of pregnancies, and loss to follow-up of study outcome. Some different selection forces may also have acted during the retrospective re-census. At any of these stages, a systematic exclusion of a particular type of participant

could have produced a biased or unrepresentative sample (Anglewicz et al., 2009). Any selection biases introduced through village selection or household selection in one way or another reduced the generalisability of the findings.

Some of the reasons for losses to follow-up during the retrospective survey might include migration, changing of names, or changing household living arrangements. Migration within the district is usually from villages to larger trading centres, although there is also seasonal migration between villages and farming areas during cultivation periods, and movements from one village to another following marriage, divorce or widowhood. Such migration may have the effect of increasing loss to follow-up during the retrospective survey visits, if mothers were out of their usual village at the scheduled time.

Another challenging aspect of follow-up was the lack of any identifying documents such as identity cards. Women may be known by different names to different people and at different times. In addition, most women did not know their exact dates of birth, but rough ages.

On identification of pregnancies to be followed up, it is not known how many pregnancies were not reported, or the characteristics of the pregnant women. It is likely that unreported pregnancies included those ending in early miscarriage or termination, and those arising during a period of absence such as farming or schooling.

The study was constrained by its staffing and supervision structure, coverage and reach, and availability of resources, which were kept low in order to try and make the intervention cost-effective and feasible to scale up. The distances covered by supervisors when visiting zones for supervision could be up to 20 kilometres, and the time and cost of fuel involved limited the number of supervisory visits that could be made. In addition, some supervisors were less willing to travel to the furthest zones, meaning that deaths may have been more under-reported in the remotest zones, making their mortality rates lower than expected (Lewycka, 2011).

Definitions of miscarriage, stillbirth and neonatal death occasionally caused confusion amongst fieldworkers, despite repeated training and monthly review meetings. In some specific areas,

chieftainship conflicts also resulted in parts of communities being prevented from taking part in the study as required.

Some variables of interest had little information and were not included in the analysis. There was no cause of death variable in the dataset that would have helped in finding the diseases that caused a lot of perinatals' deaths. There was also missing data on dates of birth and death of some infants, which resulted in exclusion of data from the sample. There is some evidence from other surveys in Malawi that respondents tend to under-report dead infants, and they are also more likely not to remember their dates of birth (NSO, 2005).

# Chapter 4

# Results and Summary

## 4.1 Descriptive summaries

Tables 4.1 and 4.2 show individual characteristics of the sample population prior to multiple adjustments of all factors that might confound or mediate the observed spatial variation within zones and TAs also regarded as sub-districts on prevalence of perinatal mortality.

Of the overall sample of 8, 320 subjects, 92 percent (7, 627) was used for analysis. Each category had a total of 7, 627 subjects. 306 of the total perinatals died representing perinatal mortality rate of 40 deaths per 1, 000 pregnancies. The variables considered were categorized into socio-demographic and delivery or clinical factors. For the socio-demographic factors, the distribution of perinatal mortality was as illustrated in table 4.1. Of the 3, 512 perinatals from mothers who were not sleeping under mosquito nets, 158 (5.5%) perinatals died whereas 148 (3.6%) of 4, 115 perinatals born from mothers who were sleeping under nets died. The perinatal mortality had almost a u-shape with the maternal age; higher in maternal age of less than 20 years (6.34%), lower for maternal age range of 20 to 35 years (3.58%) and high for maternal age of greater than 35 years (4.55%). The perinatal mortality was higher among infants born from mothers with no previous pregnancy (6.83%) compared to those born from mothers with at least one previous pregnancy (3.42%). The mortality was higher among infants born from mothers who had no ANC visit (70.00 percent) followed by those born from mothers who had their first ANC visit in first trimester with less than 4 visits (10.64%),

those born from mothers who had first ANC visit in first trimester with at least 4 visits (5.87%), those born from mothers who had first ANC visit in second trimester with less than 4 visits (4.15%), those born from mothers who had first ANC visit in second trimester with at least 4 visits (2.45%), those born from mothers who had first ANC visit in third trimester with less than 4 visits (2.42%) and lastly those born from mothers who had first ANC visit in third trimester with at least 4 visits (0.57%).

Table 4.1: Distribution of perinatal mortality by Socio-demographic factors

| *Variable description* | Total # of Perinatals | # (%) of Perinatals Dead | *p*-value |
|---|---|---|---|
| **Trading Centre** | | | |
| No | 5, 891 | 235 (3.99) | 0.851 |
| Yes | 1, 736 | 71 (4.09) | |
| **Mother slept under net** | | | |
| No | 3, 512 | 158 (4.50) | 0.045 |
| Yes | 4, 115 | 148 (3.60) | |
| **Maternal Age** | | | |
| $<$ 20 years | 868 | 55 (6.34) | $<$0.0001 |
| 20 to 35 years | 5, 813 | 208 (3.58) | |
| $>$ 35 years | 946 | 43 (4.55) | |
| **Previous Pregnancy** | | | |
| 0 | 1, 318 | 90 (6.83) | $<$0.0001 |
| $\geq 1$ | 6, 309 | 216 (3.42) | |
| **ANC visit** | | | |
| None | 30 | 21 (70.00) | $<$0.0001 |
| $1^{st}$ trimester, $<$4 visits | 357 | 30 (10.64) | |
| $1^{st}$ trimester, $\geq$4 visits | 818 | 48 (5.87) | |
| $2^{nd}$ trimester, $<$4 visits | 2, 672 | 111 (4.15) | |
| $2^{nd}$ trimester, $\geq$4 visits | 1, 592 | 39 (2.45) | |
| $3^{rd}$ trimester, $<$4 visits | 1, 982 | 48 (2.42) | |
| $3^{rd}$ trimester, $\geq$4 visits | 176 | 1 (0.57) | |

The details of perinatal mortality distribution for delivery or clinical factors are summarised in 4.2. The prevalence of death was higher among perinatals born from mothers who had no blood sample test (4.44%) compared to those born from mothers who had blood sample test (3.13%). The incidence of dying was higher among perinatals born from mothers who had no blood pressure test (9.29%) compared to infants born from mothers who had blood pressure test (2.5%). The prevalence of death was higher among perinatals born from mothers who had

no syphilis test (4.43%) compared to those born from mothers who had syphilis test (2.31%). The perinatal mortality was higher among infants born from mothers who had no abdominal examination (4.14%) than those born from mothers who had abdominal examination (2.77%). The incidence of dying was higher among perinatals born from mothers who did not receive advice on danger signs of pregnancy (19.58%) compared to those born from mothers who received advice on danger signs (2.16%). The perinatal mortality was higher among perinatals born under the supervision of non-skilled birth attendant (4.48%) compared to those born under the supervision of the skilled birth attendant (3.50%). The prevalence of dying was higher among perinatals born from mothers who had prolonged labour (15.89%) compared to those born from mothers who had normal labour duration (2.60%). The incidence of dying was higher among perinatals delivered by mothers who had 7 to 8 months gestation period (33.73%) compared to those delivered by mothers who had at least 9 months gestation period (2.63%). Lastly, the perinatal mortality was higher among perinatals delivered through other modes of delivery (20.83%) than those who delivered normally through birth canal (3.47%).

Blood sample test, blood pressure test, urine sample test, syphilis test, vaginal examination and abdominal examination were conducted to find out whether pregnant women had health problems that would have led to poor pregnancy outcomes. In so doing, health workers were able to come up with approriate treatment to improve the survival of the infants.

Table 4.2: Distribution of perinatal mortality by Clinical factors

| *Variable description* | Total # of Perinatals | # (%) of Perinatals Dead | *p*-value |
|---|---|---|---|
| **Blood sample test** | | | |
| No | 5, 135 | 228 (4.44) | 0.006 |
| Yes | 2, 492 | 78 (3.13) | |
| **Blood pressure test** | | | |
| No | 1, 701 | 158 (9.29) | <0.0001 |
| Yes | 5, 926 | 148 (2.50) | |
| **Urine sample taken** | | | |
| No | 7, 153 | 290 (4.05) | 0.466 |
| Yes | 474 | 16 (3.38) | |
| **Syphilis test** | | | |
| No | 6, 114 | 271 (4.43) | <0.0001 |
| Yes | 1, 513 | 35 (2.31) | |
| **Vaginal exam** | | | |
| No | 6, 336 | 262 (4.14) | 0.225 |
| Yes | 1, 291 | 44 (3.41) | |
| **Abdominal exam** | | | |
| No | 291 | 103 (35.40) | <0.0001 |
| Yes | 7, 336 | 203 (2.77) | |
| **Danger signs advice** | | | |
| Not received | 812 | 159 (19.58) | <0.0001 |
| Received | 6, 815 | 147 (2.16) | |
| **Malaria Prophylaxis** | | | |
| $<$ 2 SP doses | 4, 338 | 170 (3.92) | 0.634 |
| $\geq$ 2 SP doses | 3, 289 | 136 (4.13) | |
| **Birth Attendant** | | | |
| Non-skilled | 3, 975 | 178 (4.48) | 0.031 |
| Skilled | 3, 652 | 128 (3.50) | |
| **Labour Duration** | | | |
| Prolonged | 812 | 129 (15.89) | <0.0001 |
| Normal | 6, 815 | 177 (2.60) | |
| **Gestation Period** | | | |
| 7 to 8 months | 338 | 114 (33.73) | $<$ 0.0001 |
| $\geq$ 9 months | 7, 289 | 192 (2.63) | |
| **Mode of delivery** | | | |
| Other | 240 | 50 (20.83) | <0.0001 |
| Normal | 7, 387 | 256 (3.47) | |

On the other hand, there was no statistically significant association between the prevalence of the perinatal mortality and presence of trading centre, urine sample test, vaginal examination

and malaria prophylaxis.

## 4.2 Spatial clustering of perinatal mortality

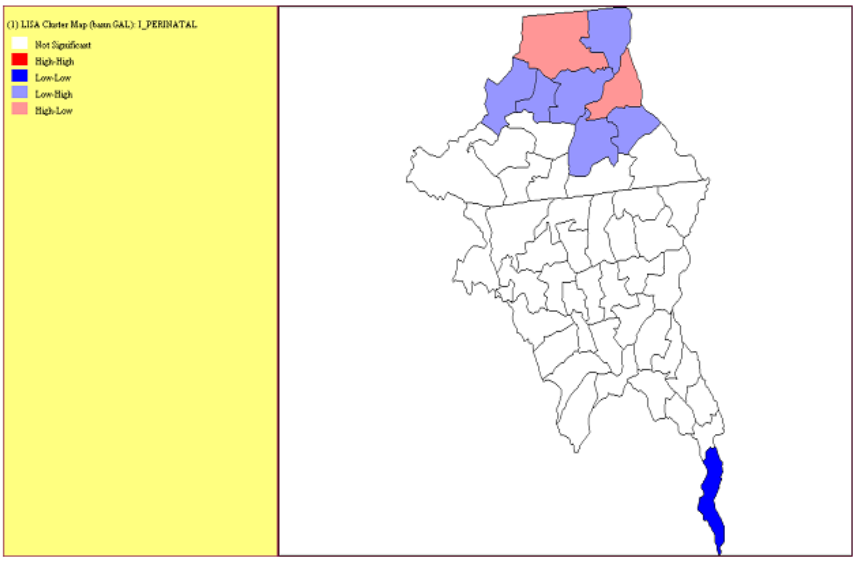



Figure 4.1: LISA cluster map of perinatal mortality

The figure 4.1 shows some spatial clustering of perinatal mortality in the study area that was developed using Local Moran LISA statistics in GeoDa (Anselin, 1995). This methodology yields a measure of spatial autocorrelation for each individual location. The significance of clustering in the locations is categorized depending on different colours: bright red for the high to high association, bright blue for low to low, light blue for low to high and light red for high to low. The high to high and low to low locations suggest clustering of similar values, whereas the high to low and low to high locations indicate spatial outliers (Anselin, 2003).

Many spatial datasets exhibit patterns of data and/or residuals in which neighbouring areas have similar values (positive spatial autocorrelation) and hence violate the core assumptions of standard regression models. One result of this feature of spatial data is to greatly over-estimate the effective sample size, and hence the degrees of freedom that may be indicated will be stated as being far higher than they should be. One possible solution to this problem

is to resample (Haining et al., 2009).

The results of clustering analysis in figure 4.1 revealed that zone number 14 in Traditional Authority Mavwere located in the southern part of the district had low to low spatial correlation, indicating that in this zone there was clustering of similar values of low perinatal mortality. Some zones in the northern part of the district in traditional authorities Mkanda and Dambe had high to low and low to high spatial correlation, indicating the presence of outliers. However, the spatial correlation was not significant in a good number of zones in the central, eastern and western parts of the study area.

## 4.3 Multivariate analysis results

Under this section, the parameter estimates of the fixed effects and relationship of nonlinear effects with perinatal mortality obtained using FB will be presented as they are almost similar with the results obtained using EB.

### 4.3.1 Model comparison

Results for model fit that include deviance, $pD$ and DIC are summarized in the table 4.3.

Table 4.3: Model comparison using DIC values.

| Model Fitted | Deviance ($\mu$) | pD | DIC | $\triangle$ DIC |
|---|---|---|---|---|
| M4 | 1654.15 | 28.47 | **1711.09** | 0.00 |
| M2 | 1654.74 | 28.42 | 1711.57 | 0.48 |
| M3 | 1654.04 | 28.99 | 1712.01 | 0.92 |
| M6 | 1655.65 | 28.53 | 1712.71 | 1.62 |
| M5 | 1657.33 | 29.12 | 1715.58 | 4.49 |
| M7 | 1658.90 | 28.35 | 1715.61 | 4.52 |
| M1 | 1684.04 | 19.94 | 1723.93 | 12.84 |
| M0 | 1685.75 | 19.58 | 1724.91 | 13.82 |
| M8 | 2560.29 | 6.72 | 2573.73 | 862.73 |

Based on the DIC values, model M0 had DIC = 1724.91, while M1 gave DIC value of 1723.93,

suggesting that incorporating maternal age as continuous variable in the model explained the risk of perinatal mortality better than having it as a categorical variable. Model M2, that combines the effect of individual characteristics and unstructured random effects gave the DIC value of 1711.57, indicating that individual characteristics alone cannot explain perinatal mortality better. After, incorporating the structured spatial effects to the individual effects in model M3, the DIC value increased from 1711.57 to 1712.01 indicating that model M2 was explaining the data better as compared to model M3. In model M4, the fit improved when both structured and unstructured spatial effects were included in the model (DIC value for model M4 was 1711.09). Looking at the difference in DIC values of the other models relative to model M4, it can be concluded that models M2, M3, M5, M6 and M7 can be weakly differentiated as they all have DIC difference values of less than 7 from the best model, whereas models M0, M1 and M8 cannot be supported. When the random and spatial effects were included in model M1 there was an increase in model complexity but also a substantial improvement in the DIC values, thereby suggesting the importance of contextual effects. Model M5 which is the same model M4 but implemented at TA level had the DIC value of 1715.58 indicating that health outcomes like perinatal mortality can be estimated better at small area-level when logistic models are used. Model M6 which is a variant of model M4 showed a higher DIC value of 1712.71 compared to model M4 itself, thereby supporting the inclusion of maternal age as a continuous variable. Model M7 which is the same best model M4 but without birth attendant variable had DIC value of 1715.61, indicating that this variable has significant impact on the occurrence of perinatal mortality and ignoring it can lead to poor estimation of the outcome. Finally, model M8 which considered spatial effects only had DIC value of 2573.73, indicating that spatial effects only cannot explain the prevalence of the health outcome better. Therefore, there is a need of incorporating fixed, continuous and spatial effects to come up with better estimation of the health outcome.

### 4.3.2 Sensitivity analysis

The performance of the models in Bayesian framework can be sensitive to the choice of the variance components priors, which may arise due to small sample sizes (Gelman, 2006). Although results are insensitive to the choice of a and b for moderate to large datasets, a sensitivity analysis is required to check the changes in the models with respect to changes in the hyper-priors (Hennerfeind et al., 2006). The sensitivity analysis was carried out with the same set of covariates as in model M4 through changing the prior distributions for the variance components using the following values (a = b = 0.001), (a = 0.5, b = 0.0005), (a = 1, b = 0.005) and (a = b = 0.01). The table 4.4 shows the sensitivity results on the choice of hyper-parameters a and b. From table 4.4, it shows that the choice of priors does not affect the estimates. The standard model which used priors: a = b = 0.001 had the lowest DIC value and can be considered the best.

Table 4.4: Sensitivity to choice of hyper-prior values for model M4

| | Hyper-priors | | | |
|---|---|---|---|---|
| Model Fit | a = b = 0.001 | a = 0.5, b = 0.0005 | a = 1, b = 0.005 | a = b = 0.01 |
| Deviance | 1654.15 | 1658.54 | 1656.09 | 1648.28 |
| pD | 28.47 | 26.33 | 27.51 | 33.55 |
| DIC | **1711.09** | 1711.21 | 1711.12 | 1715.38 |

### 4.3.3 Results for fully Bayesian (FB) approach

The results for models M0, M2, M3 and M4 are summarized in 4.5 to see the influence of incorporating nonlinear and spatial effects on parameter estimates, however, the best model **M4** is used for interpretation.

Table 4.5: Parameter estimates using FB approach for data in 2005 - 2010.

| Model | M0<br>OR (95% CI) | M2<br>OR (95% CI) | M3<br>OR (95% CI) | **M4**<br>OR (95% CI) |
|---|---|---|---|---|
| *Socio-demographic* | | | | |
| **Mother used net** | | | | |
| No | 1 | 1 | 1 | 1 |
| Yes | 0.89 (0.72, 1.12) | 0.90(0.70, 1.12) | 0.90 (0.74, 1.12) | 0.91 (0.73, 1.12) |
| **Previous Pregnancy** | | | | |
| 0 | 1 | 1 | 1 | 1 |
| $\geq 1$ | 0.69 (0.51, 0.93) | 0.71(0.51, 1.03) | 0.70 (0.50, 1.01) | **0.70** (0.51, 0.99) |
| **ANC visit** | | | | |
| None | 1 | 1 | 1 | 1 |
| $1^{st}$ trimester, <4 visits | 0.46 (0.17, 1.34) | 0.49(0.16, 1.37) | 0.50(0.16, 1.42) | 0.49 (0.15, 1.32) |
| $1^{st}$ trimester, ≥4 visits | 0.27 (0.10, 0.76) | 0.28(0.10, 0.75) | 0.28(0.10, 0.79) | **0.29** (0.10, 0.84) |
| $2^{nd}$ trimester, <4 visits | 0.26 (0.11, 0.74) | 0.27(0.10, 0.71) | 0.28(0.10, 0.76) | **0.28** (0.10, 0.79) |
| $2^{nd}$ trimester, ≥4 visits | 0.21 (0.08, 0.58) | 0.21(0.07, 0.58) | 0.21(0.07, 0.59) | **0.22** (0.08, 0.61) |
| $3^{rd}$ trimester, <4 visits | 0.18 (0.07, 0.52) | 0.18(0.07, 0.48) | 0.18(0.06, 0.50) | **0.18** (0.06, 0.55) |
| $3^{rd}$ trimester, ≥4 visits | 0.05 (0.01, 0.27) | 0.05(0.01, 0.26) | 0.06(0.01, 0.25) | **0.05** (0.01, 0.23) |
| *Clinical/Delivery* | | | | |
| **Blood sample test** | | | | |
| No | 1 | 1 | 1 | 1 |
| Yes | 1.71 (1.31, 2.26) | 1.89(1.38, 2.58) | 1.93 (1.43, 2.60) | **1.92** (1.44, 2.62) |
| **Blood pressure test** | | | | |
| No | 1 | 1 | 1 | 1 |
| Yes | 0.78 (0.60, 1.02) | 0.76(0.59, 0.99) | 0.77 (0.57, 1.00) | 0.76 (0.58, 1.01) |
| **Syphilis test** | | | | |
| No | 1 | 1 | 1 | 1 |
| Yes | 0.64 (0.45, 0.94) | 0.59(0.41, 0.83) | 0.59 (0.40, 0.86) | **0.60** (0.41, 0.85) |
| **Abdominal exam** | | | | |
| No | 1 | 1 | 1 | 1 |
| Yes | 0.32 (0.21, 0.48) | 0.33(0.22, 0.50) | 0.31 (0.21, 0.47) | **0.32** (0.21, 0.49) |
| **Danger signs advice** | | | | |
| Not received | 1 | 1 | 1 | 1 |
| Received | 0.30 (0.23, 0.39) | 0.29(0.21, 0.39) | 0.28 (0.21, 0.38) | **0.28** (0.21, 0.37) |
| **Birth Attendant** | | | | |
| Non-skilled | 1 | 1 | 1 | 1 |
| Skilled | 0.80 (0.61, 1.02) | 0.75(0.59, 0.98) | 0.73 (0.59, 0.95) | **0.73** (0.58, 0.94) |
| **Labour Duration** | | | | |
| Prolonged | 1 | 1 | 1 | 1 |
| Normal | 0.40 (0.31, 0.53) | 0.37(0.28, 0.49) | 0.37 (0.28, 0.49) | **0.37** (0.28, 0.49) |
| **Gestation Period** | | | | |
| 7 to 8 months | 1 | 1 | 1 | 1 |
| $\geq$ 9 months | 0.12 (0.09, 0.16) | 0.11(0.08, 0.15) | 0.11 (0.08, 0.15) | **0.11** (0.08, 0.14) |
| **Mode of delivery** | | | | |
| Other | 1 | 1 | 1 | 1 |
| Normal | 0.19 (0.13, 0.30) | 0.19(0.14, 0.28) | 0.18 (0.12, 0.28) | **0.18** (0.12, 0.28) |

### 4.3.4 Categorical covariates (fixed effects)

Table 4.5 provides estimates of odds ratios (OR) and 95% credible intervals (CI) where model **M4** is used for interpretation of the results. Under socio-demographic factors in this table, perinatals from mothers who had at least one previous pregnancy were associated with reduced incidence of dying (OR = 0.70, CI: 0.51, 0.99) relative to those from mothers who had no previous pregnancy. Perinatals from mothers who had their first ANC visit in first trimester with at least 4 visits were associated with reduced incidence of dying (OR = 0.29, CI: 0.10, 0.84) as well as those born from mothers who had first ANC visit in second trimester with less than 4 visits (OR = 0.28, CI: 0.10, 0.79), those born from mothers who had first ANC visit in second trimester with at least 4 visits (OR = 0.22, CI: 0.08, 0.61), those born from mothers who had first ANC visit in third trimester with less than 4 visits (OR = 0.18, CI: 0.06, 0.55) and lastly those born from mothers who had first ANC visit in third trimester with at least 4 visits (OR = 0.05, CI: 0.01, 0.23) relative to those from mothers who had no ANC visit. Generally, it has also been observed that perinatals from mothers who had at least 4 visits in a given trimester were associated with reduced perinatal mortality as compared to those who had less than 4 visits.

For clinical or obstetric factors, perinatals from mothers who had their blood samples tested were surprisingly associated with increased incidence of dying (OR = 1.92, CI: 1.44, 2.62) relative to those from mothers who did not have their blood samples not being tested. Perinatals from mothers who received syphilis test were at reduced incidence of dying (OR = 0.60, CI: 0.41, 0.85) relative to those from mothers who did not receive syphilis test. Perinatals from mothers who had abdominal examination were at reduced incidence of dying (OR = 0.32, CI: 0.21, 0.49) relative to those from mothers who had no abdominal examination. Perinatals from mothers who received advice on danger signs of pregnancy were at reduced incidence of dying (OR = 0.28, CI: 0.21, 0.37) relative to those from mothers who did not receive advice on danger signs of pregnancy. Perinatals who were delivered under skilled birth attendant were at reduced incidence of dying (OR = 0.73, CI: 0.58, 0.94) relative to those who were delivered under non-skilled birth attendant. Perinatals from mothers who

had normal labour duration were at reduced occurrence of dying (OR = 0.37, CI: 0.28, 0.49) relative to those from mothers who had prolonged labour. Perinatals from mothers who had a gestation period of at least 9 months were at reduced occurrence of dying (OR = 0.11, CI: 0.08, 0.14) relative to those from mothers who had gestation period of 7 to 8 months. Lastly, perinatals who were delivered normally through birth canal had reduced prevalence of dying (OR = 0.18, CI: 0.12, 0.28) relative to those who were delivered through other modes.

### 4.3.5 Nonlinear effects

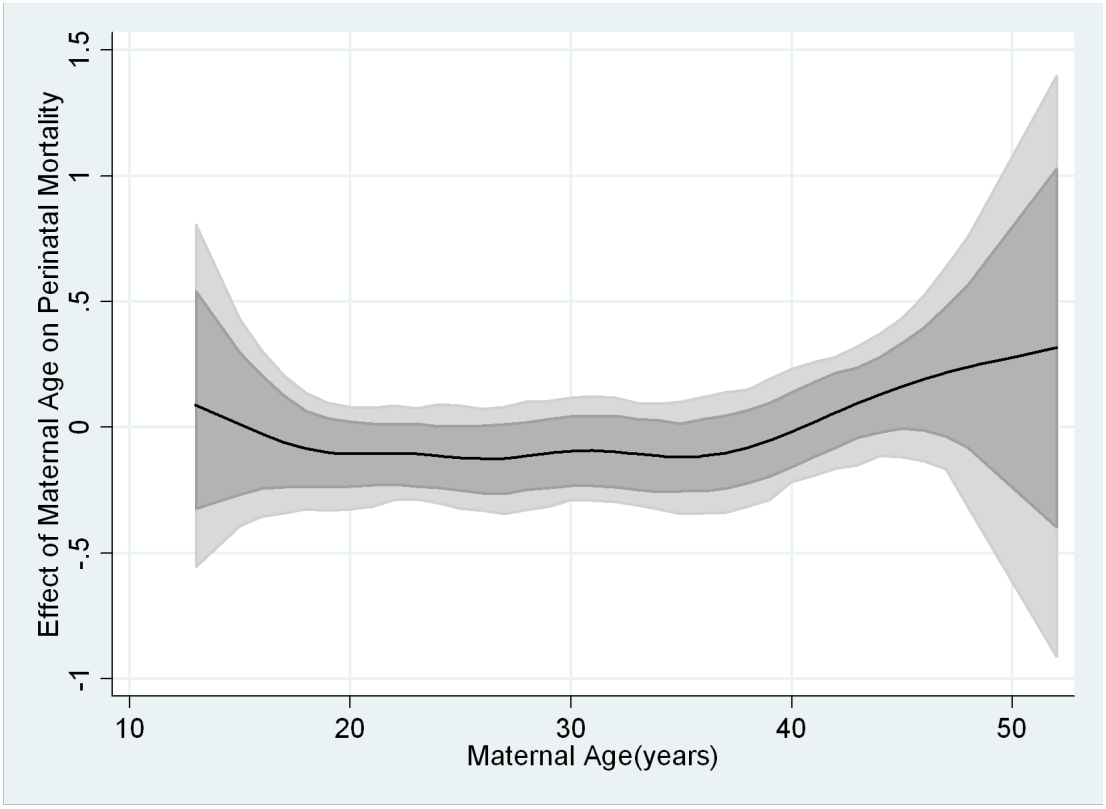



Figure 4.2: Non-linear effect of mother's age on the risk of perinatal mortality (solid centre line) with 80% and 95% confidence lines

Figure 4.2 shows that there is a u-shaped, nonlinear relationship between the effects of maternal age and perinatal mortality, that is, perinatals from mothers with the age of less than 16 years were associated with higher occurrence of perinatal mortality. Perinatals from mothers with the age range of 16 to 40 years had reduced occurrence of dying whereas those

from mothers with the age of greater than 40 years were also associated with increased prevalence of dying. The expanded 80% and 95% credible intervals from 18 years below and 45 years above in the graph above means that few data were collected from younger mothers (age $<$ 16 years) and older mothers (age $>$ 45 years).

### 4.3.6 Spatial effects

All smoothed geographical effect estimates are interpreted using maps that are developed using fully Bayesian approach as the occurrence of perinatal mortality was almost the same regardless of the type of the estimation used. In all the maps presented under this subsection, the red colour denotes regions with high perinatal mortality whereas green denotes regions with low perinatal mortality.

When structured and unstructured spatial effects only were considered, that is, without accounting for other significant covariates the pattern of perinatal mortality is as displayed in figure 4.3. Some areas in the eastern and southern parts of the district had high perinatal mortality whereas some areas in the northern part had low perinatal mortality. There was moderate perinatal mortality in the central and central west of the district.

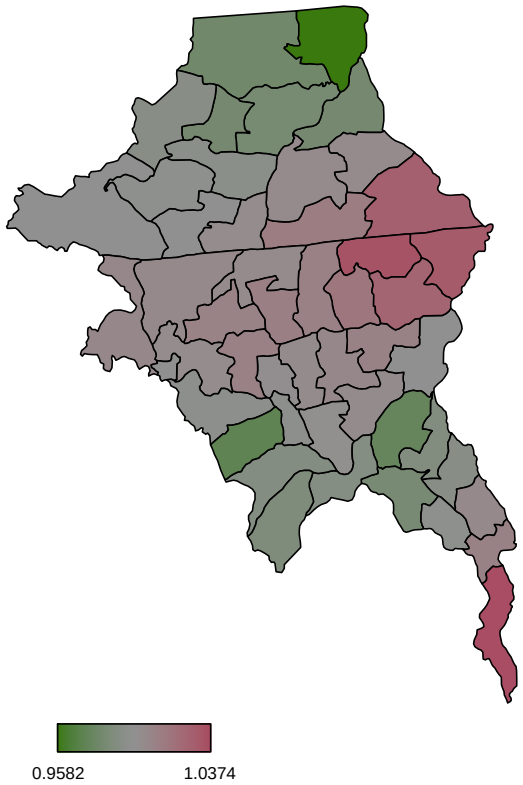



Figure 4.3: Smooth geographical effects of perinatal mortality at sub-district level basing on model **M8**.

Figure 4.4 shows the estimated smooth geographical effects at sub-district level, after controlling for other significant covariates. As depicted in the map, high perinatal mortality (OR $\geq$ 1) was observed in a number of sub-districts, particularly the zones that are located in the eastern part of the district. Low perinatal mortality was observed in zones that are in the central and western parts of the district. The low prevalence of perinatal mortality in the central and western parts of the district could be due to the availability of quality maternal services being offered and increased health care-seeking behaviours by pregnant women as compared to other areas.

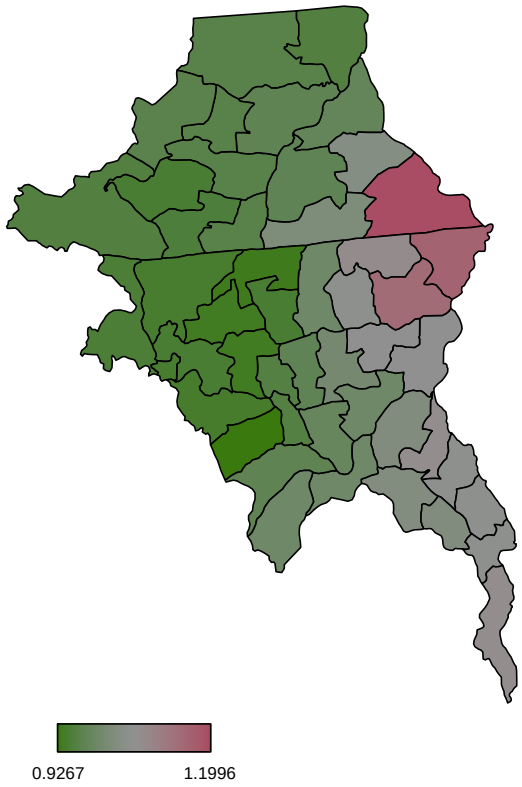



Figure 4.4: Smooth geographical effects of perinatal mortality at sub-district level basing on model **M4**.

After removing birth attendant variable from model M4 there were some slight changes in the occurrence of perinatal mortality as compared to the full model as shown in the figure 4.5. Some zones were associated with low perinatal mortality as compared to the occurrence of the same in other locations. The green colour intensity was decreasing in some zones of the central and western parts and red colour was developing on the southern part of the district indicating decrease in probability of perinatal survival and increase in probability of dying, respectively.

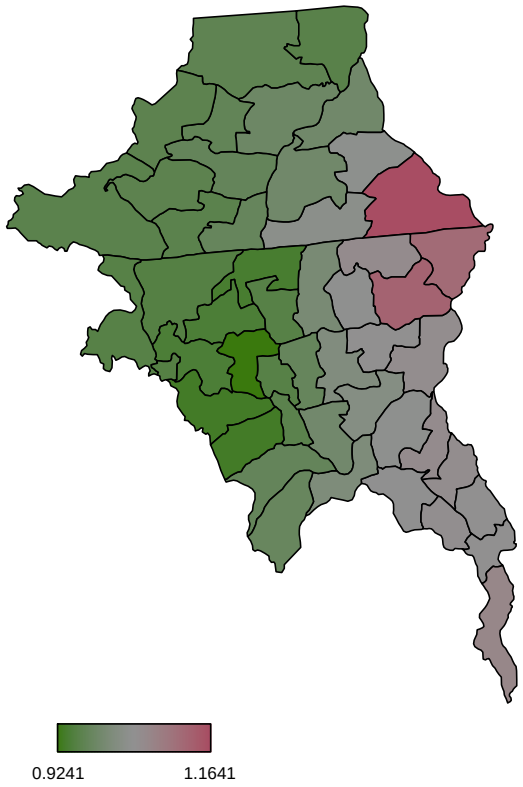
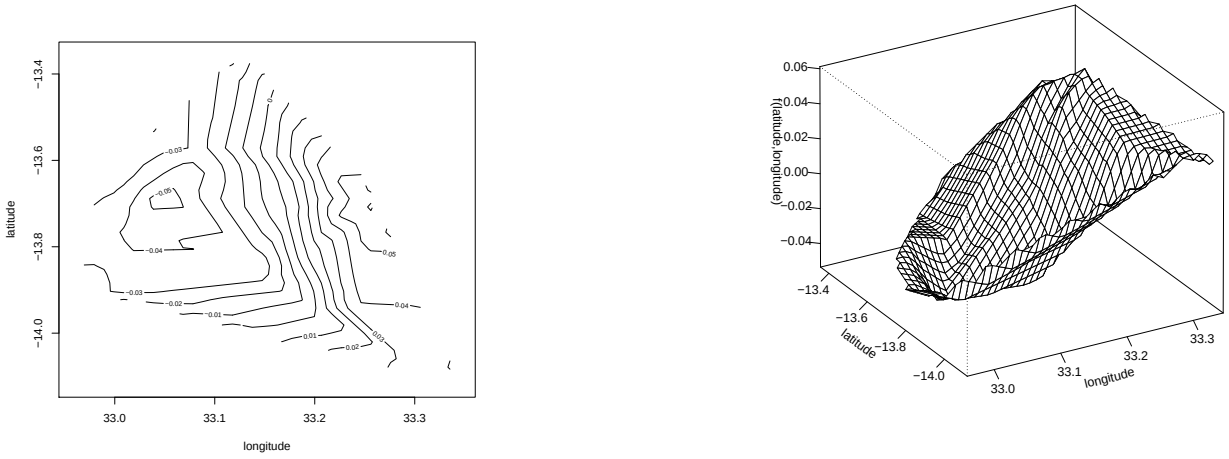



Figure 4.5: Smooth geographical effects of perinatal mortality at sub-district level basing on model **M7**.

Figure 4.6 shows the surface interaction plot of the same geographical locations. These represent other risk factors not directly observed, but had an impact on the risk of perinatal mortality risk. These might be ecological factors like varying deprivation inequalities including depth of poverty, as well as infectious diseases such as malaria, tetanus, syphilis, sepsis, HIV/Aids, pneumonia, intra-partum asphyxia and meningitis that contribute directly to perinatal mortality. These factors often display a geographical pattern. The pattern of the figures produced by contours and mesh are the same. They are indicating that there was low perinatal mortality on the western part and high on the eastern part of the Mchinji district.




(a) (b)

Figure 4.6: Surface of perinatal disparities basing on model **M4** using (a) contours and (b) mesh

# Chapter 5

# Discussion and Conclusion

## 5.1 Discussion

This study demonstrates the use of STAR models that incorporate the effects of nonlinear and the usual fixed effects of some risk factors, while accounting for both structured and unstructured spatial effects to determine the prevalence and potential risk factors of perinatal mortality (Kazembe and Mpeketula, 2010). Logistic regression models were developed and used to have an in-depth understanding of factors associated with the probability of perinatal mortality, building on the existing methodological contributions by (Fahrmeir et al., 2004; Gemperli et al., 2004; Kandala et al., 2007, 2011; Kazembe, 2009; Kazembe and Mpeketula, 2010; Kazembe et al., 2008; Kneib, 2005). However, Poisson or negative binomial models can as well be employed when dealing with area counts data.

In this study, the intervention variable was controlled for, that is, only subjects from the control zones were considered for the analysis in order to have true reflection of spatial distribution of perinatal mortality in the area.

A number of variables were used to explain the variation in the health outcome. The spatial component was specified through MRFs and the two-dimensional P-splines. However, the stationary GRF, widely used in geo-statistics is an alternative approach. The continuous variable, maternal age was estimated non-parametrically as nonlinear function using P-splines

with second order random walk priors; this is based on contributions by (Fahrmeir et al., 2004); while the categorical covariates were modelled as fixed effects using diffuse priors.

Bayesian inference was employed in all the analyses because the models were highly parameterized and analytically intractable that cannot be achieved using maximum likelihood (Fahrmeir et al., 2004, 2003; Kazembe et al., 2008). It is frequently argued that results from REML estimation procedures in GLMMs tend to be biased due to the Laplace approximation involved, especially in sparse data situations (Lin and Breslow, 1996). Although theoretical comparison of EB and FB inference reveals several differences between both inferential concepts, it should be noted that in many applications, the differences are comparably small. In addition, when the sample size is increasing these differences tend to disappear and both approaches give nearly unbiased estimates. If larger differences are observed, that may be an indicator for weakly identified model or other problems caused by model building (Kneib, 2005). Therefore, if possible it is advisable to compare the results from both approaches. In this study both EB and FB approaches were explored, and the results were almost the same.

The findings of the study show that STAR models can quantify the prevalence of health outcomes effectively as compared to the GLMs as observed from the values of Deviance Information Criterion; the STAR model has 1711.09 whereas the GLM has 1724.91. The STAR models accomodate overdispersion and heterogeneity whereas GLMs fail to do so. This makes GLMs not to fit the data well. Generally, the directions of estimates from STAR models were similar to those of GLMs although there were some minor changes.

It has also been observed that modelling continuous covariates as categorical covariates may lead to poor estimation of the health outcome as evidenced from model M6 that has DIC value of 1712.71, which is greater as compared to the value of model M4 with DIC value of 1711.09. It has also been observed that doing the analysis at large area-level may lead to poor estimation of the outcome as compared to when the analysis is done at small area-level as indicated from model M5 which has the DIC value of 1715.58 compared to the small DIC value of 1711.09. Under fully Bayesian approach it has also been observed that the choice of hyper-priors really affects the estimation of the outcome. In this study the hyper-parameters

of a = b = 0.001 lead to better estimation as compared to other priors that were considered.

The residual spatial effects identified a clear and strong spatial structure at zone level. Some areas, in the eastern and southern parts, were associated with high perinatal mortality whereas those of the northern part were associated with low perinatal mortality when structured and unstructured spatial effects only were considered. In addition, there was moderate incidence of perinatal mortality in the central and central west of the district. After controlling for other significant covariates, high perinatal mortality was observed in some parts of the district, particularly zones that are located on the eastern part of the district. Low perinatal mortality was observed in zones that are on the western part of the study area. The low prevalence of perinatal mortality in specific zones could be due to the availability of quality maternal health services being offered and increased health care-seeking behaviours by pregnant women as compared to other areas.

After removing birth attendant variable from the full model, the pattern of perinatal mortality was almost the same to the pattern of the mortality when full model was used. However, there were slight changes. The green colour intensity decreased on western part and red colour was developing on the southern part of the district indicating decrease in probability of perinatal survival and increase in the probability of dying, respectively.

Using the surface interaction plot of the geographical locations showed that there was high perinatal mortality in the eastern part of the district. The surface interaction plot represents other risk factors that were not directly observed, but had an impact on the risk of perinatal mortality. These factors might be the ecological factors like varying deprivation inequalities including depth of poverty, as well as infectious diseases such as malaria, tetanus, syphilis, sepsis, HIV/Aids, pneumonia, intra-partum asphyxia and meningitis that contribute directly to perinatal mortality. These factors often display geographical pattern.

The approximate negative linear relationship of maternal age from 13 to 30 years and approximate positive relationship of the same from 30 to 52 years with perinatal mortality suggest that the occurrence of perinatal mortality decreases with an increase in maternal age to a

certain level and starts increasing as maternal age is also increasing. From this study, it has been observed that the maternal age range that was associated with low perinatal mortality is 16 to 40 years.

The study also found several factors with significant effects on perinatal mortality. Table 4.5 shows that perinatals whose mothers had at least one previous pregnancy were associated with significant reduced perinatal mortality. This could be due to having more knowledge on the danger signs of pregnancy as well as the advantage of the previous experience of the same.

The perinatals whose mothers had their first ANC visit in first trimester with at least 4 visits, second trimester with less than 4 visits, second trimester with at least 4 visits, third trimester with less than 4 visits and third trimester with at least 4 visits were significantly associated with reduced incidence of perinatal mortality compared to those from mothers who had no ANC visit. In addition, perinatals from mothers who had at least 4 visits for a given trimester were associated with reduced occurrence of perinatal mortality as compared to those who had less than 4 visits. It is likely that those mothers who attended ANC visits were offered with essential ANC visits services like TTV, malaria prophylaxis, screening and treatment of anaemia and syphilis, and were examined for pregnancy related complications such as hypertensive disorders and mal-presentations (Graner et al., 2010). So there are many factors that can contribute to this outcome, including the quality of the personnel providing the antenatal services.

Surprisingly, perinatals from mothers whose blood samples were tested were significantly associated with increased prevalence of perinatal mortality as compared to those from mothers whose blood samples were not tested. It may happen that a good number of those who had their blood samples tested had dwindling health status, and this test was provided to find out whether they were infected with HIV or not in order to give them the appropriate care and treatment services (Lewycka et al., 2010). So, it is likely that those mothers who were diagnosed with HIV did not receive the treatment on time and their perinatals died of the same. It has been discovered that successful prevention of mother-to-child transmission of

HIV (PMTCT) prophylaxis depends on the timing of the ingestion of the drug. If the maternal dose of the drug is ingested less than 2 hours before delivery the concentration of the same in the blood may not reach enough therapeutic levels before giving birth and if the infant dose of the drug is taken after 72 hours of birth the baby may not get the full benefits of the drug (Kuonza et al., 2010). Attending more ANC sessions offers more opportunities for healthcare providers to reinforce issues such as the importance of taking the nevirapine (NVP) at the recommended times, the importance of delivering institutionally, the need to take the baby to the clinic in the event that birth takes place at home, and others which have a bearing on adherence to NVP prophylaxis.

Perinatals whose mothers were tested for syphilis were significantly associated with reduced perinatal mortality. It is likely that those mothers who were diagnosed of having syphilis received appropriate treatment and advice to quell the health problems. The findings of a meta-analysis by (Blencowe et al., 2011) correlate with the above observations and show that treatment of syphilis during pregnancy can significantly reduce syphilis related stillbirths by up to 80% (Ishaque et al., 2011).

Perinatals from mothers who had abdominal examination were associated with significant decrease in perinatal mortality. It is obviously that health personnel offering this service were able to detect the potential risks for the pregnancy and gave their clients appropriate medical care to curb the problems.

Perinatals from mothers who received advice on dangers of pregnancy were associated with significant decrease in perinatal mortality. It is obviously that those who received advice were aware of the dangers of pregnancy and were able to seek medical attention for help.

Perinatals who were delivered under skilled birth attendant were significantly associated with reduced perinatal mortality. It is likely that those babies who were born under skilled birth attendant were prevented from other infections and resuscitated during and soon after birth. Birth attendants provide a vital role on the survival of infants during birth. Over one million newborns die from complications of preterm birth, such as respiratory distress

syndrome and these babies require assistance to breathe at birth. It should be noted that due to uterine contraction during normal birth process, all fetuses experience some asphyxia (Leuthner and Utpalla, 2004). There are many reasons why a baby may not be able to take in enough oxygen before, during or just after birth. A mother may have medical conditions that can lower her oxygen levels; there may be a problem with the placenta that prevents enough oxygen from circulating to the fetus; or the baby may be unable to breathe after delivery (Majeed et al., 2007). Neonatal resuscitation is one of the effective ways to save lives of asphyxiated newborns. Resuscitation is now receiving increasing attention especially as a missed opportunity for saving lives for births already in facilities, and for improving morbidity outcomes (Lee et al., 2011). When birth attendants lack skills or perform practices that delay effective ventilation, more babies die as a result of insufficient supply of oxygen soon after delivery. Out of 136 million babies born annually, around 10 million require assistance to breathe (Lee et al., 2011); (Wall et al., 2009). There is evidence from facility-based studies in low and middle income countries that neonatal resuscitation training reduces neonatal mortality from intrapartum-related events by 30%, potentially saving 93,700 babies each year just by addressing missed opportunities for current facility births, and up to 192,000 babies at 90% coverage, only considering the effect on intrapartum-related neonatal deaths (Lee et al., 2011). However, in low income countries, particularly in South Asia and SSA resuscitation is not available for the majority of newborns (Wall et al., 2009).

On infections, more than half a million newborns are established to die each year from serious neonatal infections, accounting for about 15% of all neonatal deaths globally (Black et al., 2010). Many neonatal deaths due to tetanus and other infections are acquired postnatally. The most vulnerable time for both the mother and the newborn is during birth and in the hours and days immediately after childbirth (Ganatra et al., 2010). Clean birth and postnatal care practices in accordance with WHO's "six cleans" - hand washing of birth attendant before birth, clean birth surface, clean perineum, cutting of the umbilical cord using a clean implement, clean cord tie, and a clean cloth for drying, have been associated with dramatic reductions in the incidence of neonatal tetanus. Hand-washing with soap

results in a large reduction in hand contamination, even when washed with unclean water, and birth attendant and maternal hand washing have been associated with reductions in neonatal mortality (Blencowe et al., 2011). These practices may be influenced by a number of programmatic approaches including behaviour change communications, commodity provision, or training of attendants, or combinations of these, and the context may involve a facility birth or a home birth. Therefore, it is important that all pregnant women have access to skilled birth attendants.

Perinatals whose mothers had normal labour duration were significantly associated with reduced perinatal mortality. Prolonged labour may be associated with the size of the birth canal among other factors, whereby small-sized birth canals can result in difficulties of delivering a baby as well as birth asphyxia.

Perinatals from mothers who had a gestation period of at least 9 months were significantly associated with reduced perinatal mortality. It is likely that most perinatals who were delivered before 9 months died of immaturity-related causes. Lastly, perinatals who were delivered normally through birth canal were significantly associated with reduced perinatal mortality. It is likely that a good number of those perinatals that died and born through other modes of delivery, their mothers were attended to by non-skilled birth attendants or the health facility or places where they delivered had no EmONC, among other possible contributing factors.

## 5.2 Conclusion

The study applies a flexible Bayesian modelling approach that allows joint analysis of the nonlinear effects of continuous covariates, spatially structured variation, unstructured heterogeneity, as well as the fixed covariates to quantify small-scale geographical variability in public health outcomes. The best model, M4 has shown that perinatal mortality was high on the eastern part and low on the western part of the Mchinji district. Model M4 also reveals that the perinatal mortality prevalence was associated with parity, timing of the first and number of antenatal care visits, blood sample test, syphilis test, abdominal examination,

provision of advice on danger signs of pregnancy, birth attendant, labour duration, gestation period, mode of delivery, as well as unobserved risk factors. The possible unobservable risk factors are shown by the distinct spatial patterns exhibited by the spatial covariates; suggesting the need for further epidemiological research.

It has been observed that the two Bayesian inference approaches give almost similar results. The findings of the study have shown that modelling fixed effects only using generalized linear models cannot produce satisfactory results. Therefore, the challenge to minimize perinatal mortality requires addressing the unmeasured covariates if we are to come up with effective interventions as a nation by using modelling approaches that account for continuous as well as spatial covariates.

Targeting health interventions to poorer or higher risk individuals and/or communities and ensuring universal coverage are promising approaches for promoting equity. Successful approaches include subsidized health care and health inputs, improved geographic access to health interventions in poor communities and social marketing (Victora et al., 2003).

## 5.3 Recommendations

The eastern part of the district should be given first priority in the provision of targeted interventions as perinatal mortality was high in zones of this area. The capacities of communities in rural Malawi need to be encouraged to take control of the mother and child health issues that affect them such as the high rates of mortality and morbidity they are facing, their low practice of key care and care-seeking behaviours and their high levels of disadvantage and disempowerment through awareness campaigns on importance of seeking medical services during pregnancy and infant bearing period. Mothers who are very far away from health facilities should be encouraged to deliver under the presence of the skilled birth attendant at health facilities. Policy makers should try their best to address the issue of health inequalities as well as improving the access of high quality health services in all health facilities if we are to achieve the Millennium Development Goals 4 and 5. Nurses working in

the PMTCT clinics should ensure that HIV positive mothers are given nevirapine tablets at first contact, regardless of the stage of the pregnancy. Health promotion should be intensified at the community level to encourage ANC attendance and institutional deliveries. The government should consider adopting a policy of dispensing infant NVP doses during ANC, as is done for the maternal dose, and the possibility of incorporating trained traditional birth attendants into the PMTCT programme, so as to increase access to the ARV prophylaxis.

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# Appendix A

# Estimation of parameters with BayesX

This part demonstrates how probit models of geoadditive predictor are estimated with BayesX. The program is command line driven, i.e., the user must enter a number of commands to estimate regression models. The statements can be combined and collected in a batch file which allows one to execute all statements in one step. The following statements are part of the batch file and are required to estimate the probit model.

```
> delimiter = ;
> dataset d;
> d.infile using c:\spatialB\permcban.txt;
> map m;
> m.infile using c:\spatialB\mcban.txt;
> m.reorder;
> bayesreg m4;
> m4.outfile = c:\MC\m4;
> m4.regress perinatal = z_id(random) + z_id(spatial, map = m) + mothernet +
m_age(psplinerw2) + prev_preg + ancfvisit1 + ancfvisit2 + ancfvisit3 +
ancfvisit4 + ancfvisit5 + ancfvisit6 + ancbp + ancblood + ancfta + ancexam +
ancidanger + skilled + labourduration + gest_period + delmode +
latitude*longitude(pspline2dimrw1), family = binomialprobit iterations =
12000 burnin = 2000 step = 20 predict using d;
```

```
> m4.getsample;
> remlreg r4;
> r4.outfile = c:\MC\r4;
> r4.regress perinatal = z_id(random) + z_id(spatial, map = m) + mothernet +
m_age(psplinerw2) + prev_preg + ancfvisit1 + ancfvisit2 + ancfvisit3 +
ancfvisit4 + ancfvisit5 + ancfvisit6 + ancbp + ancblood + ancfta + ancexam +
ancidanger + skilled + labourduration + gest_period + delmode +
latitude*longitude(pspline2dimrw1), family = binomialprobit using d;
```

The first statement sets the delimiter to the ';' sign rather than the return key and allows one to split subsequent commands into several lines. The next two statements create a dataset object 'd' and read in the data using the infile command of dataset objects. The data are supposed to be stored in the ASCII file 'c:\spatialB\permcban.txt', where variables are stored column wise and observations are separated by blanks or tabs. The first line of the file contains the variable names.

In the following two statements a map object 'm' is created and the location of perinatals is read using the infile command of map objects. This information is required to estimate spatial effects. In the next statements bayesreg object 'm4' is created and model M4 is estimated. The outputs of model M4 are stored in 'c:\MC\m4'. A number of options are specified after a comma. These options define the model and details about MCMC simulation (the number of iterations, the burn in period and the thinning parameter). The dataset to be used for estimation is given after the key word 'using'. Post-estimation commands like getsample are used to stored the detailed results in the specified folder.

The last three commands re-estimate the model using mixed model technology and based on REML estimates for the variance respective to the smoothing parameters.

The univariate p-splines for the main effects of maternal age are specified by the term m_age(psplinerw2). The term `latitude*longitude(pspline2dimrw1)` is used to estimate

the spatial effect. Alternatively, bivariate p-spline `(latitude*longitude(pspline2dimrw1))` may be replaced by the Kriging term `(latitude*longitude(Kriging, full))`. In this case, the option full specifies that all observation points shall be used for the kriging estimate, i.e., no low-rank approximation is to be employed (Kneib, 2005).

Details on how to use BayesX can be found in the user manual. The latest version of BayesX manual is available at `http://www.stat.uni-muenchen.de/~lang/bayesx/`. An overview about the capabilities of BayesX is given in (Brezger and Lang, 2003).

# Appendix B

# R Package

## B.1 Drawing maps in R using BayesX output

Maps were drawn in R using the outputs from BayesX. The commands used are in the following order:

```
> library(foreign)
> library(BayesX)
> m <- read.bnd(``c:/spatialB/mcban.txt")
> drawmap(data = ``c:/MC/m4_f_z_id_spatial.res", map = m, plotvar = ``pmean",
region = ``z_id")
> drawmap(data = ``c:/MC/r4_f_z_id_spatial.res", map = m, plotvar = ``pmode",
region = ``z_id")
```

## B.2 Producing two dimension surface using BayesX output

```
> library(foreign)
> library(BayesX)
> d <- read.table(``c:/MC/m4_f_latitude_longitude_pspline.res", header = T)
```

```
> plotsurf(d, ylab = ‘‘latitude", xlab = ‘‘longitude", zlab = ‘‘f(latitude,
longitude)")
> plotsurf(d, mode=2)
> plotsurf(d, mode=3)
> n <− read.table(‘‘c:/MC/r4_f_latitude_longitude_pspline.res", header = T)
> plotsurf(n, ylab = ‘‘latitude", xlab = ‘‘longitude", zlab = ‘‘f(latitude,
longitude)")
> plotsurf(n, mode=2)
> plotsurf(n, mode=3)
```

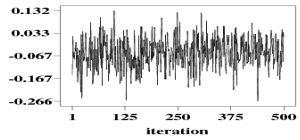
After producing the maps and diagrams, they were saved in pdf format.

# Appendix C

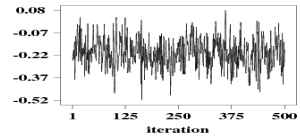
# Trace plots

To monitor convergence of parameters, trace plots were used. Figure C.1 shows trace plots of different covariates: fixed and continuous effects.

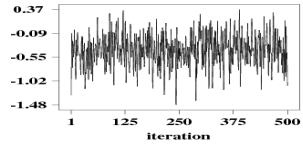
Mother slept under net



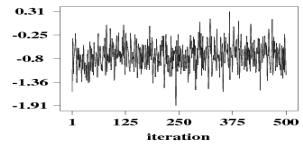

Previous pregnancy



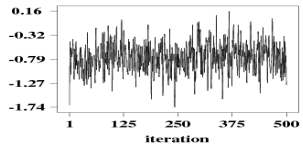

Trimester 1, < 4 visits



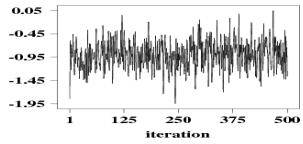

Trimester 1, ≥ 4 visits



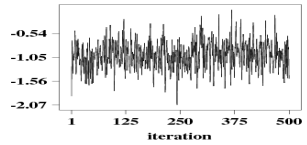

Trimester 2, < 4 visits



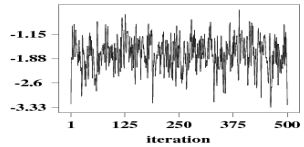

Trimester 2, ≥ 4 visits



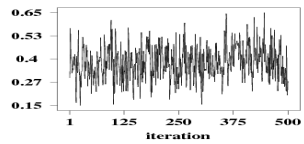

Trimester 3, < 4 visits



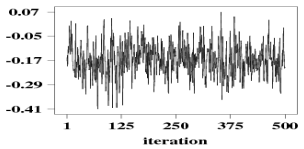

Trimester 3, ≥ 4 visits



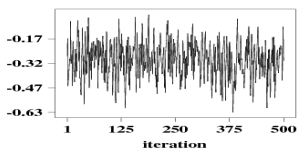

Blood sample test



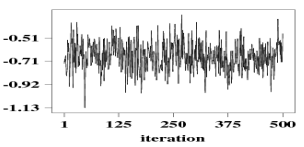

Blood pressure test



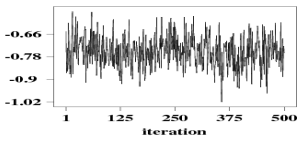

Syphilis test



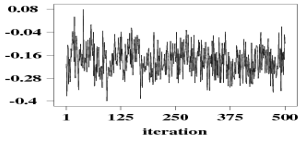

Abdominal examination



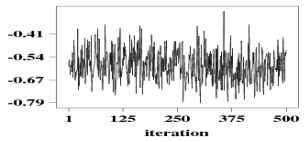

Danger signs advice



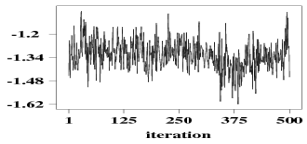

Birth attendant



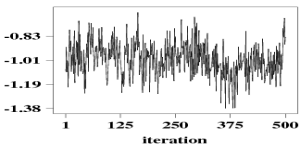

Labour duration



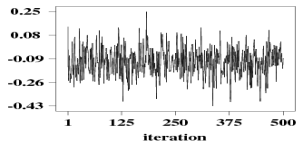

Gestation period



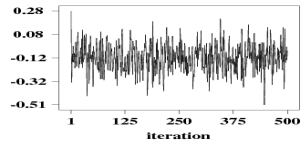

Mode of delivery




First quartile of maternal age




Median of maternal age




Third quartile of maternal age

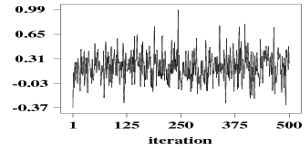



Figure C.1: Trace plots

# Appendix D

# Data Protection Policy

All protocols were followed and permission was granted by the directors of MaiMwana project to use their dataset. Below is the Data Protection Policy that was read and signed.

**RIGHTS OF PARTICIPANTS**

- To Know what information MaiMwana holds about them and why?
- To know how to gain access to the information MaiMwana holds about them.
- To know what MaiMwana is doing to ensure confidentiality.
- Right to know the results of the study.
- Right to withdraw anytime and get their Data.

## D.1 Staff Guidelines for Data Protection

### D.1.1 All Data room staff must make sure that:

- Access to the data room is strictly controlled to non MaiMwana Staff.
- Data room must be closed whenever there is no staff present.
- No unauthorized entry into the data room.

- Data collectors and clerks must be identified by personal identities.
- No copies of the database are taken offsite without authorisation.

### D.1.2 Verbal Autopsies Protection.

- All photocopies of verbal autopsies that have been reviewed will be returned immediately to Mchinji.
- Photocopied autopsies must be transferred in a secure way to The Project Directors and consultant obstetrician.
- Photocopies of perinatal verbal autopsies will be released to the directors and maternal verbal autopsies to Grace and Terek for diagnoses in Lilongwe.
- Verbal autopsy photocopies will be prepared so that names and identifying details are blacked out.
- Once the photocopies have been reviewed, they will be returned to Mchinji for archiving.
- Written diagnoses must be returned immediately to Mchinji for entry into the database.
- All open history sections of verbal autopsies will be translated into English and the English translation will be entered into the database in Mchinji.
- Photocopies of perinatal verbal autopsies translation must be kept onsite in Mchinji.
- Addition English translations of the structured part of maternal verbal autopsies will be sent to consultant obstetrician and returned immediately to Mchinji after review.

### D.1.3 General Data Protection

- The data room must maintain a closed network and the use of external disks must be controlled to reduce the likelihood of virus infection.

- The database password must be restricted to the Directors, Project Manager, Data Manager, data team and the research fellows in Mchinji.
- All data room computers must have passwords to control access and specific individuals must have the backup copies including the data manager.
- Data must always be stored in a secure environment.
- The database must have a complex password, at least six characters to prevent the password from being cracked using password crackers which are easily found on the Internet.
- If any analyses are requested to be done in London or elsewhere by the principal investigators or an approved researcher, permission must be formally requested from Charles, specifying the data variables that needs to be exported and the procedure to ensure confidentiality.
- Only the project Directors will give permission for offsite data analyses following a formal request using a specific format provided by MaiMwana. Excel files with the requested variables will be generated and sent to the person requesting the data. The person requesting the data must give the time frame and the output for data analysis.
- Data used for external research projects must be stored and disposed of in accordance with this policy.
- Exported data should be anonymous.
- Photographs and videos must be taken after consent and the request must include an explanation of the intended purpose. These photographs, videos including electronic or hard copy taken from MaiMwana clients must be taken back to the community within a month.

### D.1.4 Human Specimen

- All human specimens must be handled safely by staff and be protected to maintain potency with the following guidelines: collected specimen must be placed in a closed plastic container to protect and prevent it from contamination either from dust or other organisms; at nodal office the specimen must be placed on a rack for 24 hours to allow drying; and specimen must be wrapped in a weighing paper, stored in a plastic zip lock bag descants added and a humidity indicator card (Humonitor) placed into the bag before transporting them into the office for proper storage within 72 hours of collection (in case of Direct Blood Spot).

- Deep freezer used for storage of spacemen must be kept locked at all times and the keys must only be accessible to HSST and MHSAs.

- No food stuff or drinking water must be stored in the deep freezer with human specimen.

- A thermometer must always be in the deep freezer and recording of the temperature must be done twice a day to make sure the specimens are always at the recommended temperature of ($-20^0$C).

- Staff members must make sure that they protect themselves, study participants and the environment by following universal infection prevention (IP) guidelines.

- Informed consent form must be signed before collection of the specimen; Supervisors must monitor staff closely to ensure this is done properly.

- No name must appear on specimens, instead bar code numbers must be used to maintain confidentiality.

- When transporting the specimens to a testing laboratory cold chain must be maintained, only barcodes numbers and date of collection must appear on the specimens.

- Human specimens must not be kept for longer than necessary (according to NHSRC guidelines). Where possible, samples must be tested at a laboratory in Malawi. Where

no suitable alternative exists, samples may be transported to a testing site overseas but any remaining biological specimens must be returned after testing.

- Specimens which are no longer required must be destroyed completely preferably by incineration.

## D.2 Data Collection

- Data collectors and Clerks must be identified by personal Identity cards.
- Data must be collected, stored and used in accordance with NHSRC guidelines.
- Data must be collected with informed consent which includes scope of processing and future use.
- The data collected from participants must be adequate, relevant and not excessive.
- The data collected must not be kept longer than necessary.

## D.3 Incoming and Internal Mail:

- Staff members are discouraged from using MaiMwana email address for non MaiMwana project matters.
- The MaiMwana email address password must only be known to Project Directors, Project Manager and Departmental Heads.
- The email password must be changed on a regular basis.

## D.4 All staff members are responsible for ensuring that:

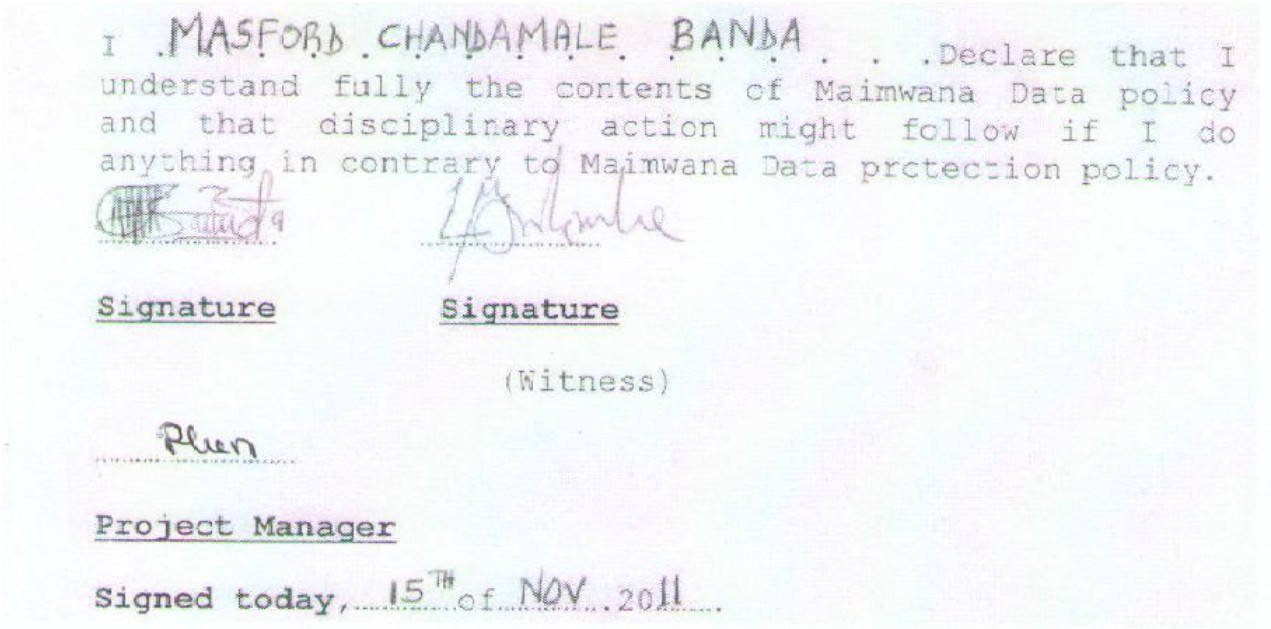
- Any Project data which they hold, whether in Electronic or Paper format is kept securely in accordance with MaiMwana data policy.

- Personal information is not disclosed either orally or in writing or accidentally or otherwise to any unauthorised third party.
- All copies of MaiMwana data that contain individual participant information should be password protected.
- They are familiar with the MaiMwana Data Protection Policy.
- Any breach of the Data Protection Policy, either deliberate or through negligence may lead to disciplinary action being taken.
- Visitors to data room staff members should be at the reception as the data room is a controlled access area.
- There is no use of data for purposes not originally stated unless with prior consent from the project directors.
- You are still bound to MaiMwana Data protection policy after leaving the institution.

## D.5 Conclusion

This policy was endorsed by the MaiMwana management on Thursday 27 March 2008 and is the formal and official MaiMwana Data Protection Policy. Any questions or concerns related to MaiMwana Data Protection Policy should be taken to the Data officer.

## D.6 Declaration



I MASFORD CHANDAMALE BANDA . . . .Declare that I understand fully the contents of Maimwana Data policy and that disciplinary action might follow if I do anything in contrary to Maimwana Data prctection policy.

Signature Signature

(Witness)

Project Manager

Signed today, 15TH of NOV. 2011