Assessing the effects of interventions on child and maternal health-related outcomes in Uganda

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Basel, den 11th, December 2018

Prof. Dr. Martin Spiess

Dekan

To my son, **Raphael**

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List of Abbreviations

ACT	Artemisinin-combination therapy
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal care
aOR	Adjusted Odds ratio
ARI	Acute respiratory infections
BCG	Bacillus Calmette Guerin
BCI	Bayesian Confidence Interval
CA	California
DHS	Demographic and Health Survey
DPT	Diphtheria, pertussis and tetanus
g/dL	grams per deciliter
HIV	Human Immunodeficiency Virus
HIV/AIDS	Human immunodeficiency virus/Acquired Immune Deficiency Syndrome
HR	Hazard ratio
IGBP	International Global Biosphere Programme
IPT	Intermittent preventive treatment
IRS	Indoor Residual Spraying
IT	Information Technology
ITN	Insecticide Treated Net
LST	Land Surface Temperature
LTR	Life time risk
MDG	Millennium Development Goals
MIS	Malaria Indicator Survey
MMR	Maternal mortality ratio
MODIS	Moderate Resolution Imaging Spectroradiometer
NDVI	Normalized Difference Vegetation Index
NPHC	National Population and Housing Census
OR	Odds ratio
ORS	Oral rehydration solution
PPHS	PhD program for Health Sciences
RDT	Rapid diagnostic test
RHF	Recommended homemade fluids
RMNCHSP	Reproductive Maternal, Newborn and Child Health Sharpened Plan
SDG	Sustainable Development Goals
SRTM	Shuttle Radar Topographic Mission
SSA	Sub-Saharan Africa
SSPH+	Swiss School of Public Health
SwissTPH	Swiss Tropical and Public Health Institute
TB	Tuberclosis
TX	Texas
UBOS	Uganda Bureau of Statistics
UK	United Kingdom
UN	United Nations
U5MR	Under-five mortality rate
USA	United States of America
USAID	United States Agency for International Development
USDI	Uganda service delivery indicators
USGSS	United States Geological Survey-Earth Resources Observation Systems

WASH	Water, Sanitation and Hygiene
WHO	World Health Organization

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Summary

In this PhD, health-related outcomes studied include the under-five mortality rate (U5MR), the prevalence of fever, diarrhoea, symptoms of acute respiratory infections (ARI) as well as maternal mortality ratio (MMR).

Every year in the world, millions of children die before their fifth birthday. In 2016, an estimated 5.6 million under-five deaths occurred with half of the burden concentrated in the sub-Saharan Africa (SSA) region. In these countries, the U5MR is unacceptably high yet progress is slowed down by the uneven distribution of key determinants of child mortality, for example, child interventions, childhood diseases and the socio-economic factors. Such imbalances lead to substantial variations in the U5MR within countries which may hinder the achievement of Sustainable Development Goal (SDG) target 3.2. In Uganda, the U5MR is much higher than the SDG target of 25 or less deaths per 1 000 live births. In addition, significant differences in the U5MR as well as determinants of U5MR are huge and disproportionately distributed within the country. A better understanding of the determinants of the existing inequalities in the under-five mortality would guide in the prioritization of effective and equitable strategies to realise mortality targets.

Another fundamental mortality indicator is the maternal mortality ratio (MMR). MMR measures the quality of the health system and also reflects inequality between sub-groups and, between and within countries. The indicator is also essential for tracking progress in development and for spurring action to improve maternal health.

According to the World Health Organisation, the MMR is highest in SSA and accounts for approximately 66% of the global maternal deaths. In SSA, direct and indirect causes of maternal deaths are the most prevalent conditions yet prevention and treatment measures are hindered by dysfunctional national health systems and a low socio-economic status. This leads to poor maternal health outcomes in SSA, resulting into vulnerable families

and increased chances of infant mortality before reaching their second birthday. Furthermore, maternal mortality deteriorates economic development since more women survive with chronic and incapacitating ill health for each maternal death.

Uganda ranks number nine among the top ten high-burdened countries and experiences a MMR far higher than the SDG target 3.1. At the same time, large regional disparities in MMR and its determinants (e.g. maternal interventions) prevail within the country. Therefore, strategies to end maternal mortality need to be implemented, in particular, approaches to address the sources of inequities. This may reduce variations in MMR within Uganda, and thus, quicken the achievement of SDG target 3.1 in the country.

The adoption of the United Nations (UN) Millennium Declaration in the late 2000, established a global partnership of countries and development partners committed to eight voluntary development goals, to be achieved by 2015. Two of the eight Millennium Development Goals (MDGs) focused on U5MR reduction and maternal health improvement. U5MR has fallen by 53% and maternal mortality by 43% since 1990 to 2015. Even though this is a cause for celebration, both declines fell short of the MDG targets of two thirds and three quarters reductions from the 1990 levels. With the end of the era of the MDGs in 2015, the international community agreed on a new framework – the SDGs. The SDG targets for under-five and maternal mortality represent a renewed commitment to the world’s children and mothers. By 2030, end preventable deaths of children under five years of age, with all countries aiming to reduce U5MR to at least 25 deaths per 1 000 live births while maternal mortality should not exceed 140 deaths per 100 000 live births.

Tracking progress towards child and maternal mortality SDG targets requires significant investment in measuring nationally representative data relevant to the estimation of mortality indicators. The implementation of the National Population and Housing Census (NPHC), nationally representative household surveys, that is, Demographic and Health

Surveys (DHS), Malaria Indicator Surveys (MIS) and the Uganda Service Delivery Indicator (SDI) Survey has resulted in rich sources of data in Uganda which has made it practical to monitor progress in mortality indicators and their determinants. Censuses collect data for each individual in the country and are therefore an important source of microdata, which enables the study of sub-national differences. The SDI survey data facilitates the assessment of health facility readiness in the country while DHS and MIS data are spatially structured and can be used to identify high risky areas as well as track progress in the distribution of the determinants of mortality such as health interventions and diseases.

Despite the rich data sources, data utilisation remains poor and information extracted by researchers is restricted to national estimates that neither take into account sub-national discrepancies nor assess the effects of interventions and childhood diseases on mortality or morbidity differentials in space. National estimates mask geographical heterogeneities that may exist at a local scale. Therefore, most important interventions at a local scale, areas affected by the disease burden as well as high mortality clusters cannot be identified. This is because the standard frequentist methods commonly employed in the analysis assume independence of observations yet the DHS and census collect mortality and morbidity data at neighbouring locations, and therefore correlated in space. This is because observations at close geographical proximity are likely to share common exposures and thus affected in a similar way. In case of mortality, spatial correlation arises from its determinants such as infectious diseases. An example is malaria which is transmitted by mosquitoes as they fly long distances in surrounding areas. Ignoring spatial correlation in the data results into imprecise effects of covariates and incorrect estimates of mortality risk which are essential for determining most important interventions, areas affected mostly by diseases and high mortality clusters.

Spatial statistical methods fitted via Markov Chain Monte Carlo simulations, are the novel approach developed to incorporate spatial correlation in space. They can estimate high mortality clusters within the country and evaluate the effects of health interventions and childhood diseases on health-related outcomes at the national and sub-national scale for targeted intervention.

The goal of this PhD thesis is to develop Bayesian spatial models to assess the ffects of interventions on child and maternal health-related outcomes at the national and sub-national scale in Uganda, through the following specific objectives; 1) to quantify the effects of childhood diseases on all-cause under-five mortality over space; 2) to estimate the effects of health interventions on all-cause under-five mortality over space; 3) to assess the contribution of childhood diseases on the geographical distribution of fever risk among children less than five years; 4) to quantify the effect of the presence of soap and water at handwashing places in households on the risk of diarrhoea and respiratory infections among children under-five years and 5) to assess the effects of maternal health interventions on all-cause maternal mortality.

In Chapter 2, Bayesian geostatistical proportional hazards models with spatially varying coefficients were applied on the 2011 DHS and 2009 MIS data to estimate the effects of childhood diseases on all-cause under-five mortality at the national and sub-national levels. The models took into account geographical misalignment in the locations of the surveys. Childhood diseases had significant but varying effects on mortality across regions. At national level, the U5M was associated with prevalence of malaria (hazard ratio (HR) = 1.74; 95% BCI: 1.42, 2.16), severe or moderate anaemia (HR =1.37; 95% BCI: 1.20, 1.75), severe or moderate malnutrition (HR = 1.49; 95% BCI: 1.25, 1.66) and diarrhoea (HR = 1.61; 95% BCI: 1.31, 2.05). The relationship between malaria and U5M was important in the regions of Central 2, East-Central, Mid-North, North-East and West-Nile. Diarrhoea was associated with under-five deaths in Central 2, East-central, Mid-Eastern and Mid-Western. Moderate/severe malnutrition was associated with U5M in East-Central, Mid-Eastern and North-East. Moderate/severe anaemia was associated with deaths in Central 1, Kampala, Mid-North, Mid-Western, North-East, South-West and West-Nile.

In Chapter 3, Bayesian geostatistical proportional hazards models with spatially varying coefficients were developed to determine interventions' effects on under-five mortality at national and sub-national levels, and to predict mortality risk at unsampled locations. The data used in the analysis were obtained from the 2011 DHS. The most important interventions at the national level were artemisinin-combination therapy (HR = 0.60; 95% BCI: 0.11, 0.79), initiation of breast feeding within one hour of birth (HR = 0.70; 95% BCI: 0.51, 0.86), intermittent preventive treatment (IPT) (HR = 0.74; 95% BCI: 0.67, 0.97) and insecticide treated nets (ITN) access (HR = 0.75; 95% BCI: 0.63 0.84). Other important health interventions had more or less comparable effects on mortality. The effects of health interventions on under-five mortality varied by region. In Central 2, Mid-Western and South-West regions, the largest reduction in the under-five mortality burden was associated with ITN access. Improved source of drinking water explains most under-five mortality reduction in Mid-North and West-Nile. Improved sanitation facilities account for the highest decline in under-five mortality in the North-East. In Kampala and Mid-Eastern, IPT had the largest impact on mortality. In Central 1 and East-Central, ORS or RHF and postnatal care were respectively associated with the highest decreases in under-five mortality.

High mortality clusters were found in the North-East, West-Nile, southern of Mid-North, East-Central along the Victoria Nile River, southern of Central 1 stretching to the South-West region and along the country border in Mid-Western between Lakes Albert and Edward. Lowest mortality hazard rates were predicted in Kampala, centre of Mid-North extending to West-Nile, North-East, Mid-Eastern and East-Central regions. Also, areas around Lake George in Mid-Western and a few spots in Central 2 were predicted with low mortality hazard rates.

In Chapter 4, we applied Bayesian geostatistical logistic models on the 2016 DHS data and quantified the contribution of childhood diseases to the geographical distribution of fever risk among children less than five years. At the national level, the population attribution fraction of diarrhoea, ARI and malaria to the prevalence of fever in the under-five was 38.12 (95% BCI: 25.15, 41.59), 30.99 (95% BCI: 9.82, 34.26) and 9.50 (95% BCI: 2.34, 25.15), respectively. The attribution of diarrhoea was common in all regions except Bunyoro, while ARI was more common in Bugisu, Karamoja and West Nile, and malaria was commonest in Bunyoro. In Lango, the attribution of diarrhoea and ARI was similar.

In Chapter 5, we analysed the 2016 DHS data and quantified the effect of the presence of soap and water at handwashing places in households on the risk of diarrhoea and ARI among the under-five using Bayesian geostatistical logistic models. The odds of diarrhoea and ARI in children who lived in households having soap and water at handwashing places were 14% and 24% less than those living in households without the intervention (adjusted odds ratio, aOR = 0.86; 95% BCI: 0.77 – 0.96) and (aOR = 0.76; 95% BCI: 0.65 – 0.88) respectively.

In Chapter 6, Bayesian negative binomial CAR models were employed to evaluate the effects of maternal health interventions on all-cause maternal mortality. Data were extracted from the 2016 DHS and 2014 NPHC. The risk of maternal mortality declined with increasing coverage of intermittent preventive treatment (Mortality rate ratio (MRR) = 88%; 95% BCI: 86%, 91%), iron supplements (MRR = 95%; 95% BCI: 93%, 98%), skilled birth attendance (MRR = 96%; 95% BCI: 94%, 98%) and family planning (MRR = 95%; 95% BCI: 92%, 98%).

The results of this thesis will guide prioritization and targeted allocation of high impact and evidence-based interventions to maximize benefits of resources. This will alleviate within country morbidity and mortality discrepancies and consequently accelerate progress towards achieving SDG targets 3.1 and 3.2 in Uganda by 2030.

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Chapter 1: Introduction

This chapter describes child and maternal health-related outcomes and their determinants. The assessed health-outcomes include the under-five mortality rate (U5MR), the prevalence of fever, diarrhoea, symptoms of acute respiratory infections as well as maternal mortality ratio (MMR).

1.1 Burden of under-five mortality

The U5MR is a key indicator for child health and well-being (Gortmaker, 1979; Mosley and Chen, 1984; United Nations, 2015a). Also, the indicator is a measure for the overall health of the general population as it correlates well with factors which influence the health status of the whole population such as malnutrition, water, sanitation and hygiene, socio-economic development, access to quality health services and quality of the environment (Reidpath and Allotey, 2003; Vella et al., 1992a). In addition, the U5MR is one of the most important among the indicators monitoring many Sustainable Development Goals (SDG) (World Health Organization, 2015b).

Remarkable progress towards Millennium Development Goals (MDG) indicates that the U5MR greatly improved since 1990 despite falling short of the MDG targets (World Health Organization, 2015b). Globally, the U5MR dropped from 93 in 1990 to 41 deaths per 1 000 live births in 2016 (Unicef, 2017). Similarly, the U5MR in majority of the regions in the world and countries improved. Sub-Saharan Africa (SSA), a region with the highest mortality burden (Figure 1.1) also experienced a decline in the U5MR from 183 to 79 deaths per 1 000 live births during the same period (Unicef, 2017).

Despite the substantial progress in reducing child mortality worldwide, the burden of U5MR remains unevenly distributed. Inequities in child mortality across regions and countries persist. In 2016, SSA had an U5MR of 79 compared to the lowest of 5 deaths per 1 000 live births in Europe. At the country level, the U5MR ranged from 2 in each of Finland, Iceland, Luxembourg and Slovenia to 133 deaths per 1 000 live births in Somalia (Unicef, 2017). As a result of the substantial under-five mortality burden worldwide, specifically in developing regions, the United Nations (UN) adopted a new development agenda – the SDGs (World Health Organization, 2015b). In this agenda, the UN incorporated and devoted target 3.2, of its third SDG to reducing the U5MR to atleast 25 deaths per 1 000 live births in every country in 2030 from the baseline year of 1990 (World Health Organization, 2015b). According to the UN, meeting the SDG target would reduce the number of under-five deaths by 10 million between 2017 and 2030 (Unicef, 2017).

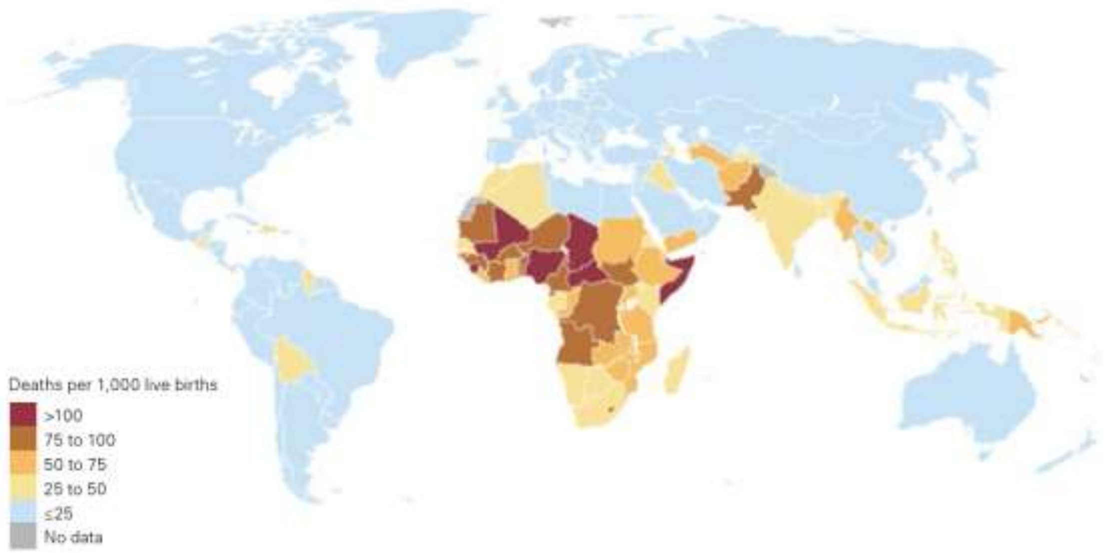

Figure 1. 1: U5MR per 1,000 live births by country, 2016; Levels & Trends in Child Mortality. Report 2017. Estimates Developed by the UN Inter-agency Group for Child Mortality Estimation.

In Uganda, the U5MR dropped from 175 in 1990 to 53 deaths per 1 000 live births in 2016 (Unicef, 2017). Equally, the 2016 Demographic and Health Survey (DHS) reports a decrease in the indicator from 183 in 1983-88 to 64 deaths per 1 000 live births in 2016 (Kaijuka et al., 1989; Uganda Bureau of Statistics (UBOS) and ICF, 2018). This decline can be attributed to the improvement in the coverage of health interventions and a decrease in the burden of childhood diseases (Kaijuka et al., 1989; Uganda Bureau of Statistics (UBOS) and ICF, 2018). Even though there is an outstanding improvement in the U5MR in Uganda, the country still falls short of the under-five mortality SDG target 3.2 (World Health Organization, 2015b). Additionally, persistent discrepancies exist in the U5MR across regions of the country. For example, in 2011, Karamoja region experienced the highest U5MR (152 per 1 000 live births) whereas the lowest rate occurred in Kampala (56 per 1 000 live births) (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Similar inequalities were observed in 2016 with U5MR varying from 102 in the North-East (Karamoja) to 64 deaths per 1 000 live births in Kampala region (Uganda Bureau of Statistics (UBOS) and ICF, 2018). All regions still face high mortality above SDG target 3.2. Also, mortality rates are substantially higher in rural areas, in households in the lower socio-economic status and children born to less educated mothers (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Thus, approaches aimed at reducing discrepancies within the country are important priorities to further accelerate the pace of progress towards SDG target 3.2 (Unicef, 2017). Specifically, factors responsible for the observed regional variations in mortality in Uganda need to be identified. This will guide the Ugandan government in designing and implementing of appropriate strategies to address U5MR in the various regions. This may reduce regional variation in all-cause under-five mortality and consequently, accelerate the achievement of the national U5MR SDG target.

1.2 Determinants of under-five mortality

Under-five mortality is known to be influenced by various factors for example, childhood diseases (Kazembe et al., 2007; Keusch, 2003; Scott et al., 2014; Walker et al., 2013), health interventions (Bbaale, 2015; Gemperli et al., 2004; Kabagenyi and Rutaremwa, 2013), socio-demographic and climatic/environmental (Burtscher, 2016; Chapur et al., 2017) factors.

1.2.1 Childhood diseases

Millions of under-five deaths occur annually, mostly from preventable or treatable conditions. Worldwide, infectious diseases, particularly pneumonia, diarrhoea and malaria, remain among the leading causes of under-five deaths (Liu et al., 2016). Most of these diseases present with the fever symptom as an indication for illness in the early stages (Armon et al., 2001; Finkelstein et al., 2000). This implies that infectious diseases also reflect the burden of fever among the under-five children. Pneumonia, diarrhoea and malaria accounted for almost a third of the global under-five deaths in 2016 (Figure 1.2) (Liu et al., 2016) while in SSA, these diseases were responsible for about 40% of deaths in the same age group during the same time (Unicef, 2017). In half of these deaths, malnutrition is an underlying factor (Unicef, 2017).

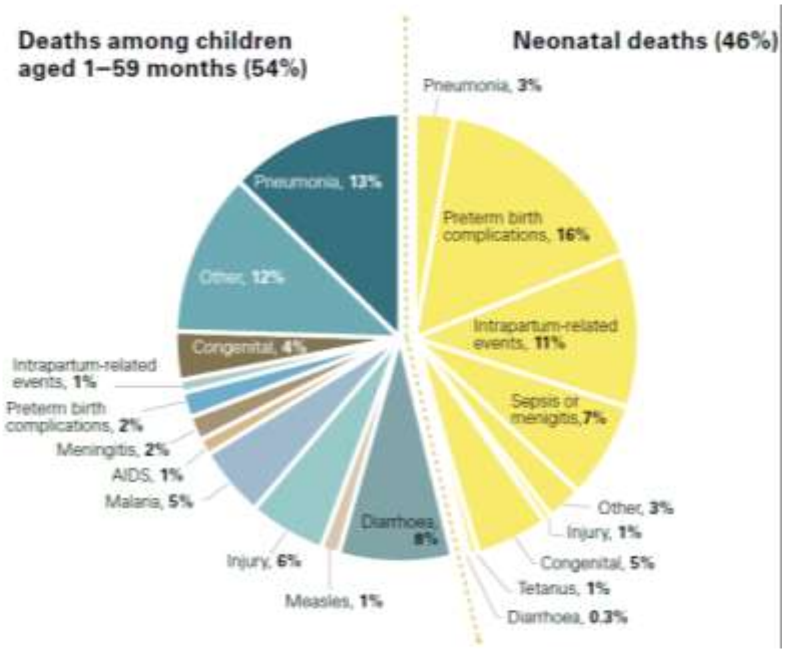

Figure 1. 2: Global distribution of deaths among children under age five, by cause, 2016; Levels & Trends in Child Mortality. Report 2017. Estimates Developed by the UN Inter-agency Group for Child Mortality Estimation.

In Uganda, malaria, anaemia, malnutrition, diarrhoea and acute respiratory infections (ARI) are the major causes of under-five mortality (Ministry of Health, 2015a). The country has registered an improvement in the burden of most childhood diseases in the past years as well as their symptoms, especially fever (Uganda Bureau of Statistics (UBOS) and ICF, 2018; Uganda Bureau of Statistics (UBOS) and ICF International, 2015). For example, the prevalence of ARI dropped from 15% in 2011 to 9% in 2016 and that of fever declined from

40% in to 33% (Uganda Bureau of Statistics (UBOS) and ICF, 2018; Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

In spite of the national improvements, the burden of childhood diseases is persistently high and unevenly distributed among regions. For instance, fever was dominant among children in Busoga (66%) and Teso (59%) regions and least prevalent in Bunyoro region (11%) (Uganda Bureau of Statistics (UBOS) and ICF, 2018). The prevalence of ARI was highest in Karamoja region (27%) and lowest in Bunyoro region (1%) (Uganda Bureau of Statistics (UBOS) and ICF, 2018). It is not known if variations in the U5MR within the country are a result of regional differences in the distribution of childhood diseases. Thus, identification of diseases which influence mortality in the various regions is necessary, so that evidence-based and disease-specific interventions to address U5MR at a local scale can be programmed and implemented.

1.2.2 Health interventions

The key to making rapid progress towards attaining SDG 3.2 is to reach every child with a priority set of high impact interventions, with emphasis on saving lives of children living in disadvantaged areas (Ministry of Health, 2009). Child survival interventions are well known and affordable, for which evidence at a global level has shown can prevent more than half of the existing childhood mortality when implemented universally (Darmstadt et al., 2005). This implies that, to accelerate child survival efforts, we do not need new science but prioritization and targeted allocation of highly cost-effective evidence-based interventions. The challenge is that most maternal and child health programs do not reach the world’s poorest families (World Health Organisation, 2012). Therefore, to curb the U5MR, focus should be placed on expanding coverage of evidence based cost-effective interventions in all areas, specifically those most in need.

Among the recommended interventions (Darmstadt et al., 2005) are; ownership and use of insecticide treated nets, residual household spraying, skilled assistance during delivery, full vaccination, appropriate treatment of malaria and respiratory infections, exclusive breast feeding, oral rehydration salts for treating diarrhoea, use of improved water sources and toilets, vitamin A and iron supplementation, deworming and universal coverage of intermittent presumptive treatment for pregnant mothers.

In Uganda, coverage of similar interventions has been scaled up and this could partly explain the marked survival gains among children less than five years (Uganda Bureau of Statistics (UBOS) and ICF, 2018; Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). For example, among the malaria interventions, the percentage of children under age five sleeping under an ITN the night before the survey increased from 43% in 2011 to 62% in 2016 (Uganda Bureau of Statistics (UBOS) and ICF, 2018; Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

Despite promising efforts to alleviate under-five mortality in the country, accelerated improvement is restricted by huge sub-national disparities. Inequities exist in access to and utilisation of many preventative and curative health services across geographical regions in Uganda. For instance, there is regional variation in the use of an ITN the night before the survey among children under age five, ranging from 47% in Karamoja region to 77% in West Nile region (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

A fundamental component of the SDGs is to effectively mitigate inequalities and ensure universal coverage of essential interventions (United Nations, 2015b). Goal 10 is specifically intended to reduce inequality within and among countries. In line with the SDGs, Uganda needs to better understand existing inequalities among children less than five years in order to prioritise effective and equitable strategies for improving their health. This is also a commitment Uganda has made in her reproductive maternal, neonatal and child health accelerated plan (Ministry of Health, 2013a). Efforts focused on reducing inequities are valuable for planning and implementing sub-national-specific interventions. This will scale up intervention coverage throughout the country and as a result improve under-five mortality in Uganda.

1.2.3 Socio-economic and demographic factors

Socio-economic factors are a key cause of child mortality inequalities between and within countries (Victora et al., 2003). This is because children born to richer families are less exposed to disease risk factors such as poor water, sanitation and hygiene (WASH) practices and undernutrition, which deteriorates body defenses of poor children (Victora et al., 2003). Additionally, poor children have limited access to curative (e.g. artemisinin-combination therapy and antibiotics) and preventive measures (e.g. insecticide treated nets and vaccinations) (Victora et al., 2003). Also, access to service is constrained since poor people tend to live in more remote and underserved areas, which normally offer a lower quality service than facilities in wealthier areas. Rural facilities are more likely run short of medical supplies and are affected by the scarcity of healthcare workers (Victora et al., 2003). In addition, higher levels of maternal education correlate with lower child mortality as it results in greater health awareness, better utilization of health facilities, higher income and the ability to purchase goods and services that improve infants' health (Jain, 1985). Moreover, socio-economic factors influence protective demographic factors against child mortality. For example, higher maternal ages, reduced number of live births and prolonged birth intervals (Cleland and Van Ginneken, 1988).

1.2.4 Climatic/environmental factors

Climatic/environmental factors, such as rainfall, temperature and altitude, are essential determinants of child mortality (Babalola et al., 2018; Chapur et al., 2017; Henry and Santos, 2013; Scovronick et al., 2018) as climatic changes can be driving forces of childhood diseases such as malaria (Thomson et al., 2005), diarrhoea (Xu et al., 2012) and respiratory infections (Zhiwei Xu et al., 2014).

1.3 Burden of maternal mortality

Maternal mortality, measured by the maternal mortality ratio (MMR) indicator (World Health Organisation, 2013a), is a measure of the quality of the health system. The indicator reflects inequality between the rich and the poor, urban and rural areas, and between and within countries (World Health Organization, 2015a). Also MMR is a valuable indicator for tracking progress in development and for spurring action to improve maternal health (World Health Organization, 2015a). Moreover, maternal mortality results in vulnerable families and increases the chances of infant mortality before reaching their second birthday. Further, it is estimated that for each maternal death, twenty and more women survive with chronic and incapacitating ill health such as fistulae (World Health Organization, 2015a).

Globally, MMR has declined from 385 in 1990 to 216 deaths per 100 000 live births in 2015 (World Health Organization, 2015a). In the same way, estimated MMR declined considerably across all MDG regions over the course of that time (World Health Organisation, 2015a). Although SSA experienced the highest MMR, the indicator decreased from 987 in 1990 to 546 deaths per 100 000 live births. Also, most countries in MDG regions experienced a decline in MMR. In Uganda, MMR dropped from 687 to 343 deaths per 100 000 live births during the same period (World Health Organization, 2015a).

Regardless of the pronounced development, none of the MDG regions achieved the MDG 5A of reducing MMR by atleast 75% between 1990 and 2015. Only nine countries (9%) attained MDG 5A (World Health Organization, 2015a). To amplify the efforts and progress catalyzed by MDG 5, SDG 3.1 establishes a new agenda for maternal health towards ending preventable maternal mortality (World Health Organization, 2015b). This SDG aims at reducing the global MMR to or less than 70 in 2030 from 385 deaths per 100 000 live births in 1990 (World Health Organization, 2015b). Further, a country-specific target of less than 140 deaths per 100 0000 live births was set (World Health Organization, 2015b). To date, most countries experience MMR far higher than the SDG target (United Nations, 2015b) and substantial differences between and within countries exist (Figure 1.3).

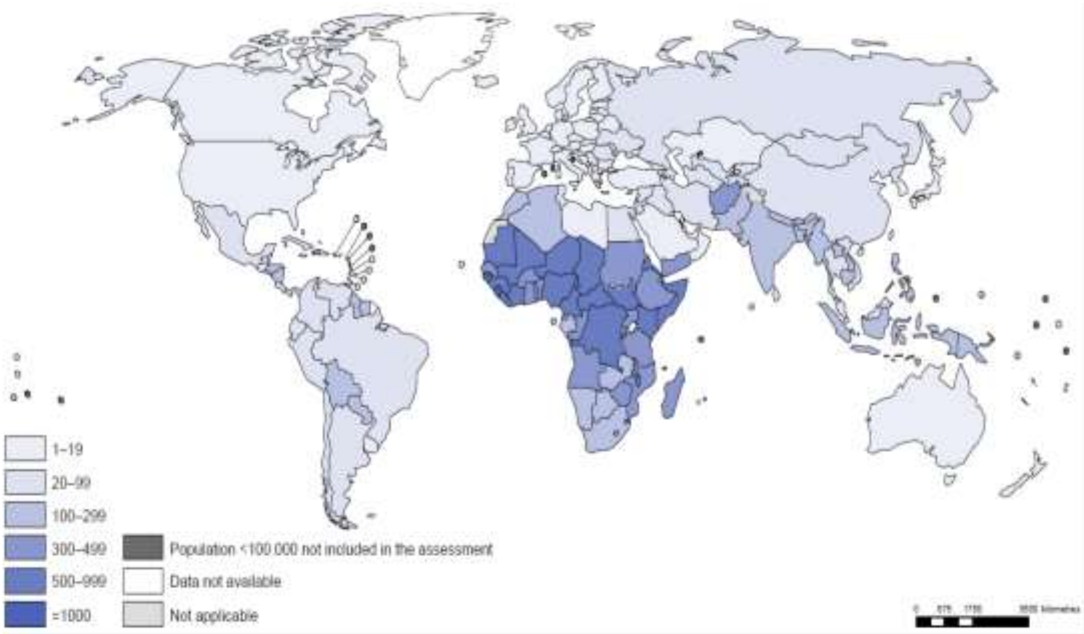

Figure 1. 3: MMR per 100 000 live births, 2015; World Health Organization Map Production: Health Statistics and Information Systems (HSI) World Health Organization.

In Uganda MMR has declined from 687 in 1990 to 336 deaths per 100 000 live births in 2016. However, large regional disparities prevail with the highest in Karamoja (588) and lowest in Teso (208) regions (Uganda Bureau of Statistics, 2016). Strategies to end preventable maternal mortality need to be implemented, in particular, approaches to address the sources of inequities (World Health Organization, 2015a). This may reduce variations in MMR within Uganda, and thus, quicken the achievement of SDG target 3.1 in the country.

1.4 Determinants of maternal mortality

Maternal mortality is affected by health interventions (Alvarez et al., 2009; Buor and Bream, 2004), health facility readiness (Mbonye et al., 2007b, 2007a) and socio-demographic factors (Mbonye, 2001).

1.4.1 Maternal health interventions

An important issue for planning of interventions is an understanding of the causes and timing of maternal deaths (Romano et al., 2010). Most maternal deaths are due to causes directly related to pregnancy and childbirth, unsafe abortion and obstetric complications such as haemorrhage, infection, hypertensive disorders of pregnancy, and obstructed labour (GBD 2013 Mortality and Causes of Death Collaborators, 2015; World Health Organisation, 2015b). Other maternal deaths result from indirect causes such as malaria, malnutrition, diabetes, hepatitis and anaemia, which are aggravated by pregnancy (World Health Organization, 2015a). As regards to the timing, majority of maternal deaths occur in the postpartum period and during child birth (Li et al., 1996). Thus, it is important to identify and implement highly effective prenatal and postnatal care interventions if sustained gains in maternal health are to be achieved.

1.4.2 Health facility assessment readiness indicators

The impact of interventions in reducing maternal mortality strongly depends on their successful integration with a functional health system (Kerber et al., 2007). Several conditions that are prevalent in Africa, such as direct and indirect causes of maternal death (Kassebaum et al., 2014), can be addressed through interventions. However, a dysfunctional health system makes access to interventions almost impossible which minimizes contact between women and the health system. In such situations, health systems breakdown and cause a dramatic rise in maternal deaths due to complications that would be easily treatable under stable conditions.

Health system challenges such as insufficient number of skilled providers, lack of standards of care and protocols, shortage of supplies and logistics (includes regular availability syphilis and Human Immune Deficiency Virus (HIV) testing kits and, essential drugs), lack of basic functional equipment (e.g. theatre), lack of functional referral systems (e.g. ambulance) and state of infrastructure of the health facility (e.g. availability of water and electricity) contribute to high maternal mortality (Kaye et al., 2003; Mbonye, 2001; Mbonye et al., 2007a, 2007b). Consequently, identifying health system factors which improve maternal outcomes can guide in increasing the efficiency of the health system. This will result in a reduced maternal mortality burden.

1.4.3 Socio-demographic factors

Socio-demographic factors such as number of prior births, area of residence, education and income level, race and ethnicity and age at birth play a major role in determining maternal health outcomes.

Women living in rural areas experience higher maternal mortality than women living in urban (Africa Progress Panel, 2010) because those living in urban areas, living in wealthier households or having higher education easily access healthcare services than their rural, poorer or less-educated counterparts (Khlat and Ronsmans, 2000). Racial and ethnic disparities increase maternal mortality in marginalized groups (Global Burden of Disease Study 2013 Collaborators, 2015). Moreover, adolescent girls under 15 years old experience the highest maternal mortality risk and complications in pregnancy. This makes childbirth a leading cause of death among adolescent girls in developing countries. Also, adolescents have higher risks for postpartum hemorrhage, puerperal endometritis, operative vaginal delivery, episiotomy, low birth weight and preterm delivery all of which lead to maternal death (Poovan et al., 1990). Also, gender-based violence, exposure to workplace threats and depression are determinants of maternal mortality. Therefore, addressing socio-demographic differentials can improve maternal health outcomes.

1.5 Measures of mortality

1.5.1 Under-five mortality indicators

Under-five mortality is death that occurs between birth and the fifth birth day and can be defined as a rate, a ratio or a probability (Unicef, 2017).

Under-five mortality rate (U5MRate) is the probability of dying between birth and exactly five years of age expressed per 1 000 live births. A live birth occurs when a fetus, whatever its gestational age, exits the maternal body and subsequently shows any sign of life, such as voluntary movement, heartbeat, or pulsation of the umbilical cord, for however brief a time and regardless of whether the umbilical cord or placenta are intact (World Health Organisation, 1993).

A rate is a measure of the frequency with which an event occurs in a defined population in a defined time. In the case of U5MRate the events are the number of deaths between age 0 and 5 years and the duration of exposure to the risk of dying which corresponds to the number of under-five person years lived, such that:

$$U5MRate = (Number\ of\ deaths\ between\ 0\ and\ 5/Total\ U5\ person\ years) * 1\ 000\ U5\ person\ years$$

A ratio has the same numerator as a rate; however, the denominator does not take into account the length of exposure. The U5MRatio is estimated as:

$$U5MRatio = (Number\ of\ deaths\ between\ 0\ and\ 5/Number\ of\ live\ births) * 1\ 000\ live\ births$$

In contrast to the concept of the rate and ratio, the concept of probability cannot apply to a population but only to a cohort. This is because the number of events in the numerator (the number of deaths between age 0 and 5), has to pertain to the number of previous trials (in this case the number of children at birth in the denominator) and this information is only available for a cohort (Preston et al., 2001).

$$Probability\ of\ dying\ between\ birth\ and\ 5$$
$$= (Number\ of\ deaths\ between\ 0\ and\ 5/Number\ of\ children\ at\ birth)$$
$$* 1\ 000\ children\ at\ birth$$

In literature under-five mortality is mostly measured as a rate (Uganda Bureau of Statistics (UBOS) and ICF, 2018; Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007; World Health Organisation, 2011). Thus, for comparability purposes, the U5MRate will be used as the measure of child mortality in this thesis.

1.5.2 Maternal mortality indicators

The four indicators developed for measurement of maternal mortality (World Health Organisation, 2013a) are described. The most commonly used indicator is the maternal mortality ratio (MMRatio), which refers to the number of maternal deaths per live birth, multiplied by a conventional factor of 100 000. The MMRatio is obtained by dividing the number of maternal deaths in a population during some time interval by the number of live births occurring in the same period.

$$MMRatio = (Number\ of\ maternal\ deaths/Number\ of\ live\ births) * 100\ 000$$

Thus, the MMRatio depicts the risk of maternal death relative to the frequency of childbearing. The MMRatio was designed to express obstetric risk. In fact, it may overestimate obstetric risk by excluding from the denominator pregnancies that do not terminate in a live birth, but that may be responsible for a maternal death. Though in theory it would be preferable to refine the denominator to include all pregnancies, in practice it is rare that suitable data on pregnancies not resulting in a live birth are available.

A related measure of maternal mortality is the maternal mortality rate (MMRate). The MMRate is an indicator of the risk of maternal death among women of reproductive age and it is usually multiplied by a factor of 1000. The MMRate is obtained by dividing the average annual number of maternal deaths in a population by the average number of women of reproductive age (typically those aged 15 to 49 years) who are alive during the observation period.

$$MMRate = (Number\ of\ maternal\ deaths/Number\ of\ women\ aged\ 15-49\ years) * 1\,000$$

Thus, the MMRate reflects not only the risk of maternal death per pregnancy or per birth, but also the level of fertility in a population. While the MMRate provides an indication of the risk of maternal death in the adult female population, it conceals the effect of differing levels of fertility in cross-country comparisons. MMRate and the MMRatio are related as follows: $MMRatio = MMRate/General\ Fertility\ Rate$, where the general fertility rate is the ratio of live births to women aged 15–49 years.

A third indicator that expresses the salience of maternal deaths relative to other causes of death among women of reproductive age is the proportion of maternal deaths among all deaths of females of reproductive age.

$$PMDF = Number\ of\ maternal\ deaths/Number\ of\ deaths\ among\ women\ aged\ 15-49\ years$$

A fourth indicator of maternal mortality, primarily used for advocacy purposes, is the Life time risk of maternal death (LTR) or probability of maternal death in a population. Whereas the MMRatio and the MMRate are measures of the frequency of maternal death in relation to the number of live births or to the female population of reproductive age, the LTR reflects the chances of a woman dying from maternal causes over the course of her 35-year reproductive lifespan. Because it is expressed in terms of the female life course, the LTR is often preferred to the MMRatio or MMRate as a summary measure of the impact of maternal mortality. Despite its interpretive appeal, the LTR can be defined and calculated in more than one way as follows:

$LTR = 35 * MMRate$ or $LTR = ((T_{15} - T_{50})/l_0) * MMRate$ or $\left((T_{15} - T_{50})/l_{15}\right)$, where

$T_{15} - T_{50}$ is a life-table quantity representing the number of woman-years lived between ages 15 and 50 years, the factor of 35 in first formula corresponds to the reproductive interval from age 15 to 50 years and l_x is the number of survivors to age x in a female life-table (Wilmoth, 2009).

The first concept ignores mortality risks by other competing causes and consequently exaggerates the LTR of maternal mortality. The other two concepts both take other competing risks into account and differ only in terms of their starting point: either birth or age 15 years, with the latter representing an approximate minimum age of reproduction (Wilmoth, 2009). However, the preferred option also does not take into account the effect of different fertility levels across age groups since its computation is based on MMRate. Thus, in this thesis, MMRatio has been considered as the measure of maternal mortality to evaluate health interventions.

1.6 Sources of data

In Uganda, monitoring of mortality and its determinants is implemented through, censuses, nationally representative household surveys, that is, Demographic and Health Surveys (DHS) and the Malaria Indicator Surveys (MIS), Demographic Surveillance Systems (DSS) and civil registration systems.

Uganda has undertaken five population censuses since independence (1962) and the most recent is the National Population and Housing Census (NPHC) of 2014 (Uganda Bureau of Statistics, 2016). The census provides several statistics among them a total population count and reliable estimates of maternal mortality, especially at sub-national scales (Uganda Bureau of Statistics, 2016). The census exercise is undertaken by the UBOS which works closely with different Government Ministries, Departments and Agencies as well as Local Governments.

To date, Uganda has conducted six DHS; 1988-89, 1995, 2000-01, 2006, 2011 and 2016 (Uganda Bureau of Statistics (UBOS) and ICF, 2018) and two MIS; MIS 2009 and MIS 2014-15 (Uganda Bureau of Statistics (UBOS) and ICF International, 2015; Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010). These surveys enable the estimation of up-to-date demographic, socio-economic, coverage of interventions and health-related indicators such as mortality measures and disease prevalences. Also, data obtained from these surveys aids the identification of most disadvantaged sub-groups, high-burden areas and track intervention scale-up within the country. DHS are implemented by national organizations: typically the Uganda Bureau of Statistics, Ministry of Planning or Ministry of Health, often in collaboration. The MIS is implemented by the UBOS and the Uganda Malaria Surveillance Project on behalf of the National Malaria Control Program.

In DSS, individuals living in a well-defined area are followed up prospectively over time. After a first population census, households are regularly visited by trained interviewers. At each visit, all vital events (e.g. live births, deaths, marriages and divorces), health data (e.g. verbal autopsies, morbidity episodes) and other data such as socio-economic activities are registered. This system offers high quality longitudinal data which is more reliable compared to cross-sectional censuses and surveys. Unfortunately, most developing countries lack surveillance sites and in countries where such sites exist, only a small proportion of the total population is covered (INDEPTH Network, 2004).

Another source of data, especially cause-specific mortality, is civil registration. According to the UN, a functional civil registration system should be present in all countries, and should constantly record all vital events and provide their legal documentation. Although civil registration is the best source of vital statistics, the system is dysfunctional or absent in most developing countries (United Nations, 2014). Despite their high quality data, the DSS and civil registration systems were not considered in this PhD thesis due to their limitations.

Data to evaluate health facility readiness were obtained from the 2013 Uganda Service Delivery Indicator (SDI) Survey (Wane, 2017). The SDI provides a set of key indicators that benchmark service delivery performance in the health and education sectors in Sub-Saharan Africa.

Environmental/climatic factors were extracted from remote sensing sources, namely; Moderate Resolution Imaging Spectroradiometer (MODIS)/Terra, United States Geological Survey-Earth Resources Observation Systems, Shuttle Radar Topographic Mission, MODIS, International Global Biosphere Programme and, the Global Rural and Urban Mapping project (http://modis.gsfc.nasa.gov/).

1.7 Rationale of the study

The study of under-five and maternal mortality has become feasible in most developing countries as the two indicators do not only reflect the health of the general population but also the economic development of countries (Reidpath and Allotey, 2003; World Health Organization, 2015a). The implementation of the NPHC, DHS, MIS and the USDI survey has resulted in rich sources of data in Uganda which has made it practical to evaluate determinants of under-five and maternal mortality.

Despite this improvement, data utilisation remains low and information extracted by researchers is restricted to national estimates that neither take into account sub-national discrepancies nor assess the effects of interventions or childhood diseases on mortality or morbidity differentials in space. Analyses of child mortality data from several studies in Africa have confirmed space variations at a local scale, for example, Health Demographic and Surveillence Survey (HDSS) sites such as Nouna HDSS in Burkina Faso (Sankoh et al., 2001), Manhica HDSS in Mozambique (Escaramís et al., 2011) and Agicourt DSS in South Africa (Musenge et al., 2013). Also, analysis of the Uganda MIS 2014–15 data showed geographical variations in child morbidities, in particular, the malaria burden at a local scale (Ssempiira et al., 2017).

Furthermore, in Uganda, analyses of DHS data at the country level indicates that the country is moving towards the SDG target of child mortality, however, there are huge variations within the country (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Moreover, few studies in Uganda assessed within country geographical variation of under-five mortality and produced country-wide mortality maps analyzing census data (Kazembe et al., 2012). However, these estimates are outdated and there is a strong need to obtain child mortality surfaces across the country, not only for assessing variations in mortality at local scales but also for guiding targeted intervention.

In Uganda, the determinants of child mortality have been widely studied including socio-demographic factors (Kabagenyi and Rutaremwa, 2013; Nasejje et al., 2015; Nuwaha et al., 2011), health interventions (Bbaale, 2015; Brenner et al., 2011; Nankabirwa et al., 2015) and childhood diseases (Nabongo et al., 2014; Vella et al., 1992b, 1992a). Nevertheless, majority of the studies have focused on aggregated effects of childhood diseases and health interventions on mortality at the national scale. National estimates mask geographical heterogeneities that may exist at a local scale. Therefore, most important interventions at a local scale and areas affected by the disease burden cannot be identified. Furthermore, previous studies ignored the geographical variations that are present in the coverage of health interventions and in the distribution of childhood diseases which may influence mortality patterns (Burke et al., 2016).

In this PhD thesis, we quantified effects of childhood diseases and health interventions on all-cause under-five mortality at national and sub-national scales, and identified diseases influencing mortality in various regions and interventions associated with largest reductions in under-five mortality at the sub-national scale. Also, the study identified areas of high under-five mortality concentration within the country. In addition, the study quantified the contribution of childhood diseases on the geographical distribution of the fever risk at the national and sub-national scales. Results can inform control programs in the development of evidence-based interventions especially at a local scale.

In Uganda, a few studies have assessed the effect of the presence of soap and water at handwashing places on the risk of diarrhoea (Zhang et al., 2013). However, the former study was school-based and included children aged 7 – 13 years excluding the under-five. Other studies used DHS data and evaluated the determinants of diarrhoea (Bbaale, 2011; Ssenyonga et al., 2009) without examining the effect of handwashing with soap and water. Another study reported higher WASH (Water, Sanitation and Hygiene) quintiles to significantly reduce the prevalence of diarrhoea (Hirai et al., 2016). However, this study did not quantify the effect of handwashing with soap and water on the risk of diarrhoea. Limited studies have assessed the determinants of ARI in Uganda (Bbaale, 2011) but little is known about the effect of the presence of soap and water at handwashing places on the risk of ARI among the under-five. In addition, previous studies on diarrhoea and ARI did not consider the spatial structure of environmental/climatic factors that drive the spread of diarrhoea and ARI risk (Siraj et al., 2014).

In this PhD, we estimated the effect of the presence of soap and water at handwashing places in households on the risk of diarrhoea and ARI among the under-five, taking into account spatial correlation in disease outcomes and potential confounding effects of socio-demographic characteristics, interventions (i.e. vaccinations, WASH and breastfeeding), health care seeking behaviour and environmental/climatic factors. Results of this study will be relevant for policy formulation and advocacy to programmes that aim to reduce the burden of diarrhoea and ARI among the under-five in Uganda. In addition, this study adds to the existing evidence that the presence of soap and water at handwashing places can reduce the risk of diarrhoea and ARI among the under-five.

Also, a few studies in Uganda have assessed the relation between health interventions and maternal mortality (Mbonye, 2001; Mbonye et al., 2007a, 2007b). However, there is paucity of literature on studies examining this relation using nationally representative data. Most studies that assessed this relation are health facility based (Mbonye, 2001; Mbonye et al., 2007a, 2007b), which only capture information on mothers with access to health facilities. Such studies are likely to under-estimate MMR as mothers who experience a higher mortality burden (e.g. the poor, those in remote areas) are less likely to deliver babies in health facilities (Uganda Bureau of Statistics (UBOS) and ICF, 2018; World Health Organization, 2015a). National studies evaluated the relation focussing on only one category of interventions (number of antenatal visits) (Atuhaire and Kaberuka, 2016). Therefore, more reliable and informed estimates of the effects of health interventions on maternal mortality need to be obtained. In this PhD thesis, we have used nationally representative data and attained more consistent estimates of the relationship between maternal mortality and health interventions. Our analysis adjusts for confounding effects of health facility readiness.

1.8 Spatial statistical methods

In Uganda, frequentist approaches assuming independence of observations have been broadly employed to assess relationships between under-five mortality, maternal mortality and their determinants (Atuhaire and Kaberuka, 2016; Ayiko et al., 2009; Bbaale, 2015; Kabagenyi and Rutaremwa, 2013; Kaberuka et al., 2017; Kampikaho and Irwig, 1990; Mbonye, 2001; Mbonye et al., 2007b, 2007a; Nabongo et al., 2014; Nankabirwa et al., 2015; Nasejje et al., 2015; Vella et al., 1992b, 1992a). The DHS and census mortality data analysed in this PhD thesis were collected at neighbouring locations, and therefore correlated in space. This is because observations at close geographical proximity are likely to share common exposures and thus affected in a similar way. In case of mortality, spatial correlation arises from its determinants such as infectious diseases. An example is malaria which is transmitted by mosquitoes as fly long distances in surrounding areas (Thomson et al., 2005).

Frequentist approaches ignore spatial correlation in the data which underestimates the standard error of the parameters and thus over-estimates the significance of the covariates (Cressie et al., 2009; Riedel et al., 2010). Spatial statistical methods are the novel approach developed to incorporate spatial correlation in the data. Spatial correlation is introduced into the models depending on the ways geographical proximity is defined. Proximity is determined by the geographical information which can be available at areal level or at point-locational level. Areal unit data are aggregated over continuous units (countries, regions, districts, census zones) which partition the whole study region. Proximity in space is defined by the neighbouring structure. Point-referenced or geostatistical data are collected at fixed locations (DHS clusters, households, villages) over a continuous study region. Proximity in geostatistical data is determined by the distance between sample locations.

Bayesian methods have been applied for modelling areal unit and geostatistical data because they allow flexible modelling and inference, and provide computational advantages via the implementation of Markov Chain Monte Carlo (MCMC) (Gelfand and Smith, 1990). The correlation structure is usually introduced in a hierarchical manner via the prior distribution of area or location-specific random effects. The choice of prior distributions or spatial models depends on the type of spatial data.

In geostatistical data, spatial correlation is introduced into the geostatistical models via the correlation matrix of location-specific random effects which are assumed to be latent data from an underlying Gaussian spatial process (Cressie, 1993; Diggle and Tawn, 1998). Correlations between pairs of locations are modeled as a function of the distance between them. The parameter function can take an exponential form suggesting a decrease in spatial dependence with increasing distance (Gemperli et al., 2006; Schur et al., 2011). In areal data, simultaneously autoregressive (SAR) models (Whittle, 1954), conditional autoregressive (CAR) models (Clayton and Kaldor, 1987) and modifications (Besag et al., 1991) have been suggested as prior specifications in the Bayesian approach.

Introduction of random effects in the CAR or geostatistical model results in highly parameterized models making inference by maximum likelihood estimation unattainable. The flexibility of the Bayesian inferential approach via MCMC simulations provides an appropriate method to deal with over-parametrized models (Gelfand and Smith, 1990). Analytical solutions of the posterior distribution of the CAR or geostatistical model parameters are intractable. The simulation based method such as Gibbs sampler and Metropolis-Hasting algorithm (MCMC) estimates model parameters through iterative sampling of the marginal posterior distribution of the parameters. The iterative process in MCMC start at an arbitrary point after which it generates a Markov until it reaches a convergence point whose distribution is that of the parameters of interest (Gelfand and Smith, 1990).

The flexibility of spatial models enables accurate estimation of national and sub-national effects of interventions and diseases on mortality as well as prediction at unsampled locations. The models have previously been applied to survey data to evaluate national and sub-national effects of interventions on health outcomes in Uganda (Ssempiira et al., 2017), Burkina Faso (Diboulo et al., 2016), Tanzania (Rumisha et al., 2014), Malawi (Kazembe et al., 2007) and in Angola, Liberia, Mozambique, Senegal, Rwanda, and Tanzania (Giardina et al., 2014). They have also been employed to predict the risk of health indicators at unsampled locations in Mali (Gemperli et al., 2004), Uganda (Ssempiira et al., 2017), Nigeria (Adigun et al., 2015), Malawi (Kazembe et al., 2006), Cote d'Ivoire (Raso et al., 2012), Tanzania (Gosoniu et al., 2012) and Zambia (Riedel et al., 2010).

1.9 Objectives of the Thesis

The goal of this PhD thesis is to assess the ffects of interventions on child and maternal health-related outcomes at national and sub-national levels in Uganda. The goal will be addressed through the following specific objectives.

1.9.1 Specific Objectives

1. To quantify the effects of childhood diseases on all-cause under-five mortality over space
2. To estimate the effects of health interventions on all-cause under-five mortality over space
3. To assess the contribution of childhood diseases on the geographical distribution of fever risk among children less than five years
4. To quantify the effect of the presence of soap and water at handwashing places on the risk of diarrhoea and respiratory infections among children under-five years
5. To assess the effects of maternal health interventions on all-cause maternal mortality

1.10 Structure of the Thesis

The thesis is organized as follows. Chapters 2 and 3 present the application of Bayesian geostatistical proportional hazards model to estimate the effects of childhood diseases and interventions on all-cause under-five mortality in Uganda. In chapter 4, the contribution of childhood diseases on the geographical distribution of fever risk among children less than five years is quantified using a Bayesian geostatistical logistic model. Chapter 5 quantifies the effect of the presence of soap and water at handwashing places on the risk of diarrhoea and ARI among children under-five years applying Bayesian geostatistical logistic models. Chapter 6 employs Bayesian negative binomial conditional autoregressive (CAR) models to evaluate the effects of maternal health interventions on all-cause maternal mortality. A general discussion, recommendation and conclusions are presented in chapter 7.

Chapter 2: Geographical distribution of the effects of childhood diseases on all-cause under-five mortality in Uganda

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Abstract

Introduction: Information on the causes of death among under-five children is key in designing and implementation of appropriate interventions. In Uganda, civil death registration is incomplete which limits the estimation of disease-related mortality burden especially at a local scale. In the absence of routine cause-specific data, we used household surveys to quantify the effects of main childhood diseases such as malaria, severe or moderate anaemia, severe or moderate malnutrition, diarrhoea and acute respiratory infections (ARIs) on all-cause under-five mortality (U5M) at national and sub-national levels. We related all-cause U5M with risks of childhood diseases after adjusting for geographical disparities in coverages of health interventions, socio-economic, environmental factors and disease co-endemicities.

Methods: Data on U5M, disease prevalence, socio-economic and intervention coverage indicators were obtained from the 2011 Demographic and Health Survey, while data on malaria prevalence were extracted from the 2009 Malaria Indicator Survey. Bayesian geostatistical Weibull proportional hazards models with spatially varying disease effects at sub-national scales were fitted to quantify the associations between childhood diseases and the U5M. Spatial correlation between clusters was incorporated via locational random effects while region-specific random effects with conditional autoregressive prior distributions modeled the geographical variation in the effects of childhood diseases. The models addressed geographical misalignment in the locations of the two surveys.

Results: The overall U5M rate was 90 deaths per 1 000 live births. Large regional variations in U5M rates were observed, lowest in Kampala at 56 and highest in the North-East at 152 per 1 000 live births. National malaria parasiteamia prevalence was 42%, with Kampala experiencing the lowest of 5% and the Mid-North the highest of 62%. About 27% of Ugandan children aged 6-59 months were severely or moderately anaemic; lowest in South-

West (8%) and highest in East-Central (46%). Overall, 17% of children were either severely or moderately malnourished. The percentage of moderately/severely malnourished children varied by region with Kampala having the lowest (8%) and North-East the highest (45%). Nearly a quarter of under-five children were reported to have diarrhoea at national level, but was high in East-Central (32%) and Mid-Eastern (33%) and lowest in South-West (14%). Overall, ARIs in the two weeks before the survey was 15%; highest in Mid-North (22%) and lowest in Central 1 (9%). At national level, the U5M was associated with prevalence of malaria (hazard ratio (HR) = 1.74; 95% BCI: 1.42, 2.16), severe or moderate anaemia (HR =1.37; 95% BCI: 1.20, 1.75), severe or moderate malnutrition (HR = 1.49; 95% BCI: 1.25, 1.66) and diarrhoea (HR = 1.61; 95% BCI: 1.31, 2.05). The relationship between malaria and U5M was important in the regions of Central 2, East-Central, Mid-North, North-East and West-Nile. Diarrhoea was associated with under-five deaths in Central 2, East-central, Mid-Eastern and Mid-Western. Moderate/severe malnutrition was associated with U5M in East-Central, Mid-Eastern and North-East. Moderate/severe anaemia was associated with deaths in Central 1, Kampala, Mid-North, Mid-Western, North-East, South-West and West-Nile.

Conclusion: The effects of childhood diseases on U5M vary by region and different diseases are related to mortality in various regions. Thus, regional disease-specific interventions may be an important strategy to accelerate progress towards the reduction of the U5M as per the SDG target by 2030.

Key words: Under-five mortality; malaria, anaemia; malnutrition; diarrhoea; respiratory infections

2.1 Introduction

The under-five mortality (U5M) is one of the numerous health challenges in Uganda, accounting for approximately 4% of the U5M burden in Sub-Saharan Africa (Unicef, 2015). In addition, the indicator is one of the most important among those monitoring many Sustainable Development Goals (SDGs) (World Health Organization, 2015b). The burden of U5M in Uganda has reduced over time. For instance, between 2006 and 2011, the under-five mortality rate (U5MR) declined from 137 to 90 deaths per 1 000 live births (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007); indicating that Uganda has made considerable progress in improving the health of the under-fives. Similarly, the leading contributors to under-five morbidity and mortality such as malaria, anaemia, malnutrition, diarrhoea and acute respiratory infections (Ministry of Health, 2013b) have dropped. For example, the prevalences of anaemia decreased from 73% to 49% (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007) and; malaria from 42% in 2009 to 19% in 2014-15 (Uganda Bureau of Statistics (UBOS) and ICF International, 2015; Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010).

Despite the huge national improvements, the burden of mortality and childhood diseases is still high and disproportionately distributed among regions. The region of Kampala experienced the lowest malaria prevalence (5%) whereas the Mid-North region had the highest (62%). The lowest malnutrition prevalence (20%) was reported in Kampala and the highest (51%) in the South-West (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Also, wide regional variations in the U5MR occurred during the same time; with the North-East experiencing the highest (152 deaths per 1 000 live births) and the lowest (56 deaths per 1 000 live births) occurring in Kampala region (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Whether regional disparities in U5MR are a result of uneven socio-economic development across regions (Uganda Bureau of Statistics, 2017; Uganda Bureau of Statistics (UBOS) and ICF, 2018), unequal access to health interventions and services (Uganda Bureau of Statistics (UBOS) and ICF, 2018), differences environmental/climatic factors or varying childhood diseases across regions needs to be examined.

In Uganda, few studies have assessed the relation between childhood diseases and U5M. Furthermore, scanty literature exists on this relation at a local scale. Most studies that evaluated the above relation have been specific to one community at a time. Recent studies are descriptive and lack statistical evidence. In a community-based cohort of infants conducted in eastern Uganda, anaemia, malaria, diarrhoea and pneumonia were reported as the major single causes of death without estimating their relation to mortality but relying purely on their prevalence (Nabongo et al., 2014). Studies providing statistical evidence are outdated. Studies in the South-West and North-West Uganda showed that lower anthropometric indicators were associated with higher U5M (Vella et al., 1992b, 1992a). This study assessed a single cause of childhood mortality and did not use nationally representative data.

Previous studies in Mali (Gemperli et al., 2004) and Malawi (Kazembe et al., 2007) looked at the relation between child mortality with exposure to malaria risk at national level but they ignored the geographical variation in the burden of childhood diseases that may influence U5M patterns (Burke et al., 2016), therefore areas affected by the disease burden could not be identified. Estimates of the effects of childhood diseases at a sub-national scale on mortality can inform disease control programmes to implement disease-specific interventions at a local scale which may reduce regional variation in all-cause U5M.

Furthermore, past studies did not consider exposure to multiple diseases adjusting for several confounders in a single analysis.

The Demographic and Health Survey (DHS) program funded by the United States Agency for International Development (USAID), conducts national, household–based surveys in low and middle income countries, collecting among other information, data on child and maternal health, disease interventions, health seeking behaviour, socio-demographic characteristics and mother's birth histories. The latter can be used to estimate child mortality.

Data on disease-specific mortality are deficient in Uganda because birth and death registries are lacking or have incomplete information. In the absence of disease-specific mortality data, we have used DHS to assess the association between all-cause U5M and childhood diseases (i.e. malaria, severe or moderate anaemia, severe or moderate malnutrition, diarrhoea and acute respiratory infections) at national and sub-national scales, and identified diseases associated with mortality in the various regions. We employed Bayesian geostatistical Weibull proportional hazards models with spatially varying covariates to quantify the effects of childhood diseases at national and sub-national scales. The models were adjusted for geographical disparities in the coverage of child and maternal interventions, socio-economic and environmental factors and disease co-endemicities. To the best of our knowledge, analyses estimating the geographical heterogeneities of different childhood diseases on U5M taking into account disease co-endemicities have not been carried out. The methodology presented in this paper can be applied to other countries with dysfunctional civil registration systems, and be used as a tool for providing information for decision making in programming of interventions at sub-national scales to address U5MR.

2.2 Materials and methods

2.2.1 Study setting

The Republic of Uganda is located in East Africa and lies across the equator. It is a landlocked country that borders Kenya to the East, Tanzania to the South, Rwanda to the South-West, the Democratic Republic of Congo to the West, and South Sudan to the North. The country has an area of 241 039 km^2 and a population of about 40 million of which 20% are under-five years of age (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

2.2.2 Data and data sources

2.2.2.1 Mortality

Data on all-cause U5M were obtained from women birth histories available in the Uganda DHS which was conducted from May to December in 2011 (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). The survey includes a representative sample of 10 086 households selected using a stratified two-stage cluster design. In the first stage, 404 enumeration areas/clusters/locations were chosen. The second stage involved selecting households from a complete listing of households in each cluster. Mortality data were collected on all 7 878 children born in the five years preceding the date of the survey. About 8 674 women aged between 15-49 years who were either routine residents or visitors present in the selected household the night before the survey were interviewed.

2.2.2.2 Childhood diseases

Data on childhood diseases (severe or moderate malnutrition, severe or moderate anaemia, acute respiratory infections (ARIs), and diarrhoea) and socio-demographic characteristics were extracted from the DHS 2011. The children's nutritional status is reported using three anthropometric indices (i.e. height-for-age, weight-for-height and weight-for-age) based on growth standards defined by World Health Organization (WHO) in 2006 (WHO Multicentre

Growth Reference Study Group, 2006). Severely or moderately malnourished children were defined as children with weight-for-age two standard deviations below the median of the WHO reference population. Haemoglobin levels were reported for children aged 6-59 months. We considered anaemic children as those with haemoglobin levels less than 10 grams per deciliter (g/dL). ARIs and diarrhoea data were available from DHS questionnaires, asking mothers whether any of their children under the age of five years had been ill with a cough accompanied by short, rapid breathing or had diarrhoea at any time during the two-week period preceding the survey.

Disease data regarding the dead children were not gathered, making it difficult to assess the disease-mortality relation at an individual level. Therefore, we treated disease prevalence at cluster level as an exposure (McGovern and Canning, 2015) linked to the individual level mortality. Disease prevalence was obtained by aggregating the binary disease status of screened children at the cluster level.

Malaria data were not available at the 2011 DHS. This information was collected in the Malaria Indicator survey (MIS) carried out in Uganda by the DHS program in 2009. To predict malaria parasite prevalence at the 2011 DHS clusters, we fitted Bayesian geostatistical models on microscopically confirmed survey data from the 2009 MIS which was carried out during November to December at 170 clusters and included malaria parasite positivity on 3 972 children.

2.2.2.3 Socio-demographic factors

Socio-demographic data primarily included maternal (education, literacy, residence, age at birth, early pregnancy termination, number of children born, working status) and child (sex, birth order, birth interval, mode of delivery) characteristics at the individual level. The household asset score was used as a socio-economic proxy.

2.2.2.4 Environmental and climatic data

Environmental and climatic predictors were extracted from remote sensing sources. Land Surface Temperature (LST), rainfall and Normalized Difference Vegetation Index (NDVI) were averaged during January to December 2009 and January to December 2011. The former climatic summaries were used in the fitting of the malaria parasite data of the 2009 MIS. The latter were considered as predictors in the mortality model based on the 2011 DHS. Land cover types were provided in 17 categories according to the International Global Biosphere Programme (IGBP) classification scheme and re-grouped into three categories, that is, urban, forest and crops. Distance to permanent water bodies was calculated based on the water category of the land cover data. Supplementary Table 2.1 contains a list of environmental/climatic data together with their spatio-temporal resolution and data source.

2.2.2.5 Intervention coverage indicators

Child, maternal and household intervention data, that is, Water, Sanitation and Hygiene (WASH), reproductive health, breastfeeding, vaccinations, micronutrients intake and treatment interventions were obtained from the 2011 DHS. The standard guidelines of the Roll Back Malaria were used to define indicators of malaria interventions (World Health Organisation, 2013b). These included use and ownership of insecticide treated nets (ITNs) and indoor residual spraying (IRS). All intervention coverage indicators were aggregated at the cluster level because interventions at individual level such as vaccination, ITN use or treatment are not available for dead children. Interventions with coverage of less than 5% (i.e. zinc; 2%) and those exceeding 95% (i.e. iodized salt; 99%) at the national level were excluded from the analysis due to lack of variation in estimating their relation with mortality. Table 2.1 provides details on the intervention indicators used in the study and their corresponding national coverage.

Table 2. 1: Intervention indicators and their national coverage, Uganda DHS 2011

Intervention	Description	Coverage (%)
Malaria		
Prop_IRS	Percentage of households sprayed with Indoor Residual Spraying (IRS) in the past 12 months	7
ITN ownership		
Prop_1ITN	Percentage of households with atleast one ITN	60
Prop_1ITN2	Percentage of households with atleast one ITN for every two people	28
Prop_ITNA	Percentage of population with access to an ITN within their household (Percentage of the population that could sleep under an ITN, if each ITN in the household were used by up to two people)	45
ITN use		
Prop_ITNS	Percentage of the population in a household that slept under an ITN the previous night of the survey	35
Prop_ITN5	Percentage of children under 5 years in a household who slept under an ITN the previous night of the survey	43
Prop_ITNU	Percentage of existing ITNs used by the population in a household the previous night of the survey	35
WASH		
Improved water	Percentage of households with improved source of drinking water	70
Improved sanitation	Percentage of households using improved sanitation facilities	16
Prop _wsoap	Percentage of households with soap or detergent and water at hand washing place	27
Reproductive health		
Family planning	Percentage of married women using any family planning method	30
ANC provider	Percentage of pregnant mothers receiving ANC from a skilled provider	95
4+ ANC visits	Percentage of pregnant women making four or more ANC visits during their entire pregnancy	48
IPT	Percentage of women who received intermittent preventive treatment for malaria during pregnancy	27
Skilled delivery	Percentage of births that took place with the assistance of a skilled provider	58
Postnatal care	Percentage of newborns receiving first postnatal checkup from a skilled provider within two days after delivery	11
Breastfeeding		
Within one day	Percentage of infants who started breastfeeding within one day of birth	89
Exclusive	Percentage of infants exclusively breastfed during the first six months after birth	63
Vaccinations		
Tetanus toxoid	Percentage of last-born child fully protected against neonatal tetanus	84
BCG	Percentage of children vaccinated against BCG	94
DPT	Percentage of children with complete vaccination of DPT	72
Polio	Percentage of children with complete vaccination of polio	63
Measles	Percentage of children vaccinated against Measles	76
Micronutrients		
VitaminA_sup	Percentage of children receiving vitamin A supplements in the past 6 months	57
Iron_sup	Percentage of children receiving Iron supplements in the past 7 days	7
Iodized salt	Percentage of children living in households with iodized of salt	99
Treatments		
Antibiotics	Percentage of children with ARIs symptoms who took antibiotics	47
ORS or RHF	Percentage of children with diarrhoea given fluid from oral rehydration solution (ORS) sachets or recommended home fluids (RHF)	48
Zinc	Percentage of children with diarrhoea given zinc sulphates	2
ACTs	Percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy (ACT)	69
Deworming	Percentage of children given deworming medication in the past 6 months	50

2.2.3 Statistical analysis

To identify the most important predictors associated with the U5M, Bayesian geostatistical variable selection was used adopting, a stochastic search approach. In particular, a binary indicator was introduced for every disease, health intervention (except ITN coverage measures), land cover and socio-demographic characteristic with values corresponding to the inclusion or exclusion of the variable from the model. We assumed that the indicator arises from a Bernoulli distribution with probability defining the variable-specific inclusion probability in the model. We have chosen a spike and slab prior for the regression coefficients, that is, a mixture of normal prior distributions with a mixing proportion equal to the inclusion probability. The spike component shrinks the regression coefficient to zero when the variable is excluded and the slab assumes a non-informative, normal prior distribution when the covariate has high inclusion probability (i.e. larger than 40%). ITN coverage measures were highly correlated (above 0.85), therefore, only one (or none) measure among those defining ownership and one (or none) among those defining use were selected. Environmental/climatic factors (LST, NDVI, distance to permanent water bodies and rainfall) were included or excluded in the model in a linear or categorical form, introducing indicators with a multinomial prior distribution with three parameters corresponding to the probabilities of exclusion of the variable, inclusion in linear and categorical form respectively. Covariates were categorized based on their quartiles.

To assess the association between U5M and childhood diseases at the national and sub-national levels, a Bayesian geostatistical proportional hazards model with a baseline Weibull hazard function was fitted. The model included intervention coverage measures, socio-demographic, climatic and environmental covariates. Climatic/environmental factors were included as proxies of other environmentally driven causes of mortality. Malaria prevalence was not available at the 2011 DHS locations. Instead the Bayesian binomial geostatistical model was fitted on the 2009 MIS data to predict the malaria prevalence. The prediction uncertainty was taken into account as a measurement error in the malaria covariate. Spatial correlation between clusters in both, the survival and the binomial geostatistical models was incorporated on locational random effects modeled by Gaussian processes with an exponential correlation function of the distance between locations. Our model assumed that the relation between childhood diseases and mortality varied across regions by including disease-specific spatially varying coefficients. Region-specific random effects with conditional autoregressive prior distributions modeled geographical variation in the effects of childhood diseases.

Descriptive data analysis was executed in STATA version 14.0 (Stata Corporation, College Station, TX, USA) and model fit was carried out in OpenBUGS 3.2.3 (Imperial College and Medical Research Council, London, UK). Maps were produced in ArcGIS version 10.5 (ArcGIS version 10.5, Esri, Redlands, CA, USA). The effects of covariates on mortality were summarized by their posterior medians and reported as hazard ratios with their corresponding 95% Bayesian credible interval (95% BCI). Effects were regarded statistically important if their credible intervals did not include one. Supplementary file 1 describes in details the Bayesian geostatistical methods.

2.3 Results

2.3.1 Descriptive data analysis

Table 2.2 summarizes childhood disease prevalences and the U5MR estimates by region and at the country level. The overall U5MR was 90 deaths per 1 000 live births. Large regional variations in childhood mortality rates per 1 000 live births were observed, lowest in Kampala (56) and highest in the North-East (152) deaths.

Table 2. 2: U5MR estimates and childhood disease prevalence at national and regional levels, Uganda DHS 2011 and MIS 2009

	Disease prevalence (%)					U5MR estimates
Geographical scale	**Malaria**	**Anaemia**	**Malnutrition**	**Diarrhoea**	**ARIs**	**per 1 000 live births**
National	42	27	17	23	15	90
Region						
Central 1	39	30	15	22	9	83
Central 2	51	32	13	21	12	79
East-Central	56	46	20	32	15	104
Kampala	5	23	8	24	14	56
Mid-Eastern	37	32	11	33	17	80
Mid-North	62	13	16	24	22	76
Mid-Western	43	16	20	19	17	95
North-East	40	35	45	20	20	152
South-West	12	8	20	14	11	99
West-Nile	46	38	23	19	14	100

ARIs: Symptoms of acute respiratory infections; Malnutrition: Severe or moderate malnutrition; Anaemia: Severe or moderate anaemia

Based on the MIS 2009 data, the microscopy-based national malaria parasiteamia prevalence was 42%. There were large regional variations with Kampala experiencing the lowest prevalence (5%) and the Mid-North the highest (62%). About 27% of Ugandan children aged 6-59 months were severely or moderately anaemic; lowest in South-West (8%) and highest in East-Central (46%). Overall, 17% of Ugandan children were either severely or moderately malnourished. The percentage of moderately/severely malnourished children varied by region with Kampala having the lowest (8%) and North-East the highest (45%). Nearly a quarter of the children under five years were reported to have diarrhoea at national level, but was high in East-Central (32%) and Mid-Eastern (33%) and lowest in South-West (14%). Overall ARIs in the two weeks before the survey was 15%, highest in Mid-North (22%) and lowest in Central 1 (9%). Figure 2.1 presents the corresponding geographical distribution of childhood diseases. The variation in the burden of childhood diseases across regions could be a contributing factor to the existing regional discrepancies in the U5MR in Uganda.

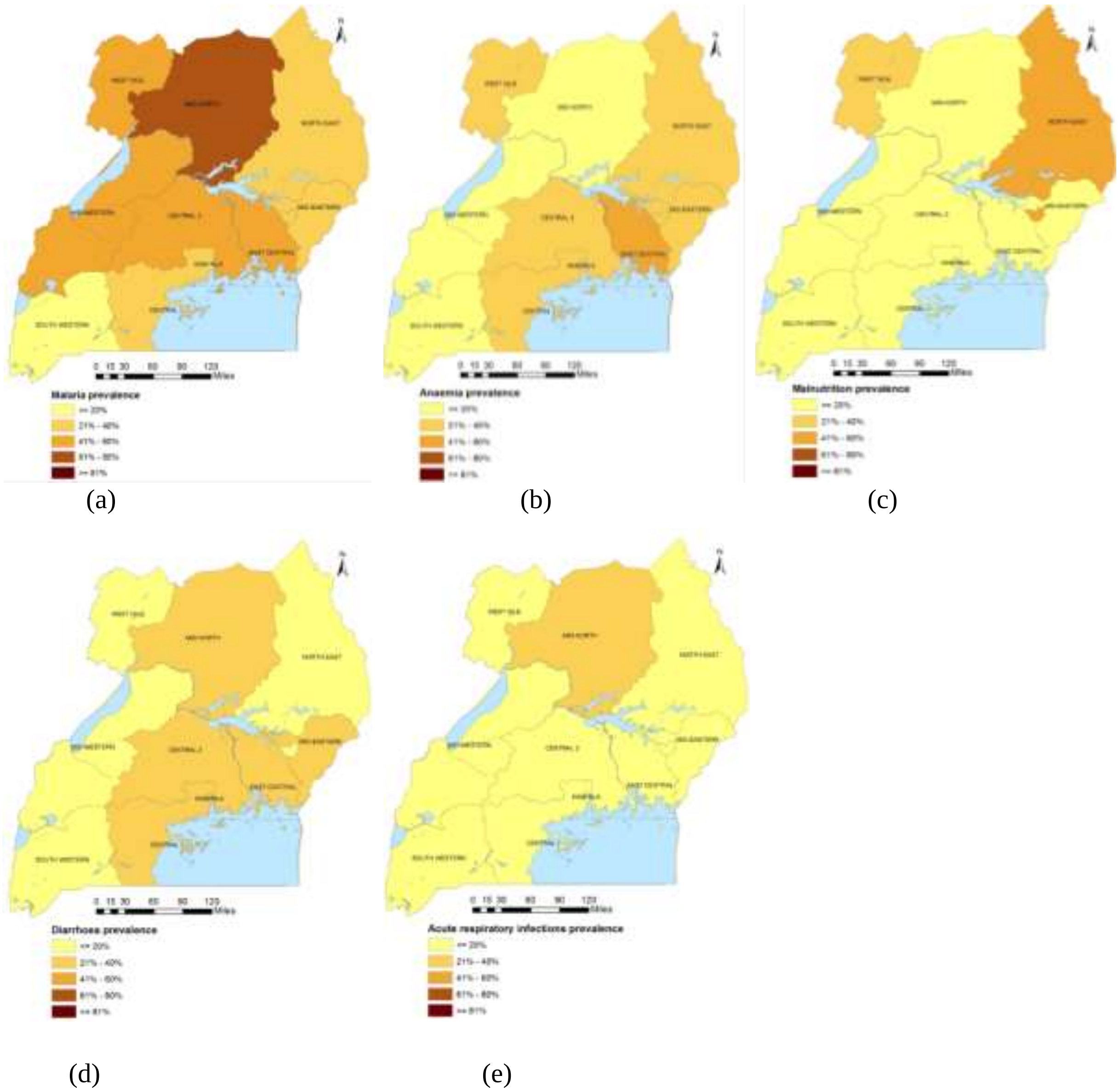

Figure 2. 1: Geographical distribution of childhood diseases by region, Uganda DHS 2011; (a) Prevalence of malaria, (b) Prevalence of anaemia, (c) Prevalence of malnutrition, (d) Prevalence of diarrhoea, (e) Prevalence of acute ARI.

2.3.2 Model-based analysis

2.3.2.1 Bayesian variable selection

Table 2.3 presents results from the Bayesian geostatistical variable selection. Socio-demographic and climatic factors, interventions and treatment indicators with posterior inclusion probabilities higher than 40% were incorporated in the final survival model. For example, the malaria intervention coverage indicators that were considered in the final model were the proportion of children under 5 years who slept under an ITN the previous night of the survey and the proportion of households sprayed with IRS. LST day and NDVI were included as categorical and linear covariates respectively.

Table 2. 3: Posterior inclusion probabilities of disease prevalence, intervention coverage indicators, socio-demographic and environmental/climatic

Variable	Inclusion probability (%)	Variable	Inclusion probability (%)
Diseases		**Treatments**	
Malnutrition	57.6[a]	Antibiotics	28.0
Malaria	63.0[a]	ORS or RHF	59.0[a]
Anaemia	69.6[a]	ACTs	15.0
ARIs	46.4[a]	Deworming	46.0[a]
Diarrhoea	68.2[a]	**Socio-economic and demographic**	
Malaria		**Child**	
Prop_IRS	59.3[a]	Sex	86.0[a]
ITN ownership		Birth order	60.2[a]
None	55.0	Birth intervals	54.2[a]
Prop_1ITN	36.7	**Maternal**	
Prop_1ITN2	0.0	Age at birth	100.0[a]
Prop_ITNA	8.3	Number of children born	100.0[a]
INT use		Education level	84.6[a]
None	8.7	Pregnancy terminated	64.6[a]
Prop_ITNS	15.0	Residence (urban vs rural)	69.0[a]
Prop_ITN5	48.0[a]	Working status	15.5
Prop_ITNU	28.3	**Household**	
WASH		Age of head	23.4
Improved water	30.0	Wealth index	68.8[a]
Improved sanitation	85.0[a]	#Children under 5 years	37.0
Prop_wsoap	13.3	**Environmental/Climatic factors**	
Reproductive health		Land cover	100.0[a]
Family planning	88.0[a]	**LST day**	
ANC provider	100.0[a]	None	0.0
4+ ANC visits	20.0	Continuous	0.0
IPT	54.5[a]	Categorical	100.0[a]
Skilled delivery	49.2[a]	**LST night**	
Postnatal care	100.0[a]	None	98.0
Breastfeeding		Continuous	2.0
Within one day	24.4	Categorical	0.0
Exclusive	45.2[a]	**NDVI**	
Vaccinations		None	5.0
Tetanus toxoid	27.0	Continuous	95.0[a]
BCG	2.0	Categorical	0.0
DPT	46.8[a]	**Rainfall**	
Polio	30.0	None	95.0
Measles	68.2[a]	Continuous	0.5
Micronutrients		Categorical	0.0
VitaminA_sup	31.0	**Distance to water**	
Iron_sup	39.0	None	100.0
		Continuous	0.0
		Categorical	0.0

[a]Selected variables with >40% inclusion probability

2.3.2.2 Effects of childhood diseases on U5M

Results (Table 2.4) indicate that at the national level, a 100% increase in the prevalence of malaria parasiteamia was associated with a 74% increase in the hazard of mortality (HR = 1.74; 95% BCI: 1.42, 2.16). Similarly, a 100% increase in the proportion of children having severe or moderate anaemia, severe or moderate malnutrition and diarrhoea was associated with a 37%, 49% and 61% rise in the hazard of mortality respectively. ARIs were neither associated with mortality at country nor at sub-national level.

Table 2. 4: Posterior estimates for the effects of childhood diseases at the national and sub-national scale on U5MR adjusted for socio-economic, demographic and environmental/climatic characteristics

	Malaria[c]	Moderate /severe anaemia[c]	Moderate /severe malnutrition[c]	Diarrhoea[c]	ARIs[c]
Geographical scale	**Hazard ratio (95% BCI)**	**Hazard ratio (95% BCI)**	**Hazard ratio (95% BCI)**	**Hazard ratio (95% BCI)**	**Hazard ratio (95% BCI)**
National	1.74 (1.42, 2.16)[a]	1.37 (1.20, 1.75)[a]	1.49 (1.25, 1.66)[a]	1.61 (1.31, 2.05)[a]	0.99 (0.31, 2.17)
Region					
Central 1	1.46 (0.70,2.38)	1.78 (1.35, 3.86)[a]	0.97 (0.63, 1.30)	1.27 (0.63, 2.85)	1.02 (0.19, 5.81)
Central 2	1.72 (1.10, 2.55)[a]	1.07 (0.93, 1.52)	1.08 (0.63, 1.52)	1.97 (1.16, 3.67)[a]	1.12 (0.19, 3.40)
East-Central	2.39 (1.41, 5.74)[a]	0.79 (0.62, 1.23)	2.98 (1.75, 4.21)[a]	1.94 (1.21, 4.57)[a]	1.21 (0.15, 3.95)
Kampala	1.20 (0.81, 1.97)	1.87 (1.33, 2.62)[a]	1.83 (0.62, 2.64)	1.07 (0.40, 3.23)	1.53 (0.17, 7.37)
Mid-Eastern	2.55 (0.80, 3.42)	0.98 (0.76, 1.53)	2.58 (1.66, 4.08)[a]	2.04 (1.27, 3.58)[a]	0.77 (0.10, 4.29)
Mid-North	1.95 (1.27, 3.35)[a]	1.28 (1.06, 1.97)[a]	0.81 (0.56, 1.19)	1.75 (0.73, 3.86)	1.01 (0.15, 2.98)
Mid-Western	1.07 (0.68, 2.23)	1.16 (1.07, 1.64)[a]	1.62 (0.88, 2.18)	2.17 (1.11, 4.13)[a]	0.91 (0.21, 3.35)
North-East	2.20 (1.31, 4.79)[a]	1.20 (1.08, 2.23)[a]	2.33 (1.33, 3.93)[a]	2.38 (0.80, 5.35)	0.90 (0.20, 5.30)
South-West	0.84 (0.59, 1.80)	1.77 (1.40, 2.67)[a]	1.27 (0.91, 1.69)	1.52 (0.59, 4.64)	1.31 (0.22, 4.56)
West-Nile	2.20 (1.06, 2.90)[a]	1.87 (1.59, 2.41)[a]	1.28 (0.85, 1.80)	1.54 (0.80, 3.02)	1.02 (0.10, 3.98)
Spatial parameters					
Variance	**Posterior median (95% BCI)**	**Posterior median (95% BCI)**	**Posterior median (95% BCI)**	**Posterior median (95% BCI)**	**Posterior median (95% BCI)**
Spatially varying[b]	0.56 (0.48, 0.71)	0.56 (0.43, 0.60)	0.68 (0.43, 0.99)	0.61 (0.38, 0.85)	0.59 (0.43, 0.76)
Range[d]	3.10 (1.42, 6.40)				
Variance in spatial process	0.49 (0.40, 0.75)				

[a]Statistically important effect; [b]Indicates the degree of variation of disease effects in space; ARIs: Symptoms of acute respiratory infections; [c]Disease prevalence was modeled on the scale of 0 to 1, therefore one unit increase in prevalence corresponds to a 100% increase which implies a shift of the current by 100%, [b]Distance after which spatial correlation becomes <5%

Sub-national analysis shows that malaria was associated with U5M in Central 2, East-Central, Mid-North, North-East and West-Nile regions. In Central 1, Kampala and South-West, only severe/moderate anaemia was associated with mortality. Anaemia also significantly increased hazards of U5M in the Mid-North, Mid-West, North-East and West-Nile regions. The prevalence of moderate/severe malnutrition in East-Central, Mid-Eastern and North-East, and diarrhoea risk in Central 2, East-Central, Mid-eastern and Mid-Western had a statistically important effect on U5M in these areas. There was no important association between the ARIs burden and U5M. Figure 2.2 demonstrates the corresponding geographical distribution of the effects of childhood diseases on U5M. The asterix (*) implies that the disease is associated with U5M in the respective region. Darker colours suggest stronger disease associations with mortality.

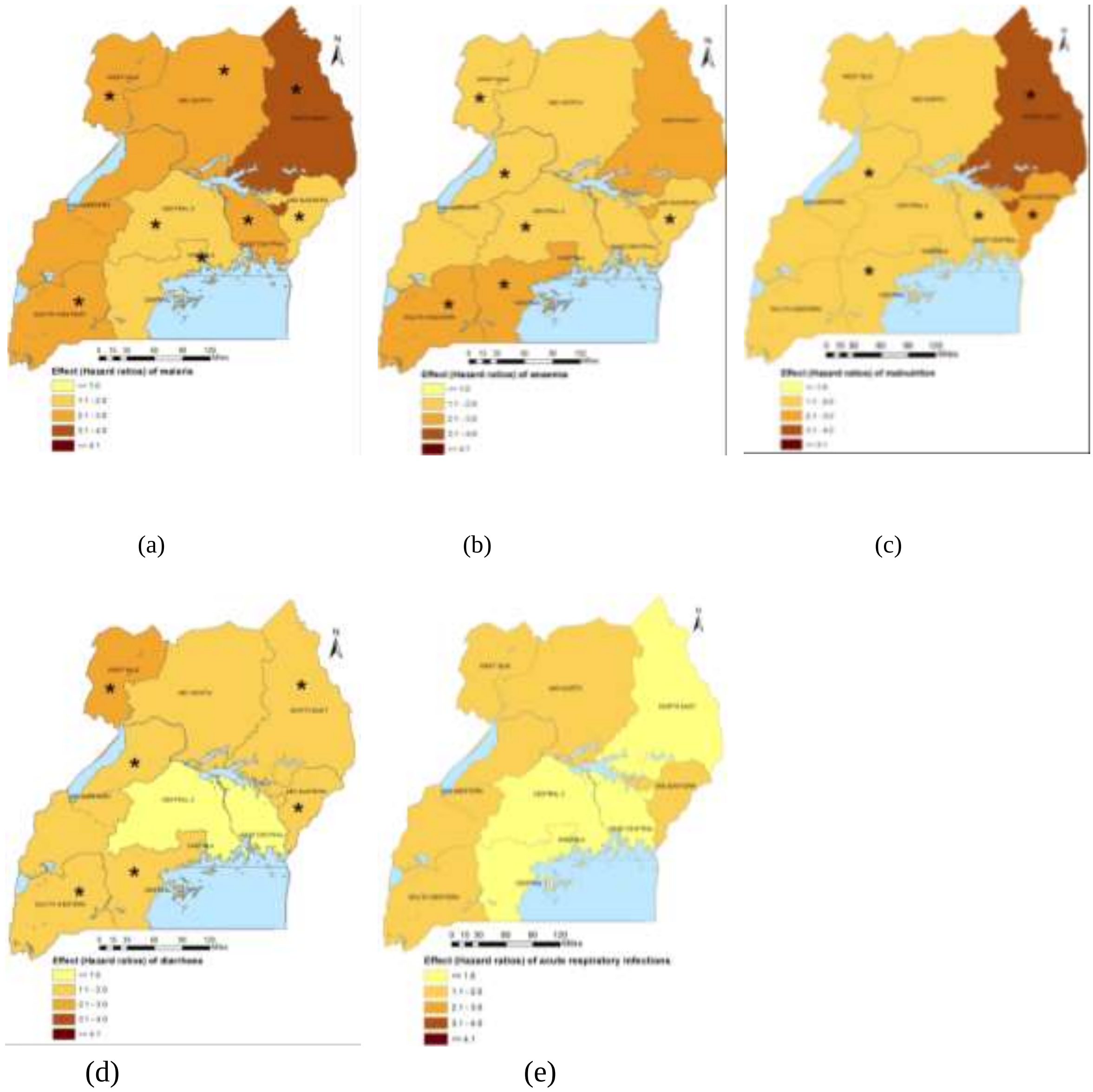

Figure 2. 2: Geographical distribution of spatially varying childhood disease effects on U5MR; (*significant driver of mortality); (a) Prevalence of malaria, (b) Prevalence of anaemia, (c) Prevalence of malnutrition, (d) Prevalence of diarrhoea, (e) Prevalence of acute ARI.

Figure 2.3 illustrates disease effects with their corresponding 95% BCI at the national and sub-national scales estimated from the Bayesian proportional hazards model. Points on the lines indicate the 2.5%, 50% and 97.5% quantiles of the posterior distribution of the hazard ratios. Lines that do not cross one indicate a statistically important effect.

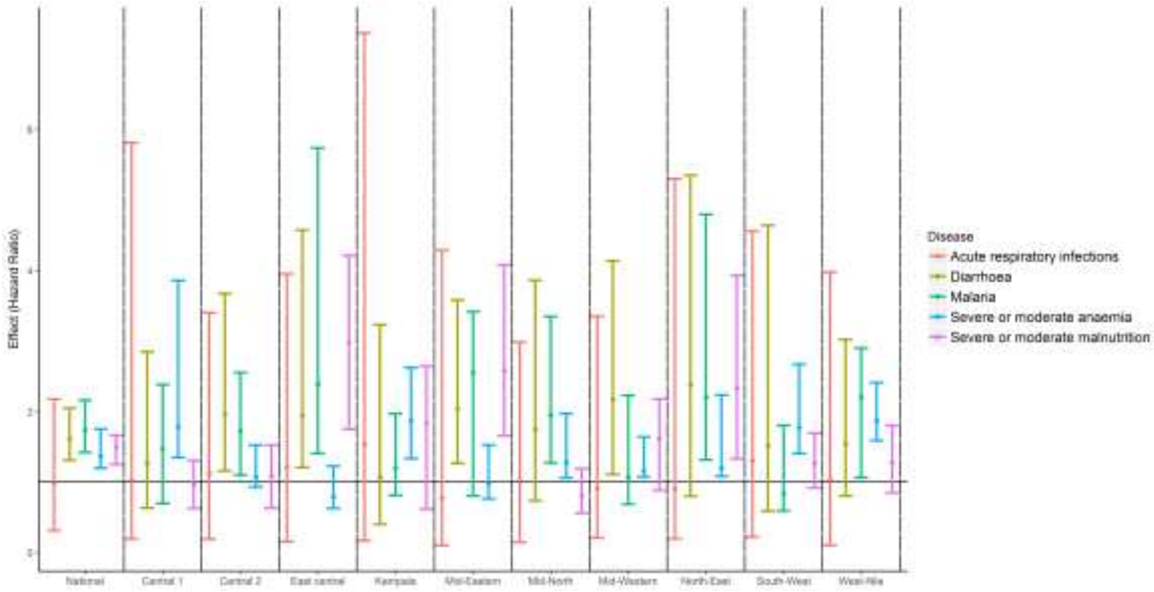

Figure 2. 3: Point estimates of disease effects on U5M with their corresponding 95% BCI at the national and regional scales estimated from the Bayesian geostatistical proportional hazards model

Table 2.5 shows that among malaria interventions, a 100% increase in the coverage of IRS is associated with a reduction in the mortality hazard by 31%, (HR = 0.69; 95% BCI: 0.61, 0.83). Reproductive health interventions were also important determinants of U5M. In particular, an increasing proportion of married women using any family planning method, proportion of pregnant mothers receiving ANC from a skilled provider and proportion of women receiving intermittent preventive treatment for malaria during pregnancy were associated with lower hazards of mortality. Child interventions considerably influenced mortality. First postnatal checkup from a skilled provider within two days after delivery, exclusive breastfeeding during the first six months after birth, complete vaccination against DPT and measles and, deworming were associated with lower hazard of mortality. Socio-economic and demographic characteristics were statistically important predictors of mortality. An increased mortality hazard was estimated for children born to mothers who once experienced a terminated pregnancy.

Table 2. 5: Posterior estimates for the effects of socio-economic, demographic and environmental/climatic factors on the U5MR

Variable	Hazard ratio (95% BCI)
Malaria[c]	
Prop_IRS	0.69 (0.61, 0.83)[a]
Prop_ITN5	1.21 (0.85, 1.63)
WASH[c]	
Improved sanitation	0.78 (0.54, 0.87)[a]
Reproductive health[c]	
Family planning	0.68 (0.41, 0.79)[a]
ANC provider	0.58 (0.23, 0.84)[a]
IPT	0.59 (0.53, 0.73)[a]
Skilled delivery	0.96 (0.80, 1.12)
Postnatal care	0.69 (0.36, 0.67)[a]
Breastfeeding[c]	
Exclusive	0.54 (0.44, 0.69)[a]
Vaccinations[c]	
DPT	0.75 (0.63, 0.96)[a]
Measles	0.71 (0.60, 0.80)[a]
Micronutrients[c]	
Deworming	0.40 (0.28, 0.48)[a]
Treatments[c]	
ORS or RHF	1.13 (0.88, 1.32)
Socio-economic and demographic	
Child	
Sex: Female vs male	
Birth order	1.19 (1.12, 1.60)[a]
>4 vs 1-4	
Birth intervals	0.54 (0.46, 0.81)[a]
24-35 vs 1-23	
36-47 vs 1-23	0.41 (0.35, 0.58)[a]
48 vs 1-23	0.37 (0.24, 0.51)[a]
Maternal	
Age at birth	0.82 (0.63, 1.21)
25-29 vs 15-24	
30-34 vs 15-24	0.69 (0.58, 0.91)[a]
35-49 vs 15-24	1.09 (0.81, 1.34)
Number of children born	1.67 (1.57, 1.76)[a]
Pregnancy terminated vs never	1.31 (1.07, 1.74)[a]
Education level: Primary vs none	0.87 (0.80, 1.10)
Secondary or higher vs none	0.81 (0.71, 0.92)[a]
Residence: Urban vs rural	0.76 (0.59, 0.91)[a]
Household: Wealth index	0.84 (0.75, 0.95)[a]
Environmental/Climatic factors	
Normalized difference vegetation index	1.47 (0.60, 2.82)
Land surface temperature (day)	
25.7 – 27.5 vs < 25.7	1.11 (0.69, 1.53)
27.6 – 30.6 vs < 25.7	1.18 (0.84, 1.63)
30.6 vs < 25.7	0.90 (0.70, 1.31)
Land cover	1.14 (0.81, 1.57)
Crops vs forest	
Urban vs forest	0.88 (0.71, 1.42)
Shape parameter[d]	0.43 (0.38, 0.49)

[c]Covariate takes values on the scale of 0 to 1, therefore one unit increase in coverage corresponds to a 100% increase which implies a shift of the current by 100%; [d]Shape parameter of the Weibull baseline hazard.

2.4 Discussion

We estimated the effects of childhood diseases in Uganda on all-cause U5M at national and subnational scales taking into account confounding effects of child and maternal interventions, socio-demographic and climatic/environmental factors that have been shown to be significantly related to U5M (Bbaale, 2015; Ezeh et al., 2015; Kabagenyi and Rutaremwa, 2013; Nafiu, 2016). We found strong geographical variation in the effects of childhood diseases on all-cause U5M across Uganda.

At the national level, malaria, diarrhoea, severe or moderate malnutrition and severe or moderate anaemia were significantly associated with U5M. In our study, almost half of the U5 children in the country had malaria which accounts for the strongest association of the disease with U5M. These findings can be explained by the rainy season during which the survey was conducted. Rainfall provides suitable conditions for development of malaria parasites within mosquitoes resulting in increased transmission (Colón-González et al., 2016; Gage et al., 2008; Rozeboom, 1960) and consequently mortality. In addition, Uganda has poor WASH practices with only fourteen percent of households having improved sanitation facilities (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). This results into rainfall pulses flushing faecal materials into waterways and concentrate micro-organisms in water sources, which increases diarrhoeal risk and death from the disease (Carlton et al., 2014). Furthermore, malnutrition is a risk factor for the major causes of U5M (Keusch, 2003; Kiwanuka, 2003) and is a consequence of poor feeding and socio-economic status (Ehrhardt et al., 2006). The inadequate young child feeding practices coupled with poor socio-economic status in Uganda (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012) could have contributed to the significant effect of malnutrition on mortality. Important relationships between U5M and malaria (Gemperli et al., 2004; Kazembe et al., 2007), diarrhoea (Walker et al., 2013), malnutrition (Vella et al., 1992b, 1992a) and anaemia (Brabin et al., 2001; Scott et al., 2014) have also been reported in other studies. Malaria, malnutrition and diarrhoea have been described as some of the major global, regional and national causes of child mortality (Liu et al., 2016, 2012).

Another crucial factor is the interplay of diseases in influencing U5M. Malnutrition is a risk factor for anaemia and malaria-associated morbidity and mortality (Caulfield et al., 2004b; Ehrhardt et al., 2006; Müller et al., 2003; Shankar, 2000). Many of the children who die from malaria also have malarial anaemia (Kiwanuka, 2003). The adverse effect of malnutrition on diarrhoea and malaria has been described (Caulfield et al., 2004a; Mockenhaupt et al., 2004; Rice et al., 2000). This implies that controlling one disease alone is not enough to significantly curb under-five morbidity and mortality as the causes are interconnected. Thus, the comprehension of the interaction of childhood diseases is important for the understanding of under-five morbidity and mortality and, for the development of effective interventions. Hence, health personnel should be trained to distinguish and treat major childhood diseases in the presence of other illnesses among children. This alongside malaria, malnutrition, diarrhoea and anaemia control measures may reduce the U5M burden related to such diseases.

Sub-national analysis showed that malaria was associated with mortality in Central 2, East-Central, Mid-North, North-East and West-Nile regions. The high prevalence of malaria parasiteamia in these regions can explain the important effect of malaria on mortality. While the Mid-North experienced the highest malaria prevalence, the largest association of the disease with mortality was not observed in this region. This suggests that high disease prevalence may not imply high mortality. Various factors (e.g. interventions), other than diseases may also play a role. The lower malaria-mortality association in the Mid-North can be attributed to the special attention the Uganda government and non-governmental organizations have given the region with regards to malaria control. For example, over sixty percent of households in this region were sprayed with IRS in the last 12 months prior to the survey compared to five percent or less in other regions (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Furthermore, the improved health facility readiness in the

Mid-North could have contributed to the reduced association between malaria and U5M despite the high malaria prevalence in the region (Ssempiira, 2018). On the other hand, East-Central had the largest malaria-mortality effect but malaria was not the most prevalent in this region. One reason that could be responsible for this finding is the low coverage of ITN (Ssempiira et al., 2017) and a weaker intervention effect on the disease risk compared to that at the national level (Ssempiira et al., 2017).

The analysis indicated significant associations between anaemia and mortality in Central 1, Kampala, Mid-North, Mid-Western, North-East, South-West and West-Nile. It is important to note that most of these regions experienced a high malaria prevalence of at least forty percent (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). It is also known that anaemia can result from malaria infection (Ezzati et al., 2004), therefore the anaemia relation to mortality in these areas may partly indicate an indirect malaria effect. Given the low prevalence of severe anaemia in these regions (i.e. less than 10%, (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012)), the majority of anaemia-related deaths are associated with moderate anaemia. This implies that even a modest improvement in haemoglobin concentration could reduce the impact of anaemia on U5M (Gera et al., 2007). The most frequently used approach to increase haemoglobin levels and reduce anaemia is universal iron supplementation starting at six months of age (Christofides et al., 2006). In Uganda, nearly eighty five percent of the under-fives did not receive iron supplementation (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012) and in most regions in which anaemia influenced mortality (Central 1, Kampala, West-Nile, Mid-Western and South-West), iron supplementation was as low as nine percent (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). This could have led to iron-deficiency diseases such as anaemia, hence the observed significant associations between anaemia and U5M.

Soil transmission helminthiasis (STH) resulting from parasitic worms may also cause anaemia. Parasitic worms, especially, hookworms are a risk factor of anaemia among children (Karagiannis-Voules et al., 2015). Such worms are transmitted by eggs present in human faeces and contaminate the soil in areas where sanitation is poor (Gyorkos and Gilbert, 2014). Given the poor WASH practices in the country, the Ugandan children are at higher risk of developing STH and STH-associated anaemia. In particular, out of the seven regions with an important association between anaemia and mortality, five have lower coverage of improved sanitation facilities varying from three to fourteen percent which is below the sixteen percent national average (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

Our results suggested that severe or moderate malnutrition was associated with mortality in East-Central, Mid-Eastern and North-East regions. These findings can be explained by the high malnutrition prevalence in the areas. Out of the three affected regions, two (East-Central and North-East) had malnutrition prevalence higher than the national average. East-Central and North-East regions are characterized by frequent dry spells and lack of agricultural extension services. This affects production and productivity resulting in poor food access and utilization, hence malnutrition (Uganda Integrated Food Security Phase Classification technical working group, 2017). Surprisingly, malnutrition is associated with mortality in regions with high food production such as the Mid-Eastern. Poor infant and young child feeding practices may partly be responsible for the persistent malnutrition. For example, nearly half of the under-fives in each of the regions where malnutrition was associated with mortality, were not exclusively breast fed in the first six months after delivery (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

Diarrhoea risk was associated with U5M in Central 2, East-Central, Mid-Eastern and Mid-Western. The almost stagnant coverage of interventions since 2006 (Uganda Bureau of

Statistics (UBOS) and ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007) proven to reduce diarrhoea-deaths in areas where they are widely used (Victora et al., 1993), could possibly have contributed to this important effect of diarrhoea on mortality. For instance, utmost, only fourteen percent of households in each of the four affected regions had improved sanitation facilities and, health care seeking for diarrhoea was poor, with about half of children having the disease in each of the four high risk regions not receiving ORS or RHF (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

Even though ARIs is among the ten leading causes of death in children under five years in Uganda (Ministry of Health, 2013b), the disease was not associated with U5M. Universal coverage of the pentavalent (Haemophilus Influenzae type B disease) vaccine could have contributed to this finding (Ministry of Health, 2013b).

The main limitation of our study is that disease data for the dead children were not available and therefore we were not able to estimate the disease-related mortality using disease information at individual level. Instead, we treated the disease prevalence at the cluster level as an exposure and quantified the associations with U5M, adjusting for birth-related factors at the individual level, maternal and household characteristics as well as coverage of interventions at cluster level. Our results are therefore prone to ecological fallacy; however, they inform about geographical distribution of the effects of childhood diseases on U5M in Uganda. The methodology presented in this paper can be applied to other countries with dysfunctional civil registration systems, and be used as a tool for providing information for decision making in programming of interventions at sub-national scales to address U5MR.

2.5 Conclusion

This study has demonstrated that the relation between childhood disease burden and mortality varies across regions in Uganda and identified the diseases related to mortality by region. This information can be used by control programs in the development of locally adapted and evidence-based interventions. This may reduce within country U5M inequalities and consequently result into accomplishing national SDG mortality targets.

Disease-specific interventions should be strengthened specifically in the affected regions. Interventions related to malaria, in particular, IRS should be reinforced in Central 2, East-Central, Mid-North, North-East and West-Nile. The coverage of iron supplementation and deworming should be increased especially during pregnancy and infancy in Central 1, Kampala, Mid-North, Mid-Western, North-East, South-West and West-Nile to lessen anaemia-mortality. Balanced investment in nutrition and education in nutrition practices mainly in more malnourished regions (East-Central, Mid-Eastern and North-East) would alleviate deaths related to malnutrition. Scaling up coverage of diarrhoea interventions, such as ORS or RHF and improved sanitation facilities in Central 2, East-Central, Mid-Eastern and Mid-Western, and educating the population on the benefits of hygienic practices will prevent diarrhoea.

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Declarations

Declarations of interest

None

Authors' contributions

All authors take responsibility for the structure and content of the paper. BBN conceptualized the research, managed and analyzed the data, developed the methodology and implemented it in software, interpreted results and wrote the first draft of the manuscript. Author JS participated in manuscript editing. Authors FEM and SK formulated research goals and objectives, and also participated in the process of acquisition of project financial support. PV was the lead author who conceived the research, formulated research goals and objectives, acquired project financial support, led methodology development, model fitting and result interpretation and manuscript writing. All authors read and approved the submitted manuscript.

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Ethical approval and consent to participate

In this research article secondary data that was made available to us by the Uganda Bureau of Statistics (UBOS) and the DHS Program (www.dhsprogram.com) was used. According to survey reports, ethical approval and consent to participate was obtained by the above bodies from the Institutional Review Board of International Consulting Firm (ICF) of Calverton, Maryland, USA, and from Makerere University School of Biomedical Sciences Higher Degrees Research and Ethics committee (SBS-HDREC) and the Uganda National Council for Science and Technology (UNCST). Information on ethical approval and consent to participate is published in the 2011 DHS (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012) and 2009 MIS reports (Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010).

Consent for publication

Not applicable.

Competing risks

The authors declare that they have no competing interests.

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Availability of data

The data that support findings of this article are available at the DHS MEASURE website (www.dhsprogram.com) with request for access and following instructions at https://dhsprogram.com/data/available-datasets.cfm

2.6 Supplementary files

Supplementray Table 2. 1: Remote sensing data sources[a]

Source	Data type	Temporal resolution	Spatial resolution
MODIS/Terra[b]	LST[l]	8 days	1km
MODIS/Terra[b]	NDVI[m]	16 days	1km
U.S. Geological Survey-Earth Resources Observation Systems (USGSS)	Rainfall	10 days	8x8km^2
Shuttle Radar Topographic Mission (SRTM)	Altitude	NA	1x1km^2
MODIS,IBGD type	Land cover Water bodies	NA	0.5x0.5km^2
Global Rural and Urban Mapping project	Urban Rural extent	NA	1x1km^2

NA: Not applicable; Land cover groups (forest, crops, urban); [a]Land cover data accessed in June 2011 and other data accessed in November 2013; [b]Moderate Resolution Imaging Spectroradiometer (MODIS)/Terra, available at: http://modis.gsfc.nasa.gov/; [l]Land surface temperature (LST) day and night; [m]Normalized difference vegetation index

Supplementary file 2. 1: Bayesian geostatistical methods

B.1. Bayesian variable selection

A Bayesian stochastic search variable selection approach was used to determine the most important predictors of under-five mortality (George and McCulloch, 1993). ITN coverage measures were highly correlated with more than 85%, therefore, only one (or none) ITN measure among those defining ownership and one (or none) ITN measure among those defining use (Ssempiira et al., 2017) was selected. For each ITN coverage measure X_p in the ownership group, a categorical indicator I_p, was introduced to represent exclusion of the variable from the model ($I_p = 1$), or inclusion of one of the ITN ownership measure i.e. Prop_ITNA ($I_p = 2$), Prop_1ITN2 ($I_p = 3$) and Prop_1ITN ($I_p = 4$). A similar definition was adopted for the ITN use coverage measure i.e. exclusion of the variable from the model ($I_p = 1$), inclusion of Prop_ITN5 ($I_p = 2$), Prop_ITNS ($I_p = 3$) and Prop_ITNU ($I_p = 4$). The ITN measure with the highest probability of inclusion in each category was included in the final model. For the environmental/climatic variables except of land cover, variable selection compared their linear and categorical forms and selected the one that had the highest probability of inclusion or neither of the two forms. The categorical forms were generated based on the quantiles of variables. We introduced an indicator I_p for each environmental/climatic covariate X_p which defines exclusion of the variable from the model ($I_p = 1$), inclusion in a categorical ($I_p = 2$) or linear ($I_p = 3$) form. For diseases, socio-demographic, land cover, health interventions other than ITN coverage measures, we introduced a binary indicator parameter I_p suggesting presence ($I_p = 1$) or absence ($I_p = 0$) of the predictor from the model. I_p has a probability mass function $\prod_{j=1}^{p} \pi_j^{\delta_j(I_p)}$, where π_j denotes the inclusion probabilities, $j = (1,2,3,4)$, e.g. for ITN coverage measures so that $\sum_{j=1}^{p} \pi_j = 1$ and $\delta_j(.)$ is the Dirac function, $\delta_j(I_p) = \begin{cases} 1, if\ I_p = j \\ 0, if\ I_p \neq j \end{cases}$. We assumed a spike and slab prior for regression coefficient β_p corresponding to the corresponding covariate, X_p i.e. for the coefficient β_p of the predictor in linear form we take $\beta_p \sim \left(1 - \delta_1(I_p)\right) N\left(0, u_0 \tau_p^2\right) + \delta_1(I_p) N(0, \tau_p^2)$ proposing a non-informative prior for β_p in case X_p is included in the model in a linear form (slab) and an informative normal prior with variance close to zero (i.e. $u_0 = 10^{-3}$) shrinking β_p to zero (spike) if X_p is excluded from the model. Similarly, for the coefficient $\{\beta_{p,l}\}_{l=1,..,L}$ corresponding to the categorical form of $\underline{X}_p$ with L categories, we assume that $\beta_{p,l} \sim \delta_2(I_p) N\left(0, \tau_{p,l}^2\right) + \left(1 - \delta_2(I_p)\right) N\left(0, \vartheta_0 \tau_{p,l}^2\right)$. For inclusion probabilities of ITN use and ownership, a non-informative Dirichlet distribution was adopted with hyper parameters $\alpha = (1,1,1,1)^T$, that is, $\boldsymbol{\pi} = (\pi_1, \pi_2, \pi_3, \pi_4)^T \sim Dirichlet(4, \alpha)$. A similar distribution was adopted for the inclusion probabilities of environmental/climatic factors. For diseases, socio-demographic, land cover, health interventions other than ITN coverage measures, a Bernoulli prior with an equal inclusion or exclusion probability was assumed for the indicator i.e. $I_p \sim bern(0.5)$. Also, inverse Gamma priors with parameters (2.01, 1.01) were assumed for the precision hyper parameters τ_p^2. The predictors identified as important are those with posterior inclusion probability greater than or equal to 40% (Diboulo et al., 2015; Giardina et al., 2014).

B.2. Geostatistical proportional hazards model with spatially varying covariates

A Bayesian geostatistical proportional hazards model (Banerjee et al., 2015) was fitted to assess the association between under-five mortality and childhood diseases, and to identify diseases associated with mortality at the national and sub-national level. Let $s = \{s_1, s_2, \dots, s_m\}^t, s_i \in D \subset R^2$ be the set of locations at which mortality data are observed, $t_j(s_i)$ be the observed number of months lived or the censoring time for child j at location s_i, $\boldsymbol{X_j}(s_i)$ be the vector of intervention coverage indicator, socio-demographic and climatic factors and $Z_d(s_i)$ be the prevalence of disease d at location s_i.We modeled the hazard of death by the equation, $h\big(t_j(s_i)\big) = h_0\big(t_j(s_i)\big) \exp\Big(\boldsymbol{\beta}^T \boldsymbol{X_j}(s_i) + \sum_{d=1}^{D}\big(b_d + \varepsilon_{dk(i)}\big)^T Z_d(s_i) + W(s_i)\Big)$ and assumed a Weibull baseline hazard i.e. $h_0\big(t_j(s_i)\big) = r(t_j(s_i))^{r-1}$ where r is the shape parameter, $\boldsymbol{\beta}^T = \big(\beta_1, \dots, \beta_p\big)$ is the vector of regression coefficients with $\exp(\beta_l)$, $l = 1, \dots p$, correspond to the hazard ratio (HR). $W(s_i)$ is a cluster-specific random frailty which captures spatial correlation in mortality i.e. clusters in closer proximity are expected to have similar mortality hazard due to common exposures. We modeled $\boldsymbol{W}(s) = (W(s_1), W(s_2), \dots, W(s_m))^T$ by a Gaussian process, i.e. $\boldsymbol{W}(s) \sim N(0, \Sigma)$, with an exponential correlation function of the distance d_{kl} between locations s_k and s_l, that is $\Sigma_{kl} = \sigma^2 \exp(-d_{kl}\rho)$ (Banerjee et al., 2015). The parameter σ^2 gives the variance of the spatial process and ρ is a smoothing parameter that controls the rate of correlation decay with distance. For the exponential correlation function, $\frac{-\log(0.05)}{\rho}$ determines the distance at which the correlation drops to 0.05 (i.e. effective range of spatial process). Our model assumed that the relation between childhood diseases and mortality varied across regions by including disease specific spatially varying coefficients, $b_d + \varepsilon_{kd}$, where b_d is the effect of the disease $d = 1, \dots D$ on child mortality at global (national) level and $\boldsymbol{\varepsilon_d} = (\varepsilon_{d1}, \dots, \varepsilon_{dk})^{\boldsymbol{T}}$ are the varying effects at regional (sub-national) levels $k = 1, \dots K$ with $k(i)$ indicating the region k corresponding to the location s_i.We introduced spatial dependence among the regions via a conditional autoregressive (CAR) prior for $\boldsymbol{\varepsilon_d}$, that is $\boldsymbol{\varepsilon_d} \sim N(\mathbf{0}, \Omega_d)$ with $\Omega_d = \sigma_d^2(I - \gamma C)^{-1}\Delta$. σ_d^2 is the variance of spatially varying disease effects, Δ is a diagonal matrix with entries $\Delta_{kk} = {g_k}^{-1}$where g_k is the number of neighbors of region k, γ measures overall spatial dependence and C is an adjacency proximity matrix with normalized entries that is $C_{kl} = \omega_{kl}/g_k$, ω_{kl} is 1 if region k neighbors l and 0 otherwise (Banerjee et al., 2015). To complete Bayesian model formulation, we assumed inverse gamma priors for all spatial variances with known parameters, i.e. $\sigma^2, \sigma_d^2 \sim IG(2.01, 1.01)$, a uniform prior distribution for $\rho \sim U(a, b)$, where a and b chosen such as the effective range is within the maximum and minimum distances of the observed locations (Thomas et al., 2004) and a uniform prior for $\gamma \sim U(\lambda_1^{-1}, \lambda_2^{-1})$ where λ_1, λ_2 are the smallest and largest eigen value of $\Delta^{-1/2}\mathrm{C}\Delta^{1/2}$ (Banerjee et al., 2015). The shape parameter was assigned an exponential prior $r \sim Exp(0.01)$. Non-informative normal priors were adopted for the regression coefficients $\beta_l, b_d \sim N(0, 10^3)$ for $l = 1, \dots p$ and $d = 1, \dots D$.

The joint posterior distribution of the model is given by

$$\prod_{\boldsymbol{i}} [\, t_j(s_i)\, |\boldsymbol{\beta}, b_d, W(s_i)\, \varepsilon_{dk}, \boldsymbol{X_j}(s_i), \boldsymbol{Z_d}(s_i), r\,][\,\boldsymbol{W}(s)|\sigma^2, \rho][\boldsymbol{\varepsilon_d}|\, \sigma_d^2, \gamma][\boldsymbol{\beta}, b_d, \sigma^2, \sigma_d^2, \gamma, \rho, r]$$

B.3. Modelling geographical misalignment of malaria survey and mortality data

We extended the above model to take into account geographical misalignment between the mortality clusters of the 2011 DHS and the 2009 MIS. Let $s' = \{s_1', s_2', \dots, s_n'\}^t, s_i \in D \subset R^2$ be the set of locations with the observed malaria survey locations which are different than the locations s. Let $N(s_i')$ be the number of children screened for malaria at location s_i' and

$Y(s_i')$ be the number of those found positive to malaria parasites. We assumed that $Y(s_i')$ has a binomial distribution, $Y(s_i') \sim Bn(N(s_i'), Z_1(s_i'))$ where $Z_1(s_i')$ is the malaria parasite prevalence at s_i'. We introduce location-specific environmental/climatic covariates $\boldsymbol{\Psi}(s_i')$ and spatial random effects, $w(s_i')$ on the logit scale via $LZ_1(s_i') = logit(Z_1(s_i')) = \boldsymbol{\Psi}^{\boldsymbol{T}}(s_i')\boldsymbol{\alpha} + w(s_i')$, where $\boldsymbol{a}$ is the vector of regression coefficients, $\boldsymbol{a} = (a_1, a_2, \dots, a_q)^T$. Spatial correlation is modelled by a Gaussian process on $\boldsymbol{w}(s') = (w(s_1'), w(s_2'), \dots, w(s_m'))^T$ as described for the proportional hazards model, that is, $\boldsymbol{w}(s') \sim N(0, \Sigma_w)$ where $(\Sigma_w)_{i'j'} = \sigma_w^2 \exp(-\phi d_{i'j'})$. Similar to the prior specification of the mortality covariance parameters, we assume an inverse gamma prior distribution for σ_w^2 , and normal prior distributions for a_l that is $a_l \sim N(0, 10^3), = 1, \dots q$.

Let $\boldsymbol{\Psi}(s) = (\Psi(s_1), \Psi(s_2), \dots, \Psi(s_m))^T$ and $\boldsymbol{LZ_1}(s) = (LZ_1(s_1), LZ_1(s_2), \dots, LZ_1(s_m))^T$ be the vectors of the malaria-related environmental/climatic covariates and the predicted malaria covariate on the logit scale at the mortality locations s, respectively. Then, $LZ_1(s_i) = \boldsymbol{\Psi}^{\boldsymbol{T}}(s_i)\boldsymbol{\alpha} + w(s_i)$ where $\boldsymbol{w}(s) = (w(s_1), w(s_2), \dots, w(s_m))^T$ is the vector of malaria-related spatial random effects predicted at mortality locations s. Conditional on $\boldsymbol{w}(s')$ and the covariance parameters of the malaria spatial process, $\boldsymbol{w}(s)$ have a Gaussian distribution and therefore the predicted malaria covariate $\boldsymbol{LZ_1}(s)$ at the mortality locations s will be also Gaussian,

$\boldsymbol{LZ_1}(s)|\boldsymbol{\alpha}, \boldsymbol{w}(s'), \boldsymbol{\Psi}(s), \phi, \sigma_w^2, \sim N(\boldsymbol{\Psi}^{\boldsymbol{T}}(s)\boldsymbol{\alpha} + \Sigma_{w'w}\Sigma_{w'}^{-1}\boldsymbol{w}(s'), \Sigma_w - \Sigma_{w'w}\Sigma_{w'}^{-1}\Sigma_{ww'})$ where $(\Sigma_{w'w})_{ij} = (\Sigma_{ww'})_{ji} = \sigma_w^2 exp(-\phi d_{i'j})$.

The joint posterior distribution is then given by

$$\prod_{\boldsymbol{i}} [\, t_j(s_i) \,|\boldsymbol{\beta}, b_d, W(s_i)\, \varepsilon_{dk}, \boldsymbol{X_j}(s_i), \boldsymbol{Z_d}(s_i), r\,][\, \boldsymbol{W}(s)|\sigma^2, \rho][\boldsymbol{\varepsilon_d}|\, \sigma_d^2, \gamma]$$

$$[\boldsymbol{LZ_1}(s)|\boldsymbol{a}, \boldsymbol{w}(s'), \boldsymbol{\Psi}(s), \phi, \sigma_w^2,][\boldsymbol{w}(s')|\phi, \sigma_w^2][\boldsymbol{a}, \boldsymbol{\beta}, b_d, \sigma^2, \sigma_d^2, \sigma_w^2, \phi, \gamma, \rho, r]$$

Model parameters were estimated using Markov Chain Monte Carlo (MCMC) simulation (George and McCulloch, 1993). We run a two chain algorithm for 250 000 iterations with an initial burn-in of 20,000 iterations. Convergence was assessed by visual inspection of trace and density plots and analytically by the Gelman and Rubin diagnostic (Rubin and Gelman, 1992).

Chapter 3: Geographical variations of the effects of health interventions on all-cause under-five mortality in Uganda

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Abstract

Background: To mitigate the under-five mortality (U5M) rate, assessing effects of health interventions especially at local scales, is critical because national averages can obscure important sub-national disparities. Sub-national estimates can guide control programmes to choose and implement interventions that are relevant at a local scale. The purpose of our study was to quantify the effects of interventions on U5M rate at national and sub-national scales, and to identify interventions associated with largest reductions in U5M rate at the sub-national scale.

Methods: Data on U5M, intervention and socio-demographic indicators were obtained from the 2011 Uganda Demographic and Health Survey (DHS). Climatic data were extracted from remote sensing sources. Bayesian geostatistical Weibull proportional hazards models with spatially varying effects at sub-national scales were used to quantify associations between all-cause U5M and interventions at national and regional levels. Bayesian variable selection was used to select most important determinants of mortality. High mortality clusters within the country were identified by means of Bayesian kriging.

Results: At the national level, interventions associated with highest reduction in U5M were artemisinin-combination therapy (Hazard ratio (HR)=0.60; 95% BCI: 0.11, 0.79), initiation of breastfeeding within one hour of birth (HR=0.70; 95% BCI: 0.51, 0.86), intermittent preventive treatment (IPT) (HR=0.74; 95% BCI: 0.67, 0.97) and insecticide treated nets (ITN) access (HR=0.75; 95% BCI: 0.63, 0.84). Effects of interventions on U5M varied between regions. In Central 2, Mid-Western and South-West, largest reduction in U5M was associated with ITN access. In Mid-North and West-Nile, improved source of drinking water explained most U5M reduction. In North-East, improved sanitation facilities accounted for the highest decline in U5M. In Kampala and Mid-Eastern, IPT had the largest impact on mortality. In Central 1 and East-Central, Oral Rehydration Solution and postnatal care were associated with highest decreases in U5M respectively. Highest mortality clusters were concentrated in North-East, West-Nile, Mid-North, East-Central, Central 1, South-West and Mid-Western.

Conclusion: Effects of interventions on U5M varied between regions, with high mortality clusters within regions. Therefore, designing and implementing region-specific interventions and targeting high mortality clusters, by improving coverage of most important interventions may be an essential step towards reducing U5M in Uganda.

Key words: DHS, Under-five mortality, interventions, sub-national scale, geographical variations, high mortality clusters, Bayesian proportional hazards geostatistical models, Uganda

3.1 Introduction

The under-five mortality rate (U5MR) is one of the fundamental indicators of a child's health and economic development of the general population (Mosley and Chen, 1984). The government of Uganda has progressed in reducing the U5MR although the burden is still high. According to the Demographic and Health Surveys (DHS), Uganda's U5MR declined from 137 in 2006 to 90 deaths per 1 000 live births in 2011 (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007). During the same period, health interventions coverage also improved country-wide. For example, the percentage of children receiving vitamin A supplements in the past 6 months increased from 36% to 57%. The percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy increased from a mere 3% to 69%. Other health interventions improved as well (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007).

Despite the recent progress at the national level, there are remarkable sub-national variations in under-five mortality and health intervention coverage. The lowest U5MR of 56 and the highest of 152 deaths per 1 000 live births occurred in Kampala and the North-East regions respectively. The coverage of vitamin A supplements was 30% in Central 1 compared to 74% in the North-East and skilled delivery varied from 31% in the North-East to 93% in Kampala. Substantial variations in U5MR and the coverage of other health interventions are also observed in other regions (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Such disparities may result into discrepancies in the effects of interventions at regions hence variations in regional mortality rates. This implies that estimates of the geographical variations of the effects of health interventions on the U5MR inform about the effectiveness of interventions at a local scale. Therefore, a step towards reducing under-five mortality is to improve the effectiveness of interventions at a sub-national scale. Moreover, U5MRs may depend on other factors, such as the socio-economic geographic disparities (Bbaale, 2015), making the effect of interventions at the national level different from that at the local scale. This suggests the need to estimate intervention effects adjusting for socio-economic confounders.

In Uganda, there is sparsity in the literature of studies estimating the relation between under-five mortality and health interventions at a local scale. In addition, most studies that assessed the under-five mortality and health interventions relation were not carried out at the national scale. For example, Bacillus Calmette Guerin (BCG) vaccination was associated with a lower rate of death among children aged between one and five years in a community-based prospective cohort study in Eastern Uganda (Nankabirwa et al., 2015). A volunteer community health worker child health promotion model was related to child mortality declines in rural South-Western Uganda (Brenner et al., 2011).

Household surveys provide the best source of national data to monitor progress of the U5MR and the implemented interventions. Uganda has conducted the national DHS in 2011 and it provides the most reliable mortality and interventions data with national coverage. To date, a few national studies in Uganda used DHS data to quantify the relationship between health interventions and child mortality. However, these studies assessed only one category of child health interventions i.e. vaccinations (Bbaale, 2015). Furthermore, previous research in other settings has used DHS data to evaluate effects of health interventions on under-five mortality at the global (McGovern and Canning, 2015) and sub-continental (Corsi and Subramanian, 2014) level. However, former studies did not take into account geographical variations in the coverage of health interventions that may influence under-five mortality patterns (Kazembe and Mpeketula, 2010). To our understanding, analyses quantifying the effects of health interventions on under-five mortality at a sub-national scale have not been carried out. Sub-national estimates of the geographical distribution of the effects of health interventions can guide control programmes to choose and implement most important interventions at a local scale. Moreover, limited studies in Uganda have assessed spatial variations in under-five mortality to identify high mortality clusters. For instance, Kazembe et al used census data to assess within country geographical variation of under-five mortality and produced a country-wide mortality map (Kazembe et al., 2012). However, this study did not identify areas of high under-five mortality concentration within regions.

The objective of the present study is to estimate geographical variation in the effects of health interventions (i.e. control interventions of malaria, Water, Sanitation and Hygiene (WASH), reproductive health, breastfeeding, vaccinations, micronutrient supplementation and treatments) on U5MR at the national and sub-national scale, to identify interventions associated with the largest reduction in mortality at a sub-national scale, and to estimate hotspots of the under-five mortality in Uganda. Bayesian geostatistical Weibull proportional hazards models were applied to the DHS data and spatially varying covariates were introduced to assess the effects of interventions at a local scale. The models were adjusted for socio-demographic and environmental/climatic factors. Bayesian kriging was used to estimate hotspots of under-five mortality. Results can inform control programs to select locally adapted interventions which may reduce regional variation in all-cause under-five mortality, and consequently result into achieving national Sustainable Development Goal mortality target of reducing U5MR to no more than 25 deaths per 1 000 live births by 2030 (World Health Organization, 2015b).

3.2 Materials and methods

3.2.1 Country profile

Uganda lies across the equator right in the heart of Africa in East Africa. The country is bordered by Democratic Republic of Congo in the West, Kenya in the East, Rwanda in the South West, Tanzania in the South and Sudan in the north making Uganda a land locked country in East Africa. Uganda is roughly the size of England, covering a total area of about 241,000 square kilometres, with a population of approximately 44 million people. The country is divided into 116 districts grouped into 15 regions. Uganda's population is largely young with 50% aged between 0 – 15 years. The population of children less than five years is nearly 20% (Uganda Bureau of Statistics (UBOS) and ICF, 2018)

3.2.2 Ethical approval

We used secondary data in this research article that was made available to us by the Uganda Bureau of Statistics (UBOS) and the DHS Program (www.dhsprogram.com). Ethical approval has been obtained by the above bodies that collected the primary data.

3.2.3 Data and sources

3.2.3.1 Mortality

All-cause child mortality data was obtained from women birth histories available in the 2011 DHS which took place from May to December in 2011. A representative sample of 10 086 households was selected for the 2011 UDHS using a stratified two-stage cluster design. In the first stage, 404 clusters were selected from a list of clusters for the 2009/10 Uganda National Household Survey. The second stage involved selecting households from a complete listing of households in each cluster. Nearly, 8 674 women aged 15-49 who were either permanent residents of the households or visitors who slept in the households the night before the survey were eligible to be interviewed on characteristics regarding their children. Mortality data were collected on 7 878 children representing the number of children born in the period of five years preceding the date of the survey.

3.2.3.2 Health interventions

The DHS captures data relating to a number of health interventions including malaria, micronutrients intake and treatments depending on whether they were used in the previous night of the survey, seven days or six months and two weeks prior to the survey. Such coverages may not reflect the extent of intervention utilization in the five years preceding the survey. Thus, to obtain representative estimates of intervention coverages for the period of five years preceding the 2011 DHS, we averaged health intervention coverages of the 2006 and 2011 DHS. The 2006 DHS collected data on malaria control interventions different from those in the 2011 DHS, that is, households with at least one Insecticide Treated Nets (ITN), under-fives sleeping under an ITN and Indoor Residual Spraying (IRS). For consistency, interventions of the 2009 Uganda Malaria Indicator Survey (MIS) were utilized since they were matching with those in the 2011 DHS.

Health interventions considered in this paper comprise of malaria, Water, Sanitation and Hygiene (WASH) practices, reproductive health, breastfeeding, vaccinations, micronutrients supplementation and treatments of diseases. Coverages of all health interventions were aggregated at the cluster level (McGovern and Canning, 2015) because data on various interventions such as the vaccination status of dead children are not reported at an individual level in the DHS.

Data on malaria interventions were collected by means of household questionnaires and included use and ownership of ITN and IRS. Standard guidelines of the Roll Back Malaria were followed in the generation of malaria intervention coverage indicators (World Health Organisation, 2013b). The ITN use indicators derived in this analysis comprised the percentage of children less than 5 years and the percentage of the population who slept under an ITN on the night preceding the survey and the percentage of ITN used by the population in a household the previous night of the survey. The indicator on IRS coverage was generated as the percentage of households sprayed in the past 12 months. ITN ownership indicators included the percentage of households with at least one ITN, the percentage of households with one ITN for every two people, and the percentage of the population with access to an ITN within their household. WASH interventions included the percentage of households with an improved source of drinking water, the percentage of households with improved sanitation facilities and the percentage of households with both water and soap/detergent at hand washing places.

Data on the coverage of reproductive health, breastfeeding, vaccinations, micronutrients supplementation and treatment interventions were collected from all eligible women using the woman's questionnaire. They comprise; reproductive health interventions (the percentage of married women using any family planning method, percentage of pregnant mothers receiving antenatal care (ANC) from a skilled provider, the percentage of pregnant women making four or more ANC visits during their entire pregnancy, the percentage of women who received intermittent preventive treatment for malaria during pregnancy, the percentage of births that took place with the assistance of a skilled provider and the percentage of newborns receiving first postnatal checkup from a skilled provider within two days after delivery, breastfeeding (the percentage of infants who started breastfeeding within one hour of birth and the percentage of infants exclusively breastfed during the first six months after birth), vaccinations (the percentage of last-born child fully protected against neonatal tetanus, the percentage of children vaccinated with BCG and measles, the percentage of children with complete vaccination of DPT and polio), micronutrients supplementation (the percentage of children receiving vitamin A supplements, the percentage of children receiving iron supplements in the past 7 days and the percentage of children living in households with iodized of salt) and treatments of diseases (the percentage of children with symptoms of acute respiratory infections (ARIs) who took antibiotics, the percentage of children with diarrhoea given fluid from oral rehydration solution (ORS) sachets or recommended home fluids (RHF), the percentage of children with diarrhoea given zinc sulphates, the percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy and those dewormed in the past 6 months).

Interventions with coverage equal to or greater than 95% and those lacking sufficient coverage within the regions were excluded from the analysis due to lack of variation in estimating their relation with mortality. These were the percentage of households sprayed with IRS in the past 12 months (%H_IRS, 7%), the percentage of pregnant mothers receiving ANC from a skilled provider (ANC provider, 95%), the percentage of children living in households with iodized salt (iodized salt; 99%) and the percentage of children with diarrhoea given zinc sulphates (Zinc; 2%). Table 3.1 provides a list of health interventions assessed in the study.

Table 3. 1: Health interventions, Uganda DHS 2006, 2009 and 2011

Intervention	Description of the intervention
Malaria	
%H_IRS	Percentage of households sprayed with Indoor Residual Spraying (IRS) in the past 12 months
%H_1ITN	Percentage of households with atleast one ITN
%H_1ITN2	Percentage of households with atleast one ITN for every two people
%P_ITNA	Percentage of population with access to an ITN within their household (Percentage of the population that could sleep under an ITN, if each ITN in the household were used by up to two people)
%P_ITNS	Percentage of the population in a household that slept under an ITN the previous night of the survey
%P_ITN5	Percentage of children under 5 years in a household who slept under an ITN the previous night of the survey
%P_ITNU	Percentage of existing ITNs used by the population in a household the previous night of the survey
WASH	
Improved water	Percentage of households with improved source of drinking water
Improved sanitation	Percentage of households using improved sanitation facilities
P_wsoap	Percentage of households with soap or detergent and water at hand washing places
Reproductive health	
Family planning	Percentage of married women using any family planning method
ANC provider	Percentage of pregnant mothers receiving ANC from a skilled provider
4+ ANC visits	Percentage of pregnant women making four or more ANC visits during their entire pregnancy
IPT	Percentage of women who received intermittent preventive treatment for malaria during pregnancy
Skilled delivery	Percentage of births that took place with the assistance of a skilled provider
Postnatal care	Percentage of newborns receiving first postnatal checkup from a skilled provider within two days after delivery
Breastfeeding	
Within one hour	Percentage of infants who started breastfeeding within one hour of birth
Exclusive	Percentage of infants exclusively breastfed during the first six months after birth
Vaccinations	
Tetanus toxoid	Percentage of last-born child fully protected against neonatal tetanus
BCG	Percentage of children vaccinated against BCG
DPT	Percentage of children with complete vaccination of DPT
Polio	Percentage of children with complete vaccination of polio
Measles	Percentage of children vaccinated against measles
Micronutrients	
VitaminA_sup	Percentage of children receiving vitamin A supplements in the past 6 months
Iron_sup	Percentage of children receiving iron supplements in the past 7 days
Iodized salt	Percentage of children living in households with iodized of salt
Treatments	
Antibiotics	Percentage of children with ARIs symptoms who took antibiotics
ORS or RHF	Percentage of children with diarrhoea given fluid from oral rehydration solution (ORS) sachets or recommended home fluids (RHF)
Zinc	Percentage of children with diarrhoea given zinc sulphates
ACT	Percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy (ACT)
Deworming	Percentage of children given deworming medication in the past 6 months

3.2.3.3 Environmental/climatic factors

Environmental/climatic factors were obtained from remote sensing sources and aggregated at the cluster level. Temporal predictors such as Land Surface Temperature (LST), rainfall and Normalized Difference Vegetation Index (NDVI) were averaged during January to December 2011. Land cover types were provided in 17 categories according to the International Global Biosphere Programme (IGBP) classification scheme and re-grouped into three categories, that is, urban, forest and crops. Distance to permanent water bodies was calculated based on the water category of the land cover data. Supplementary Table 3.1 contains a list of environmental/climatic factors together with their spatio-temporal resolutions and data sources.

3.2.3.3 Demographic and socio-economic factors

Demographic and socio-economic proxies including maternal (education, literacy, residence, age at birth, early pregnancy termination, number of children born, working status) and child (sex, birth order, birth interval, mode of delivery) characteristics were incorporated in the analysis at an individual level and were captured using the household questionnaire. The household asset score was aggregated at the cluster level and considered in the analysis as a socio-economic proxy.

3.2.4 Statistical analysis

A Bayesian geostatistical proportional hazards model assuming a baseline Weibull hazard function was fitted to quantify the associations between health interventions' coverage and U5MR, and to identify the most important interventions. Environmental/climatic, demographic and socio-economic factors were included in the model as potential confounders. Spatial correlation between clusters was modeled by a Gaussian process with a covariance matrix measuring correlation between any pair of clusters by an exponential function of the distance between them. Our model assumed that the relation between health interventions and mortality varied across regions by including spatially varying coefficients to capture the intervention effects. Spatial dependence in the interventions' effects was modeled by region-specific random effects assuming conditional autoregressive prior distributions.

To identify the most important interventions and characteristics associated with the under-five mortality, Bayesian geostatistical variable selection was used adopting a stochastic search approach. The selection consisted of introducing a binary indicator parameter for each of socio-demographic, IRS and land cover variables with values defining the covariate-specific inclusion probability in the model. We assumed that the indicator arises from a Bernoulli prior distribution with probability defining the variable-specific inclusion probability in the model. We have chosen a spike and slab prior for the regression coefficients which is a mixture of normals with mixing proportion equal to the inclusion probability. The spike component shrinks the regression coefficient to zero when the variable is excluded and the slab assumes a non-informative normal prior distribution when the variable has high inclusion probability (i.e. equal to or larger than 50%). Environmental/climatic indicators (LST, NDVI, distance to permanent bodies and rainfall) were included or excluded in the model in a linear or categorical form. We introduced indicators with a multinomial prior distribution with three parameters corresponding to the probabilities of exclusion of a variable, inclusion in linear or categorical form. ITN coverage indicators were highly correlated with more than 85%, therefore, only one (or none) ITN indicator among those measuring ownership and one (or none) ITN indicator among those defining use was selected. The ITN indicator with the highest probability of inclusion in each category was included in the final model. Health intervention indicators were standardized and a separate model adjusting for possible confounders was fitted for each selected intervention.

Under-five baseline mortality rates at unsampled locations were predicted by means of Bayesian kriging over a grid of 61 062 pixels at a 2 by 2 km spatial resolution covering the entire country. Bayesian kriging was performed in R computing and statistical software version 3.1.3 (R Development Core Team, 2018). Maps were generated using ArcGIS version 10.5 (ArcGIS version 10.5, Esri, Redlands, CA, USA). Descriptive data analysis was carried out in STATA version 14.0 (Stata Corporation, College Station, TX, USA). Bayesian variable selection and model fit were implemented in OpenBUGS 3.2.3 (Imperial College and Medical Research Council, London, UK). The effects of health interventions on U5MR were summarized by posterior medians of their hazard ratios (HR) and the corresponding 95% Bayesian credible intervals (95% BCI). An estimate is considered statistically significant if its 95% BCI excludes one. Details on the Bayesian geostatistical methods are provided in supplementary file 3.1.

3.3 Results

Table 3.2 provides a summary of the U5MR estimates and the coverage of health interventions at regional and country levels. The overall U5MR was 90 deaths per 1 000 live births. There were large regional variations in mortality rates with the lowest (56) in Kampala and the highest (152) deaths per 1 000 live births in the North-East. The discrepancies in U5MR across regions suggest that mortality rates may be influenced by region-specific factors. Supplementary Figure 3.1 presents the corresponding geographical variation in the U5MR in Uganda.

Table 3. 2: U5MR and coverage of interventions (%) at the regional and country levels, Uganda DHS 2006 and 2011

Malaria	Central1	Central2	Kampala	East-Central	Mid-Eastern	North-East	Mid-North	West-Nile	Mid-Western	South-West	Country
%H_IRS	1	3	5	1	2	2	49	1	0	1	**7**
%H_1ITN	47	42	54	36	58	67	65	67	51	51	**54**
%H_1ITN2	24	21	37	11	19	27	23	25	21	20	**22**
%P_ITNA	37	33	47	23	38	47	45	47	38	37	**39**
%P_ITNS	27	24	40	19	33	45	34	40	29	26	**31**
%P_ITN5	47	43	62	36	50	58	53	60	50	45	**38**
%P_ITNU	27	24	40	19	33	45	35	41	28	26	**31**
WASH											
Improved water	45	69	90	78	83	85	76	71	58	45	**69**
Improved sanitation	25	25	17	15	9	3	5	4	9	7	**14**
P_wsoap	45	27	42	12	9	2	10	5	32	16	**27**
Reproductive health											
Family planning	35	35	48	28	23	8	17	14	27	28	**27**
ANC provider	89	94	97	92	95	97	96	98	95	95	**95**
4+ ANC visits	52	49	64	44	39	56	48	62	46	45	**48**
IPT	18	19	23	15	26	29	19	18	27	24	**23**
Skilled delivery	57	60	91	61	47	31	42	47	44	37	**50**
Postnatal care	11	8	29	8	14	19	13	11	9	1	**11**
Breastfeeding											
Within one hour	42	52	56	55	41	70	40	38	55	45	**48**
Exclusive	56	64	65	53	58	52	58	57	56	48	**52**
Vaccinations											
Tetanus toxoid	71	80	80	80	81	93	82	85	79	80	**80**
BCG	81	92	93	92	97	100	95	98	93	86	**93**
DPT	59	63	71	57	70	90	70	72	74	70	**68**
Polio	51	57	64	54	62	65	58	61	69	71	**61**
Measles	67	69	77	65	70	91	76	71	79	69	**72**
Micronutrients											
VitaminA_sup	30	36	41	56	50	74	54	42	55	37	**47**
Iron_sup	4	4	3	5	8	12	12	9	5	3	**7**
Iodized salt	99	98	100	98	99	100	99	96	94	96	**98**
Treatments											
Antibiotics	55	49	72	33	46	30	43	54	58	42	**47**
ORS or RHF	44	52	48	49	44	77	53	46	37	28	**46**
Zinc	1	2	2	2	1	1	2	3	3	0	**2**
ACT	39	34	42	34	31	81	43	40	37	30	**36**
Deworming	47	45	58	40	48	65	44	38	51	41	**46**
Mortality rates											
U5MR	83	79	56	104	80	152	76	100	95	99	**90**

Among the malaria interventions, the percentage of households with at least one ITN has the highest coverage reaching 54% and ranges from 36% in East-Central to 67% in each region of North-East and West-Nile. IRS is the malaria intervention with the lowest coverage of 7% varying from 0% in Mid-Western to 49% in the Mid-North.

Overall, nearly seven out of every ten households had an improved source of drinking water, but the percentage of households having improved sanitation facilities was lower (14%) and varied from 3% in the North-East to 25% in each region of Central 1 and Central 2.

Amongst the reproductive health interventions, ANC services had the highest coverage with 95% of pregnant women in the country receiving services from a skilled provider. There were no outstanding regional differences. Postnatal care was the least implemented with 11% of the newborns receiving the intervention within the country. The lowest coverage was observed in South-West (1%) and the highest of 29% in Kampala. Initiation of breast feeding was not widespread throughout the country with 48% of infants breastfed within one hour after delivery. The lowest coverage of 38% was observed in the West-Nile and the highest of 70% in the North-East.

Among vaccinations, BCG had the highest coverage (93%) and ranged from 81% in Central 1 to 100% in the North-East. The polio vaccine was the least effected with 61% nationally and varied from 51% in Central 1 to 71% in South-West.

Almost all children (98%) lived in households that use iodized salt. There was no variation in the use of iodized salt by region. Iron supplementation coverage was the lowest micronutrient intake nationally (7%) with Kampala and South-West having the lowest coverages of 3% per region compared with the North-East and Mid-North which had the highest of 12% in each region.

Treatments for ARI symptoms (47%), diarrhoea (46%) and deworming (46%) were approximately at the same level. However, the percentage of children who took antibiotics for ARIs ranged from 30% in the North-East to 72% in Kampala. South-West experienced the lowest percentage of children given ORS or RHF for diarrhoea (28%) while North-East had the highest of 77%. Country wide, 36% of children with fever during the two weeks prior to the survey took artemisinin-combination therapy (ACT) and varied from 30% in South-West to 81% in the North-East. Supplementary Figures 3.2 – 3.8 display the corresponding geographical distribution. The differences in the coverage of health interventions could be partly responsible for the observed disparities in the U5MR within Uganda (Supplementary Figure 3.1).

Table 3.3 presents results from the Bayesian geostatistical variable selection. Variables selected with 50% or higher inclusion probabilities were incorporated in the final model. For example, the WASH practices interventions that were incorporated into the final model were improved source of drinking water and improved sanitation facilities.

Table 3. 3: Posterior inclusion probabilities of health interventions, socio-economic and demographic characteristics

Variable	Inclusion probability (%)	Variable	Inclusion probability (%)
Malaria		T***reatments***	
ITN access		Antibiotics	55.0*
None	8.4	ORS or RHF	57.0*
%H_1ITN	27.2	ACTs	61.0*
%H_1ITN2	4.0	Deworming	81.0*
%P_ITNA	60.4*	***Socio-economic and demographic***	
ITN use		**Child**	
None	3.1	Sex	73.2*
%P_ITNS	19.1	**Maternal**	
%P_ITN5	12.3	Age at birth	100.0*
%P_ITNU	65.5*	Number of children	100.0*
WASH		Education level	70.2*
Improved water	66.6*	Residence (urban vs rural)	59.6*
Improved sanitation	52.2*	Working status	34.0
P_wsoap	23.8	**Household**	
Reproductive health		Age of head	0.0
Family planning	69.0*	Wealth index	81.2*
4+ ANC visits	25.0	***Environmental/Climatic factors***	
IPT	60.8*	Land cover	33.0
Skilled delivery	70.0*	**LST day:** None	73.0
Postnatal care	76.4*	LST day continuous	27.0
Breastfeeding		LST day categorical	0.0
Within one hour	73.8*	**LST night:** None	90.6
Exclusive	100.0*	LST night continuous	8.1
Vaccinations		LST night categorical	1.3
BCG	22.0	**NDVI:** None	41.2
DPT	83.0*	NDVI continuous	58.8*
Polio	14.8	NDVI categorical	0.0
Measles	83.4*	**Rainfall:** None	80.3
Micronutrients		Rainfall continuous	12.2
VitaminA_sup	60.0*	Rainfall categorical	8.5
Iron_sup	38.6	**d_water:** None	100.0
		d_water continuous	0.0
		d_water categorical	0.0

*Selected variables with >=50% inclusion probability: LST - Land surface temperature: NDVI – Normalized difference in vegetation index: d_water -Distance to permanent water bodies

Results (Tables 3.4 and 3.5) show that amongst national effects, ACT, (HR = 0.60; 95% BCI: 0.11, 0.79); initiation of breast feeding within one hour of birth, (HR = 0.70; 95%

BCI: 0.51, 0.86); intermittent preventive treatment (IPT), (HR = 0.74; 95% BCI: 0.67, 0.97) and ITN access, (HR = 0.75; 95% BCI: 0.63 0.84) were the most important interventions. The effects of other health interventions which had an important association with child mortality at the national level, were more or less comparable and ranged from a hazard ratio of 0.80 to 0.89.

Table 3. 4: Posterior estimates for the effects of interventions at the national and sub-national scale on the U5MR adjusted for socio-economic, demographic and environmental/climatic factors

	Malaria		WASH		Reproductive health			
Geographical scale	**%P_ITNA HR (95% BCI)**	**%P_ITNU HR (95% BCI)**	**Improved water HR (95% BCI)**	**Improved sanitation HR (95% BCI)**	**Family planning HR (95% BCI)**	**IPT HR (95% BCI)**	**Skilled delivery HR (95% BCI)**	**Postnatal care HR (95% BCI)**
National	[a]0.75 (0.63, 0.84)*	0.88 (0.83, 0.94)*	0.76 (0.70, 0.81)*	0.86 (0.74, 0.91)*	1.04 (0.92, 1.10)	0.74 (0.67, 0.97)*	0.84 (0.78, 0.90)*	0.80 (0.74, 0.89)*
Region								
Central 1	0.54 (0.35, 0.81)*	0.56 (0.51, 0.63)*	0.99 (0.91, 1.14)	1.13 (0.89, 1.36)	1.29 (0.82, 2.08)	0.73 (0.51, 0.98)*	1.09 (0.84, 2.26)	0.82 (0.61, 0.96)*
Central 2	0.63 (0.51, 0.85)*	0.94 (0.85, 1.07)	0.87 (0.67, 0.98)*	0.99 (0.79, 1.23)	0.70 (0.46, 0.85)*	0.82 (0.57, 1.72)	1.06 (0.80, 1.22)	0.73 (0.63, 0.97)*
East-Central	0.98 (0.73, 1.33)	1.02 (0.90, 1.13)	0.82 (0.70, 0.91)*	1.25 (0.76, 1.90)	1.20 (0.85, 1.98)	0.83 (0.58, 1.12)	1.25 (0.94, 1.62)	0.76 (0.65, 0.95)*
Kampala	0.70 (0.51, 0.87)*	0.81 (0.73, 0.97)*	0.77 (0.69, 0.92)*	0.89 (0.66, 1.17)	0.85 (0.73, 0.97)*	0.25 (0.14, 0.44)*	0.81 (0.72,0.92)*	0.58 (0.50, 0.78)*
Mid-Eastern	1.04 (0.45, 2.36)	0.87 (0.67, 1.31)	0.71 (0.59, 0.77)*	0.84 (0.65, 1.11)	1.29 (0.93, 1.88)	0.35 (0.23, 0.73)*	1.15 (0.72, 1.58)	0.92 (0.68, 1.17)
Mid-North	0.82 (0.54, 1.15)	0.77 (0.62, 0.87)*	0.50 (0.38, 0.57)*	1.02 (0.76, 1.29)	1.03 (0.79, 1.28)	1.12 (0.64, 1.50)	0.81 (0.61, 0.95)*	1.05 (0.58, 1.29)
Mid-Western	0.46 (0.21, 0.84)*	1.02 (0.91, 1.35)	1.04 (0.81, 1.41)	1.01 (0.77, 1.17)	1.00 (0.48, 1.56)	0.60 (0.46, 0.85)*	0.49 (0.40, 0.68)*	0.70 (0.45, 0.84)*
North-East	1.49 (0.96, 2.14)	1.23 (0.99, 1.39)	1.09 (0.92, 1.42)	0.50 (0.39, 0.66)*	0.77 (0.62, 0.89)*	0.83 (0.56, 1.28)	0.77 (0.68, 0.86)*	1.06 (0.87, 1.35)
South-West	0.34 (0.22, 0.63)*	0.75 (0.64, 0.87)*	0.89 (0.80, 1.02)	0.51 (0.28, 0.67)*	1.38 (0.83, 2.08)	0.82 (0.46, 1.32)	0.68 (0.52, 0.82)*	0.71 (0.56, 1.21)
West-Nile	1.24 (0.93, 1.87)	0.95 (0.83, 1.05)	0.30 (0.23, 0.48)*	0.69 (0.53, 0.87)*	0.81 (0.65, 0.96)*	0.68 (0.45, 0.93)*	0.69 (0.23, 0.98)*	0.82 (0.60, 1.24)
Spatial parameters	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**
Spatially varying[b]	0.65 (0.43, 0.90)	0.49 (0.43, 0.54)	0.59 (0.45, 0.64)	0.63 (0.57, 1.11)	0.59 (0.38, 0.84)	0.58 (0.48, 1.03)	0.54 (0.35, 0.84)	0.51 (0.37, 0.47)
Spatial process	0.29 (0.16, 0.34)	0.30 (0.21, 0.36)	0.21 (0.15, 0.25)	0.23 (0.19, 0.27)	0.27 (0.19, 0.31)	0.15 (0.11, 0.20)	0.31 (0.19, 0.41)	0.29 (0.16, 0.34)
Range (km)[c]	3.33 (0.55, 5.83)	1.06 (0.32, 4.21)	0.46 (0.35, 3.83)	0.56 (0.36, 1.84)	0.81 (0.31, 1.38)	0.37 (0.32, 3.49)	0.71 (0.32, 3.18)	3.33 (0.53, 5.83)
Other parameters								
Shape parameter[d]	0.44 (0.41, 0.48)	0.41 (0.36, 0.49)	0.35 (0.32, 0.38)	0.38 (0.28, 0.42)	0.30 (0.27, 0.36)	0.37 (0.31, 0.43)	0.44 (0.39, 0.47)	0.46 (0.42, 0.53)

*Significant and protective, HR; Hazard ratio, %P_ITNA; Percentage of population with access to an ITN within their household, %P_ITNU; Percentage of existing ITNs used by the population in a household the previous night of the survey, [a] Intervention coverage was modeled on a standardized scale; therefore results are interpreted as associations. The coverage of P_ITNA was associated with a reduction in the mortality rate of 0.25; (HR = 0.75; 95% BCI: 0.63, 0.84), [b]Indicates the degree of variation of intervention effects in the country, [c]Measures distance after which spatial correlation between mortality at clusters becomes negligible and [d]Describes the trend in the baseline mortality hazard over time

Table 3. 5: Posterior estimates for the effects of interventions at the national and sub-national scale on the U5MR adjusted for socio-economic, demographic and environmental/climatic factors

	Breastfeeding	Vaccinations		Micronutrients	Treatments		
Geographical scale	**Within one hour HR (95% BCI)**	**DPT HR (95% BCI)**	**Measles HR (95% BCI)**	**VitaminA_sup HR (95% BCI)**	**Deworming HR (95% BCI)**	**ORS or RHF HR (95% BCI)**	**ACT HR (95% BCI)**
National	0.70 (0.51, 0.86)*	0.85 (0.72, 0.97)*	0.82 (0.69, 0.89)*	0.88 (0.78, 0.97)*	0.89 (0.84, 0.94)*	0.86 (0.78, 0.92)*	0.60 (0.11, 0.79)*
Region							
Central 1	0.55 (0.51, 0.92)*	0.60 (0.44, 0.81)*	0.63 (0.39, 0.88)*	0.74 (0.58, 0.97)*	0.76 (0.37, 1.69)	0.30 (0.21, 0.74)*	0.41 (0.11, 0.94)*
Central 2	0.63 (0.54, 1.43)	0.95 (0.75, 1,23)	0.79 (0.48, 1.47)	0.86 (0.64, 1.15)	1.25 (0.78, 1.89)	1.27 (0.79, 1.42)	0.56 (0.31, 1.10)
East-Central	0.88 (0.73, 1.72)	0.74 (0.55, 1.07)	0.97 (0.61, 1.36)	1.09 (0.81, 1.53)	1.08 (0.93, 1.24)	1.35 (0.89, 2.72)	0.84 (0.54, 1.52)
Kampala	0.53 (0.39, 0.91)*	0.82 (0.70, 1.25)	0.63 (0.29, 0.94)*	0.77 (0.56, 1.17)	0.72 (0.60, 0.89)*	0.34 (0.18, 0.72)*	0.32 (0.09, 0.80)*
Mid-Eastern	0.93 (0.83, 1.90)	0.67 (0.47, 0.93)*	1.38 (0.85, 2.01)	1.12 (0.64, 2.20)	0.50 (0.23, 1.42)	2.30 (0.79, 2.72)	1.33 (0.78, 1.78)
Mid-North	0.91 (0.83, 1.46)	0.69 (0.38, 0.85)*	0.71 (0.47, 1.31)	1.05 (0.73, 1.63)	1.16 (0.79, 1.88)	1.05 (0.46, 1.34)	0.77 (0.40, 1.66)
Mid-Western	0.71 (0.68, 1.27)	1.12 (0.76, 1.42)	0.88 (0.55, 1.21)	1.12 (0.78, 1.63)	0.93 (0.73, 1.14)	0.92 (0.68, 1.21)	0.49 (0.22, 0.79)*
North-East	0.98 (0.91, 1.69)	0.96 (0.73, 1.32)	1.29 (0.93, 1.60)	1.31 (0.93, 1.65)	1.18 (0.99, 1.30)	1.10 (0.86, 1.42)	0.89 (0.72, 1.44)
South-West	0.56 (0.42, 0.82)*	1.61 (0.63, 2.25)	0.64 (0.38, 0.92)*	0.63 (0.43, 0.81)*	0.74 (0.62, 0.92)*	0.75 (0.54, 0.85)*	0.40 (0.23, 0.61)*
West-Nile	0.63 (0.55, 0.98)*	0.86 (0.62, 0.98)*	0.65 (0.29, 1.23)	0.49 (0.34, 0.67)*	0.85 (0.73, 0.98)*	0.75 (0.28, 1.75)	0.66 (0.29, 3.81)
Spatial parameters	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**
Spatially varying[b]	0.50 (0.33, 0.72)	0.62 (0.43. 0.80)	0.52 (0.34, 1.12)	0.56 (0.36, 0.75)	0.58 (0.36, 0.98)	0.79 (0.52, 0.92)	0.66 (0.42, 1.56)
Spatial process	0.13 (0.09, 0.22)	0.27 (0.19, 0.36)	0.23 (0.18, 0.30)	0.15 (0.12, 0.22)	0.27 (0.22, 0.34)	0.20 (0.18, 0.24)	0.36 (0.27, 0.51)
Range (km)[c]	0.71 (0.31, 3.78)	0.45 (0.31, 0.48)	0.70 (0.33, 1.51)	0.48 (0.31, 1.82)	0.57 (0.35, 1.56)	0.44 (0.35, 1.68)	0.60 (0.32, 2.01)
Other parameters							
Shape parameter[d]	0.37 (0.34, 0.41)	0.41 (0.33, 0.45)	0.40 (0.38, 0.44)	0.42 (0.38, 0.46)	0.35 (0.31, 0.42)	0.37 (0.32, 0.43)	0.44 (0.40, 0.53)

*Significant and protective, HR; Hazard ratio, ORS or RHF; Percentage of children with diarrhoea given fluid from ORS sachets or recommended home fluids, ACT; Percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy, [b]Indicates the degree of variation of intervention effects in the country, [c]Measures distance after which spatial correlation between mortality at clusters becomes negligible and [d]Describes the trend in the baseline mortality hazard over time

Sub-national analysis (Tables 3.4 and 3.5) indicates that in Central 2, Mid-Western and South-West regions, the largest reduction in the under-five mortality burden was associated with ITN access. The intervention also had a large effect on under-five mortality in Central 1 and Kampala. Improved source of drinking water explains most under-five mortality decrease in Mid-North and West-Nile. Improved source of drinking water was in addition associated with under-five mortality in Central 2, East-Central, Kampala and Mid-Eastern. Improved sanitation facilities were associated with the highest decline in under-five mortality in the North-East. The coverage of improved sanitation facilities also had an important association with mortality in South-West and West-Nile. In Kampala and Mid-Eastern, IPT had the largest impact on child mortality. The relation between IPT and mortality was statistically important in Central 1, Mid-Western and West-Nile. In Central 1 and East-Central, ORS or RHF and postnatal care were respectively associated with the highest decreases in under-five mortality. The coverage of postnatal had an important effect on child mortality in Central 1, Central 2, Kampala and Mid-Western. ORS or RHF was as well associated with lower mortality hazards in Kampala and South-West. There was no important association between family planning and under-five mortality at the national level. However, the intervention had an important effect on mortality in Central 2, Kampala, North-East and West-Nile. Supplementary Figures 3.9 – 3.13 summarize graphically the spatially varying effects of all interventions on U5MR.

Table 3.6 shows that socio-demographic and environmental/climatic factors were important determinants of under-five mortality. For instance, children born to mothers residing in urban areas had lower hazards of mortality relative to those in rural areas. Environmental/climatic factors were associated with lower hazards. Children living in areas with a higher NDVI have increased survival times.

Table 3. 6: Posterior estimates for the effects of socio-economic, demographic and environmental/climatic factors adjusted for in each health intervention model

	Malaria		WASH		Reproductive health			
	%P_ITNA	%P_ITNU	Improved water	Improved sanitation	Family planning	IPT	Skilled delivery	Postnatal care
Variable	HR (95% BCI)	HR (95% BCI)	HR (95% BCI)	HR (95% BCI)	HR (95% BCI)	HR (95% BCI)	HR (95% BCI)	HR (95% BCI)
Socio-demographic factors								
Child								
Sex								
Male	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Female	0.82(0.76,0.90)*	0.89(0.75,0.96)*	0.84(0.73,0.98)*	0.80(0.78,0.94)*	0.86(0.73,0.93)*	0.78(0.73,0.86)*	0.85(0.72,0.91)*	0.81(0.78,0.98)*
Maternal								
Age at birth								
15-24	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
25-29	0.60(0.51,0.72)*	0.61(0.55,0.69)*	0.62(0.48,0.71)*	0.59(0.52,0.66)*	0.62(0.46,0.75)*	0.69(0.54,0.73)*	0.63(0.49,0.80)*	0.67(0.60,0.73)*
30-34	0.51(0.42,0.58)*	0.38(0.35,0.46)*	0.38(0.31,0.45)*	0.44(0.37,0.51)*	0.43(0.30,0.59)*	0.49(0.42,0.52)*	0.45(0.32,0.62)*	0.52(0.47,0.57)*
35-49	0.62(0.58,0.69)*	0.50(0.41,0.59)*	0.50(0.44,0.56)*	0.52(0.44,0.58)*	0.48(0.33,0.71)*	0.61(0.48,0.71)*	0.50(0.34,0.73)*	0.71(0.62,0.77)*
#Children born	1.44(1.36,1.57)*	1.53(1.48,1.62)*	1.52(1.43,1.62)*	1.53(1.36,1.56)*	1.53(1.29,1.73)*	1.45(1.32,1.59)*	1.49(1.30,1.71)*	1.38(1.30,1.49)*
Residence								
Rural	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Urban	1.10(0.85,1.55)	1.03(0.86,1.25)	1.16(0.99,1.36)	1.11(0.92,1.26)	1.18(0.82,1.64)	1.20(1.01,1.38)	1.13(0.85,1.49)	1.00(0.96,1.12)
Education level								
None	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Primary	1.14(0.89,1.45)	1.14(0.89,1.45)	1.12(0.88,1.42)	1.13(0.89,1.43)	1.16(0.91,1.49)	1.13(0.89,1.44)	1.19(0.93,1.51)	1.11(0.87,1.41)
Secondary+	1.22(0.87,1.70)	1.22(0.87,1.71)	1.22(0.87,1.70)	1.21(0.86,1.69)	1.26(0.90,1.78)	1.21(0.86,1.69)	1.30(0.93,1.83)	1.20(0.86,1.68)
Household								
Wealth index	0.90(0.82,0.98)*	0.91(0.81,0.98)*	0.86(0.81,0.92)*	0.86(0.82,0.96)*	0.90(0.78,0.97)*	0.88(0.78,0.94)*	0.95(0.84,1.07)	0.84(0.81,0.90)*
Environmental/climatic factors								
NDVI	0.85(0.80,0.96)*	0.98(0.89,1.02)	0.83(0.77,0.92)*	0.95(0.92,1.02)	1.00(0.85,1.17)	0.95(0.90,0.98)*	0.95(0.86,1.05)	0.89(0.84,0.96)*

*Statistically significant

Table 3. 7: Posterior estimates for the effects of socio-economic, demographic and environmental/climatic factors adjusted for in each health intervention model

	Breastfeeding	Vaccinations		Micronutrients	Treatments		
	Within one hour	DPT	Measles	VitaminA_sup	Deworming	ORS or RHF	ACT
Variable	**HR (95% BCI)**	**HR (95% BCI)**	**HR (95% BCI)**	**HR (95% BCI)**	**HR (95% BCI)**	**HR (95% BCI)**	**HR (95% BCI)**
Socio-demographic factors							
Child							
Sex							
Male	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Female	0.86(0.72,0.98)*	0.91(0.87,0.96)*	0.79(0.65,0.92)*	0.87(0.69,0.98)*	0.84(0.77,0.91)*	0.85(0.62,0.99)*	0.78(0.69,0.85)*
Maternal							
Age at birth							
15-24	1.0	1.0	1.0	1.0	1.0	1.0	1.0
25-29	0.69(0.51,0.72)*	0.62(0.51,0.69)*	0.69(0.58,0.82)*	0.63(0.55,0.68)*	0.59(0.53,0.75)*	0.58(0.49,0.67)*	0.61(0.53,0.71)*
30-34	0.49(0.42,0.58)*	0.48(0.38,0.54)*	0.45(0.39,0.57)*	0.41(0.35,0.54)*	0.41(0.34,0.54)*	0.41(0.32,0.51)*	0.37(0.31,0.43)*
35-49	0.62(0.47,0.79)*	0.47(0.36,0.57)*	0.57(0.49,0.64)*	0.48(0.34,0.55)*	0.40(0.36,0.59)*	0.45(0.33,0.56)*	0.42(0.36,0.55)*
#Children born	1.46(1.28,1.51)*	1.59(1.48,1.67)*	1.39(1.30,1.45)*	1.54(1.34,1.78)*	1.69(1.57,1.72)*	1.59(1.44,1.79)*	1.63(1.56,1.70)*
Residence							
Rural	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Urban	1.06(0.87,1.45)	0.90(0.86,0.97)*	1.04(0.80,1.26)	1.23(0.89,1.47)	1.03(0.95,1.12)	1.18(0.80,1.62)	0.98(0.85,1.11)
Education level							
None	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Primary	1.25(0.91,1.47)	1.18(0.92,1.51)	1.18(0.92,1.52)	1.35(0.99,163)	1.15(0.90,1.47)	1.16(0.91,1.49)	1.29(0.93,1.67)
Secondary+	1.36(0.98,1.70)	1.27(0.90,1.79)	1.27(0.90,1.79)	1.27(0.94,1.67)	1.23(0.87,1.72)	1.24(0.88,1.73)	1.38(0.98,1.96)
Household							
Wealth index	0.91(0.80,0.98)*	0.93(0.81,0.98)*	0.93(0.87,0.96)*	0.87(0.81,0.98)*	0.92(0.91,0.98)*	0.88(0.82,0.97)*	1.03(0.92,1.21)
Climatic/Environmental factors							
NDVI	0.97(0.90,1.11)	1.06(0.99,1.15)	1.02(0.89,1.09)	0.98(0.88,1.10)	1.02(0.95,1.11)	1.01(0.86,1.13)	0.97(0.87,1.10)

*Statistically important

Highest mortality clusters are found in the North-East, West-Nile, areas around Lake Kyoga in the southern of Mid-North, East-Central in locations along the Victoria Nile River, the southern part of Central 1 stretching to the South-West region and along the country border in Mid-Western between Lakes Albert and Edward (Figure 3.1). Lowest mortality rates were estimated in Kampala, a large share of the Mid-North, areas around Lake Kyoga in the North-East, Mid-Eastern and East-Central, in the Mid-Western region around Lake George and a few spots in Central 2.

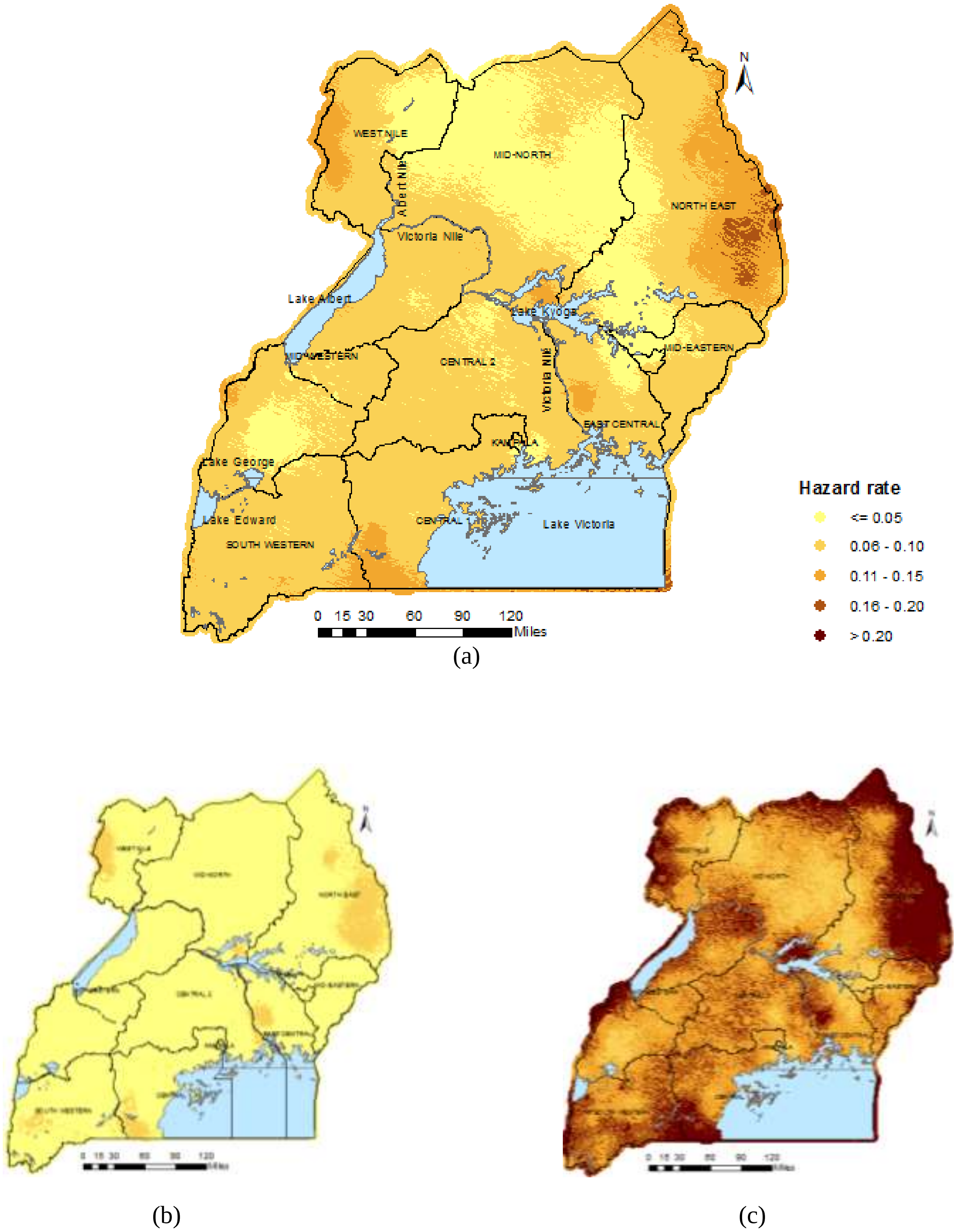

Figure 3. 1: Geographical distribution of predicted baseline mortality hazard rates on a log scale; (a) median, (b) 2.5th percentile and (c) 97.5th percentile.

3.4 Discussion

We quantified the effects of health interventions on all-cause under-five mortality at national and sub-national scales in Uganda. The analysis took into account confounding effects of socio-demographic and environmental/climatic factors which have been shown to be significantly related to mortality (Chin et al., 2011; Ezeh et al., 2014; Gebretsadik and Gabreyohannes, 2016; Kabagenyi and Rutaremwa, 2013; Nafiu, 2016; Nasejje et al., 2015; Rutstein, 2005; Thomson et al., 2005). We found strong geographical variations in the effects of health interventions on all-cause under-five mortality across Uganda. Also, the study identified areas of high under-five mortality concentration in the country.

Findings at the national level indicated that ACT, initiation of breast feeding within one hour of birth, IPT, ITN access and improved source of drinking water were the health interventions associated with a highest reduction in under-five mortality. However, these interventions were poorly implemented in the country with coverage below fifty percent yet the prevalences of diseases targeted by these interventions are high (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). For example, malaria prevalence was at least forty percent nationally and in eighty percent of the regions (Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010). Other interventions which were associated with a significant reduction in mortality include ITN use, improved sanitation facilities, skilled delivery, postnatal care, complete DPT and measles vaccination, vitamin A supplementation, deworming medication and ORS or RHF. These variables are among the essential health interventions that have been associated with a decrease in child mortality in a review by Lassi et al (Lassi et al., 2014). Also these findings are similar to results reported from analyses of DHS data (Bbaale, 2015) and community-based studies in Uganda (Brenner et al., 2011; Nankabirwa et al., 2015). Similar results were reported in other settings. For instance, Masanja et al in Tanzania (Masanja et al., 2008) analysed DHS data and found that increased coverage of key child-survival interventions, such as ITN, vitamin A supplementation, immunisation, and exclusive breastfeeding accelerated progress in reducing under-five mortality in Tanzania. In addition, analysis of cohort studies in Burkina Faso (Vaugelade et al., 2004), randomised control trials in Guinea Bissau (Aaby et al., 2010) and systematic reviews (Ent et al., 2011; Higgins et al., 2016) reported vaccinations to be associated with declines in child mortality. Our findings showed that DPT and measles vaccination are not among the most important interventions although the interventions were extensively implemented. This could be related to the untimely receipt of the vaccines which might have hindered optimal immune response to the vaccines. According to guidelines developed by the World Health Organization (World Health Organisation, 2018), children are considered fully vaccinated when they have received a vaccination against tuberculosis (BCG), three doses each of the diphtheria, pertussis, and tetanus (DPT) and polio vaccines, and a measles vaccination by the age of 12 months. At the time of the survey, only half of the children had received all basic vaccinations by the appropriate age of 12 months (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Untimely vaccinations contribute to coverage figures leading to an overestimation of actual population immunity (Akmatov et al., 2008; Babirye et al., 2012; Fadnes et al., 2011).

Results at the sub-national scale showed that effects of interventions on under-five mortality vary across regions in Uganda. This could partly explain the observed disparities in the U5MR between regions. ITN access had the largest association with mortality in Central 2, Mid- Western and South-West; IPT was most important in Kampala and Mid-Eastern; improved source of drinking water was most influential in Mid-North and West-Nile; ORS or RHF had a leading association in Central 1; postnatal care in East-Central and improved sanitation facilities in the North-East. Despite the important effects of malaria and diarrhoea interventions on mortality, their coverage is low in most regions (Uganda Bureau of Statistics

(UBOS) and ICF International Inc, 2012). ITN access varied from twenty three percent in East-Central to forty seven percent in each of the regions; Kampala, North-East and West-Nile. IPT ranged from eighteen percent in Central 1 and West-Nile to twenty nine percent in the North-East. More than fifty percent of children having diarrhoea were not given fluid from ORS sachets or RHF in seven out of the ten regions. Postnatal care varied from one percent in South-West to twenty nine percent in Kampala. Only fourteen percent of households had improved sanitation facilities in the country. Outstanding are the Mid-Eastern, North-East, Mid-North, West-Nile, Mid-Western and South-West regions with less than ten percent of households in each region having improved sanitation facilities. On the other hand, prevalences of malaria and diarrhoea are high across regions. The prevalence of malaria was at least forty percent in eight out of the ten regions (Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010). Also, in half of the regions, the prevalence of diarrhoea exceeds that of the national average of twenty three percent (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

Study results confirmed earlier findings that household socio-economic status is protective against under-five mortality. The improved socio-economic status boosts the effect of interventions despite their low coverages. Better socio-economic status has been shown to reduce under-five mortality (Ezeh et al., 2015; Kaberuka et al., 2017; Kanmiki et al., 2014). In Central 2, Mid-Western and South-West in which ITN access had the largest association with mortality, over sixty five percent of households in the three regions fall either in the middle, fourth or highest wealth quintile (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). More than sixty five percent of households in East-Central, in which postnatal care had a leading effect, are in the middle, fourth or highest wealth quintile (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). IPT had a strongest association with mortality in Kampala and over ninety percent of households in this region are in the highest quintile (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). In Central 1 where ORS or RHF was most important, over sixty five percent of households either belong to the fourth or highest wealth quintile (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). The improved socio-economic status in these regions might have contributed to the success of the poorly implemented interventions. The North-East in which coverage of several interventions was satisfactory (e.g. improved source of drinking water, DPT and measles vaccination, deworming, ORS or RHF and ACT), over eighty percent of households in this region are in the lowest wealth quintile (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). The high poverty level in the North-East could have hindered the effectiveness of many interventions which were adequately implemented in this region.

The country-wide mortality map identifies hotspots of under-five mortality and can be used as a practical tool by control programmes to improve coverage of important interventions at high mortality clusters and reduce the within country child mortality differentials. The map indicated that hotspots are found in the North-East, West-Nile, around Lake Kyoga in the southern of Mid-North, in East-Central along the Victoria Nile River, the southern of Central 1 stretching to the South-West region and along the country border in Mid-Western between Lakes Albert and Edward. Lowest mortality hazard rates were found in Kampala, centre of Mid-North extending to West-Nile, North-East, Mid-Eastern and East-Central regions. Also, areas around Lake George in Mid-Western and a few spots in Central 2 were predicted with low mortality hazard rates. The regions in which our study found hotspots of mortality have been reported to be at high risk by Kazembe et al (Kazembe et al., 2012) (e.g. North-East, South-West and East-Central), when they investigated geographical inequalities in under-five mortality using census data. Similarly, we did not find hotspots in regions which Kazembe et al (Kazembe et al., 2012) reported to be at the lowest risk such as Kampala.

The hotspots in high risk regions can be attributed to the low coverage of child health interventions (e.g. family planning, poor sanitation facilities, IPT, postnatal care and iron supplementation), poor socio-economic status and the high burden of childhood diseases. Increased implementation of such interventions has been reported to reduce child mortality (Blencowe et al., 2011; Ettarh and Kimani, 2012; Fegan et al., 2007; Jones et al., 2003). In half of the regions having hotspots (North-East, West-Nile, Mid-North and Mid-Eastern), over seventy percent of households fall in the lowest or second lowest wealth quintile (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). The North-East where mortality concentration is highest, eight in ten households are in the lowest quintile and about sixty percent of the women had no education at all. In the rest of the high risk regions, about forty percent of women just had some primary education. In almost all of the regions having hotspots, at least forty percent of children less than five years were malnourished or had malaria and more than half were anaemic (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012).

The low mortality risk in Kampala and Central 2 can be attributed to the higher socio-economic status compared to other regions. In Kampala, the capital and most urban, over ninety percent of households are in the highest wealth quintile. Sixty percent of households in Central 2 are either in the fourth or highest wealth quintile. Also, the growing of high protein and energy foods such as millet and sorghum in the low mortality areas in the Mid-North and West-Nile might be responsible for the low mortality rates in these areas. These foods contain all the ingredients of a balanced diet recommended for children (Saleh et al., 2013; Singh, 2016). Furthermore, there is plenty of fish in areas around lakes in Mid-Eastern, East-Central and Mid-Western. Fish is rich in nutrients which are essential for the health of children

(Hellberg et al., 2012). The low mortality hazard rates in the North-East area bordering Mid-North could be a spillover effect from the Mid-North as the neighbouring population can tap resources from the Mid-North.

The main constraint in our research is that data on several health interventions for dead children were not available in the DHS; therefore, the intervention-mortality relation could not be estimated using interventions data at an individual level. Therefore, we aggregated intervention coverages at the cluster level and explained variation in under-five mortality within the country by the variation in intervention coverage between clusters while adjusting for socio-demographics and environmental/climatic factors. The findings are inclined to the ecological fallacy. Regardless of these limitations, the approach demonstrated in this paper enables estimation of the geographical variations in the effects of health interventions on the U5MR, which informs countries about the effectiveness of interventions at a local scale so that appropriate interventions can be implemented at a sub-national level.

3.5 Conclusion

We demonstrated that the effects of health interventions on under-five mortality vary across regions in Uganda and identified interventions associated with largest reductions in under-five mortality by region. The study has also pointed out high under-five mortality clusters in Uganda. These findings can guide control programmes to choose and implement more relevant interventions at a local scale, especially at high mortality clusters. This may reduce within country under-five mortality inequalities and consequently result into achieving national SDG mortality targets.

The coverage of interventions associated with the highest reduction in mortality in each region should be improved while targeting high mortality clusters. In Central 2, Mid-Western and South-West regions, ITN access should be strengthened. There is a need to increase coverage of improved sources of drinking water in Mid-North and West-Nile while focus should be placed on improved sanitation facilities in the North-East. IPT coverage should be scaled up in Kampala and Mid-Eastern; however, ORS or RHF and postnatal care should be prioritized in Central 1 and East-Central respectively. Also, the Uganda government should improve the socio-economic status of regions to enhance intervention performance and improve mortality rates.

Although it has been proven that health interventions diminish mortality; their impact is influenced by external factors including the health system and socio-economic status which differ between regions. Therefore, the one-fit-for-all approach may not yield the maximum out of the implemented interventions. These results can aid disease control programmes to identify the region-specific interventions associated with largest reduction in mortality.

Acknowledgements

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Declarations

Declarations of interest

None

Author contributions

BBN: Conceptualisation, data management and analysis, methodology development and implementation, results interpretation and writing original draft of the manuscript.

JS: Writing – review and manuscript editing.

FEM and SK: Formulation of research goals and objectives and acquisition of project financial support.

PV: Lead author, Conceptualisation, formulation of research goals and objectives, acquisition of project financial support, lead methodology development and implementation, result interpretation, writing – original draft of manuscript, review and editing.

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Ethical approval and consent to participate

In this research article secondary data that were made available to us by the Uganda Bureau of Statistics (UBOS) and the DHS Program (www.dhsprogram.com) were used. According to survey reports, ethical approval and consent to participate was obtained by the above bodies from the Institutional Review Board of International Consulting Firm (ICF) of Calverton, Maryland, USA, and from Makerere University School of Biomedical Sciences Higher Degrees Research and Ethics committee (SBS-HDREC) and the Uganda National Council for Science and Technology (UNCST). Information on ethical approval and consent to participate is published in the 2006, 2011 DHS (Uganda Bureau of Statistics (UBOS) and

ICF International Inc, 2012; Uganda Bureau of Statistics (UBOS) and Macro International Inc, 2007) and 2009 MIS reports (Uganda Bureau of Statistics (UBOS) and ICF Macro, 2010).

Consent for publication

Not applicable.

Competing risks

The authors declare that they have no competing interests.

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Availability of data

The data used in this article were requested from the DHS program website (www.dhsprogram.com), but the "Data terms of use" do not permit us to distribute these data as per access instructions (https://dhsprogram.com/data/Access-Instructions.cfm). However, data are available at the DHS MEASURE website (www.dhsprogram.com) and can be accessed upon request and following instructions at https://dhsprogram.com/data/Access-Instructions.cfm.

3.6 Supplementary files

Supplementary Table 3. 1: Remote sensing data sources[a]

Source	Data type	Temporal resolution	Spatial resolution
MODIS/Terra[b]	LST[l]	8 days	1km
MODIS/Terra[b]	NDVI[m]	16 days	1km
U.S. Geological Survey-Earth Resources Observation Systems (USGSS)	Rainfall	10 days	8x8km^2
Shuttle Radar Topographic Mission (SRTM)	Altitude	na	1x1km^2
MODIS,IBGD type	Land cover Water bodies	na	0.5x0.5km^2
Global Rural and Urban Mapping project	Urban Rural extent	na	1x1km^2

na: Not applicable; Land cover groups (forest, crops, urban); [a]Land cover data accessed in June 2011 and other data accessed in November 2013; [b]Moderate Resolution Imaging Spectroradiometer (MODIS)/Terra, available at: http://modis.gsfc.nasa.gov/; [l]Land surface temperature (LST) day and night; [m]Normalized difference vegetation index

Supplementary file 3. 1: Bayesian geostatistical methods

Geostatistical proportional hazards model with spatially varying covariates

A Bayesian geostatistical proportional hazards model (Banerjee et al., 2015) was fitted to assess the association between under-five mortality and health interventions, and to identify interventions which contribute most to mortality at the sub-national level. Let $s = \{s_1, s_2, \dots, s_m\}^t, s_i \in D \subset R^2$ be the set of locations at which mortality data are observed, $t_j(s_i)$ be the observed number of months lived or the censoring time for child j at location s_i, $\boldsymbol{X_j}(s_i)$ be the vector of socio-demographic and climatic factors and $Z_d(s_i)$ be the coverage of intervention d at location s_i.We modeled the hazard of death by the equation, $h\big(t_j(s_i)\big) = h_0\big(t_j(s_i)\big) \exp\Big(\boldsymbol{\beta}^T \boldsymbol{X_j}(s_i) + \sum_{d=1}^{D} \big(b_d + \varepsilon_{dk(i)}\big)^T Z_d(s_i) + W(s_i)\Big)$ and assumed a Weibull baseline hazard i.e. $h_0\big(t_j(s_i)\big) = r\big(t_j(s_i)\big)^{r-1}$ where r is the shape parameter, $\boldsymbol{\beta}^T = \big(\beta_1, \dots, \beta_p\big)$ is the vector of regression coefficients with $\exp(\beta_l), l = 1, \dots p$, correspond to the hazard ratio (HR). $W(s_i)$ is a cluster-specific random frailty which captures spatial correlation in mortality i.e. clusters in closer proximity are expected to have similar mortality hazard due to common exposures. We modeled $\boldsymbol{W}(s) = (W(s_1), W(s_2), \ldots, W(s_m))^T$ by a Gaussian process, i.e. $\boldsymbol{W}(s) \sim N(0, \Sigma)$, with an exponential correlation function of the distance d_{kl} between locations s_k and s_l, that is $\Sigma_{kl} = \sigma^2 \exp(-d_{kl}\rho)$ (Banerjee et al., 2015). The parameter σ^2 gives the variance of the spatial process and ρ is a smoothing parameter that controls the rate of correlation decay with distance. For the exponential correlation function, $\frac{-\log(0.05)}{\rho}$ determines the distance at which the correlation drops to 0.05 (i.e. effective range of spatial process). Our model assumed that the relation between health interventions and mortality varied across regions by including intervention specific spatially varying coefficients, $b_d + \varepsilon_{kd}$, where b_d is the effect of intervention $d = 1, \ldots D$ on child mortality at global (national) level and $\boldsymbol{\varepsilon_d} = (\varepsilon_{d1}, \ldots, \varepsilon_{dk})^{\boldsymbol{T}}$ are the varying effects at regional (sub-national) levels $k = 1, \ldots K$ with $k(i)$ indicating the region k corresponding to the location s_i.We introduced spatial dependence among the regions via a conditional autoregressive (CAR) prior for $\boldsymbol{\varepsilon_d}$, that is $\boldsymbol{\varepsilon_d} \sim N(\boldsymbol{0}, \Omega_d)$ with $\Omega_d = \sigma_d^2 (I - \gamma C)^{-1} \Delta$. σ_d^2 is the variance of spatially varying disease effects, Δ is a diagonal matrix with entries $\Delta_{kk} = {g_k}^{-1}$where g_k is the number of neighbors of region k, γ measures overall spatial dependence and C is a proximity matrix with normalized entries that is $C_{kl} = \omega_{kl}/g_k$, ω_{kl} is 1 if region k neighbors l and 0 otherwise (Banerjee et al., 2015). To complete Bayesian model formulation, we assumed inverse gamma priors for all spatial variances with known parameters, i.e. $\sigma^2, \sigma_d^2 \sim IG(2.01, 1.01)$, a uniform prior distribution for $\rho \sim U(a, b)$, where a and b chosen such as the effective range is within the maximum and minimum distances of the observed locations (Thomas et al., 2004) and a uniform prior for $\gamma \sim U(\lambda_1^{-1}, \lambda_2^{-1})$ where λ_1, λ_2 are the smallest and largest eigen value of $\Delta^{-1/2} C \Delta^{1/2}$ (Banerjee et al., 2015). The shape parameter was assigned an exponential prior $r \sim Exp(0.01)$. Non-informative normal priors were adopted for the regression coefficients $\beta_l, b_d \sim N(0, 10^3)$ for $l = 1, \dots p$ and $d = 1, \dots D$.

The joint posterior distribution of the model is given by

$\prod_{\boldsymbol{i}} [\, t_j(s_i) \,|\boldsymbol{\beta}, b_d, W(s_i)\, \varepsilon_{dk}, \boldsymbol{X_j}(s_i), \boldsymbol{Z_d}(s_i), r\,][\, \boldsymbol{W}(s)|\sigma^2, \rho][\boldsymbol{\varepsilon_d}|\, \sigma_d^2, \gamma][\boldsymbol{\beta}, b_d, \sigma^2, \sigma_d^2, \gamma, \rho, r]$.

Model parameters were estimated using Markov Chain Monte Carlo (MCMC) simulation (O'Hara R and Sillanpää M, 2009). We run a two chain algorithm for 250 000 iterations with an initial burn-in of 20,000 iterations. Convergence was assessed by visual inspection of trace and density plots and analytically by the Gelman and Rubin diagnostic (Raftery and Lewis, 1992).

Bayesian kriging

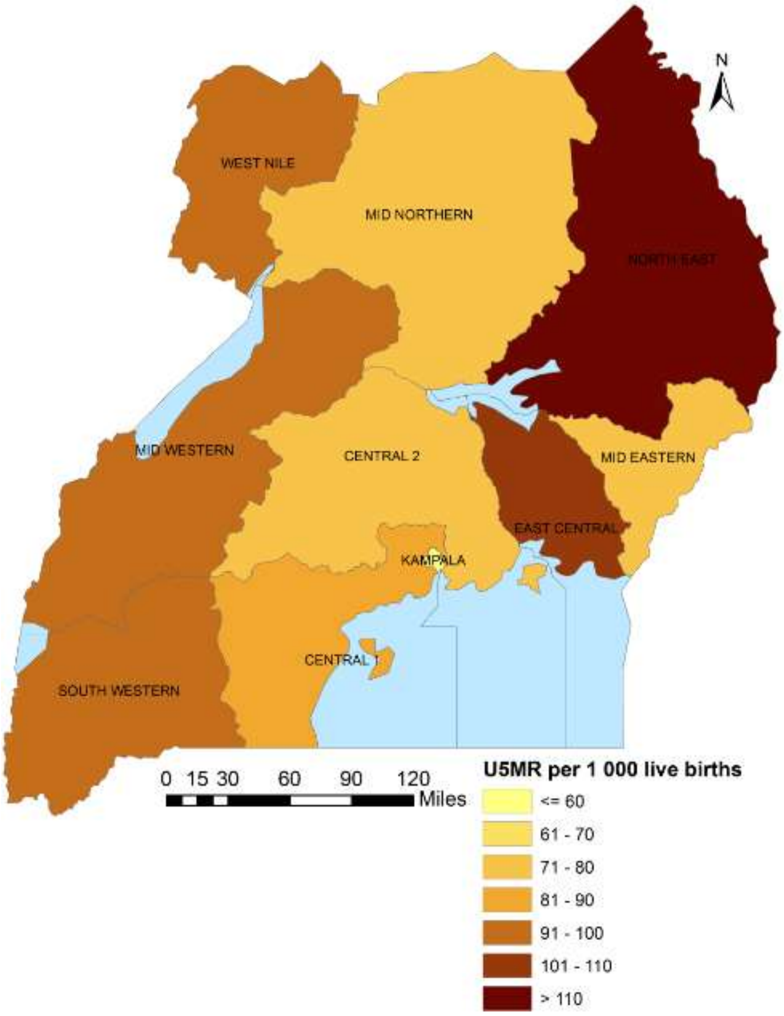
To produce a smooth map of under-five mortality risk, we used Bayesian kriging (Cressie, 2015) and predicted mortality risk at unsampled locations over a grid of 61,062 pixels at a 2x2 km^2 grid covering the entire country. Specifically, predictions of mortality risk, $T(s_0) = T(s_{01}), T(s_{02}), \dots, T(s_{0l})$ at any unsampled location, $\boldsymbol{s}_0 = (s_{01}, s_{02}, \dots, s_{0l})$ were obtained by the posterior predictive distribution $[T(s_0)|W(s_0), r]$*$[W(s_0)|W(s), \sigma_w]$*$[\theta|T(s)]$. W(s_0) and $W(s)$ have a Gaussian joint distribution and the conditional distribution given by $[W(s_0)|W(s), \sigma_w]$. θ denotes the parameter vector $\theta = (r, W(s), \sigma_w^2, W(s_0), \sigma_{w_0}^2)^t$.

Bayesian variable selection

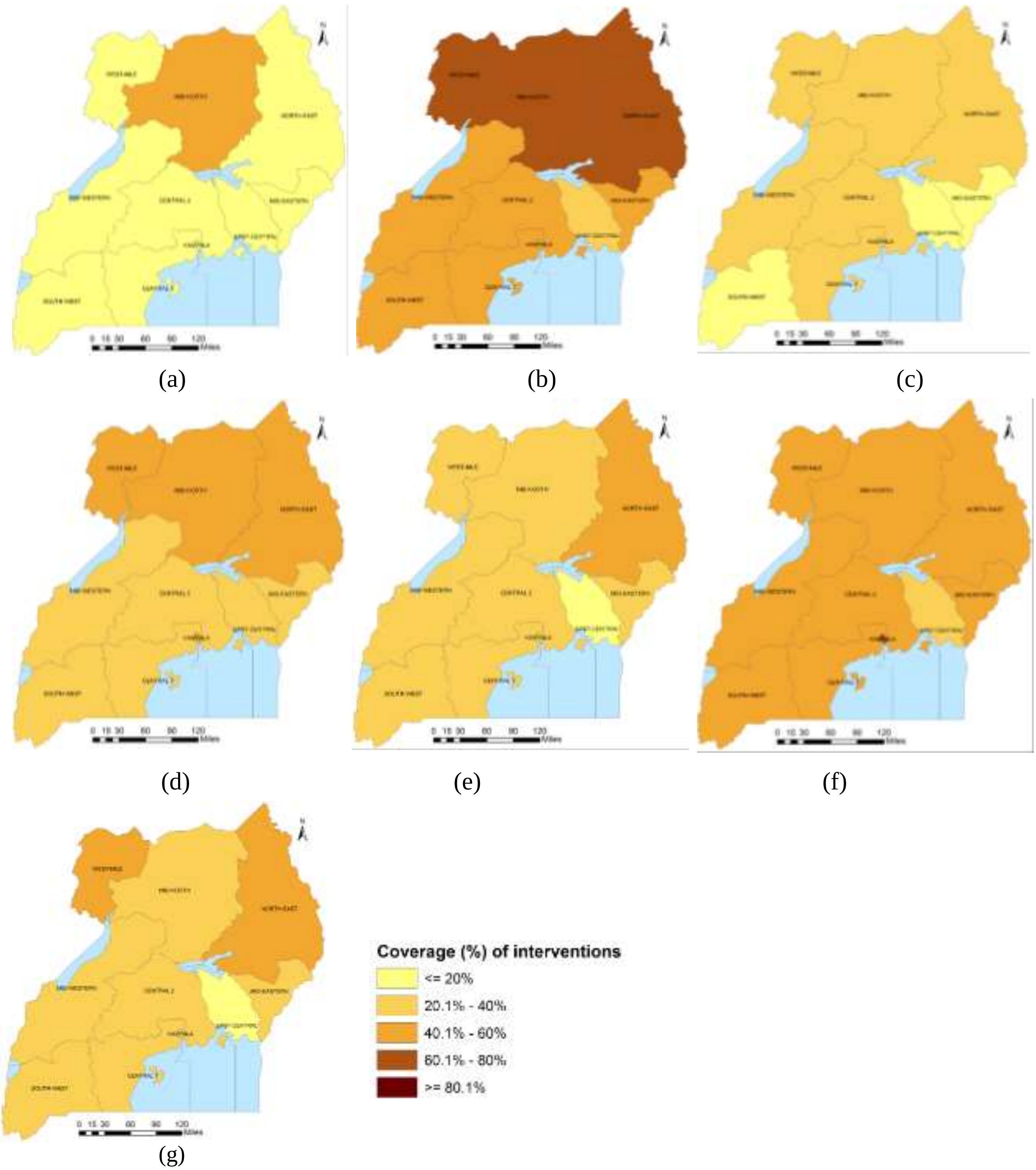
A Bayesian stochastic search variable selection approach was used to determine the most important predictors of under-five mortality (George and McCulloch, 1993). ITN coverage measures were highly correlated with more than 85%, therefore, only one (or none) ITN measure among those defining ownership and one (or none) ITN measure among those defining use (Giardina et al., 2014; Ssempiira et al., 2017) was selected. For each ITN coverage measure X_p in the ownership group, a categorical indicator I_p, was introduced to represent exclusion of the variable from the model ($I_p = 1$), or inclusion of one of the ITN ownership measure i.e. Prop_ITNA ($I_p = 2$), Prop_1ITN2 ($I_p = 3$) and Prop_1ITN ($I_p = 4$). A similar definition was adopted for the ITN use coverage measure i.e. exclusion of the variable from the model ($I_p = 1$), inclusion of Prop_ITN5 ($I_p = 2$), Prop_ITNS ($I_p = 3$) and Prop_ITNU ($I_p = 4$). The ITN measure with the highest probability of inclusion in each category was included in the final model. For the environmental/climatic variables except land cover, variable selection compared their linear and categorical forms and selected the one that had the highest probability of inclusion or neither of the two forms. The categorical forms were generated based on the quartiles of variables. We introduced an indicator I_p for each environmental/climatic covariate X_p which defines exclusion of the variable from the model ($I_p = 1$), inclusion in a categorical ($I_p = 2$) or linear ($I_p = 3$) form. For diseases, socio-demographic, land cover, health interventions other than ITN coverage measures, we introduced a binary indicator parameter I_p suggesting presence ($I_p = 1$) or absence ($I_p = 0$) of the predictor from the model.

I_p has a probability mass function $\prod_{j=1}^{p} \pi_j^{\delta_j(I_p)}$, where π_j denotes the inclusion probabilities, $j = (1,2,3,4)$, e.g. for ITN coverage measures so that $\sum_{j=1}^{p} \pi_j = 1$ and $\delta_j(.)$ is the Dirac function, $\delta_j(I_p) = \begin{cases} 1, if\ I_p = j \\ 0, if\ I_p \neq j \end{cases}$. We assumed a spike and slab prior for regression coefficient β_p corresponding to the corresponding covariate, X_p i.e. $\beta_p \sim \left(1 - \delta_1(I_p)\right) N\left(0, u_0 \tau_p^2\right) + \delta_1(I_p) N(0, \tau_p^2)$ proposing a non-informative prior for β_p in case X_p is included in the model and an informative normal prior with variance close to zero (i.e. $u_0 = 10^{-3}$) shrinking β_p to zero if X_p is excluded from the model. Similarly, for the coefficient $\{\beta_{p,l}\}_{l=1,..,L}$ corresponding to the categorical form of $\underline{X_p}$ with L categories, we assume that $\beta_{p,l} \sim \delta_2(I_p) N\left(0, \tau_{p,l}^2\right) + \left(1 - \delta_2(I_p)\right) N\left(0, \vartheta_0 \tau_{p,l}^2\right)$.

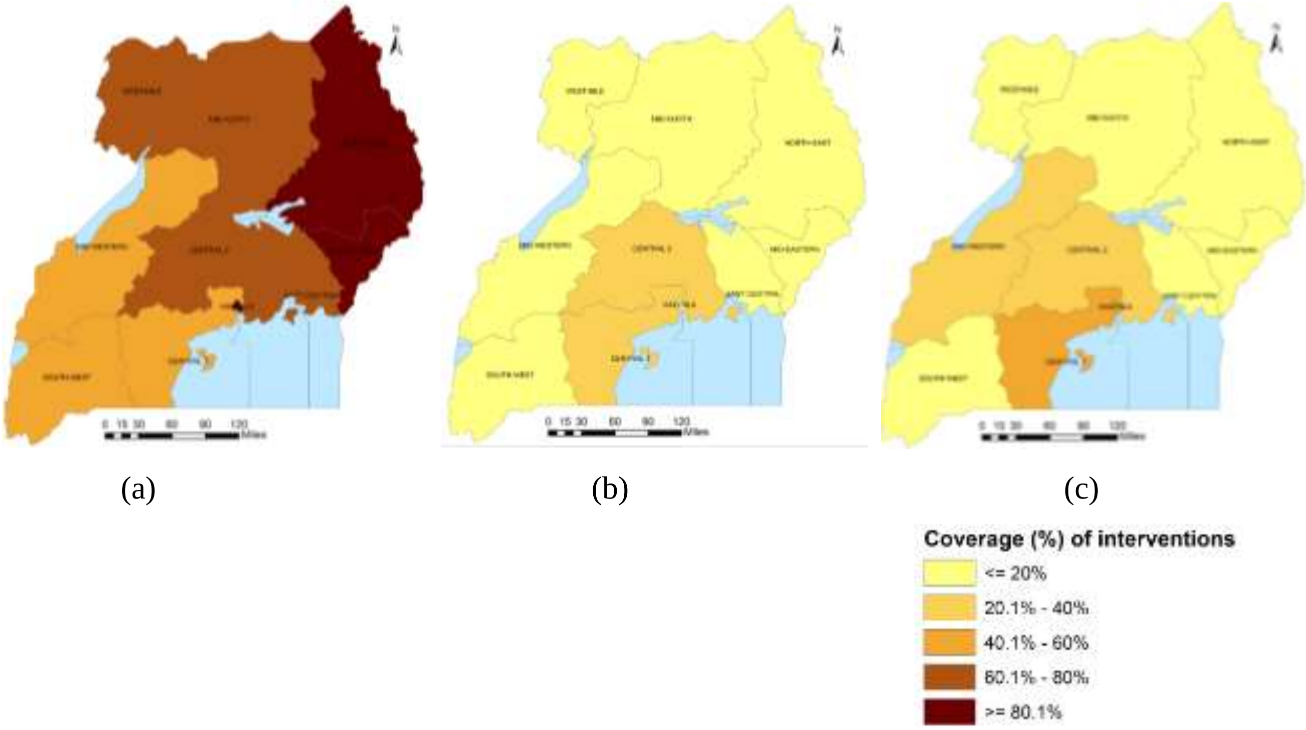
For inclusion probabilities of ITN use and ownership, a non-informative Dirichlet distribution was adopted with hyper parameters $\alpha = (1,1,1,1)^T$, that is, $\boldsymbol{\pi} = (\pi_1, \pi_2, \pi_3, \pi_4)^T \sim Dirichlet(4, \alpha)$. A similar distribution was adopted for the inclusion probabilities of environmental/climatic factors. For diseases, socio-demographic, land cover, health interventions other than ITN coverage measures, a Bernoulli prior with an equal inclusion or exclusion probability was assumed for the indicator i.e. $I_p \sim bern(0.5)$. Also, inverse Gamma priors with parameters (2.01, 1.01) were assumed for the precision hyper parameters τ_p^2. The predictors identified as important are those with posterior inclusion probability greater than or equal to 40% (Diboulo et al., 2015; Giardina et al., 2014; Ssempiira et al., 2017).



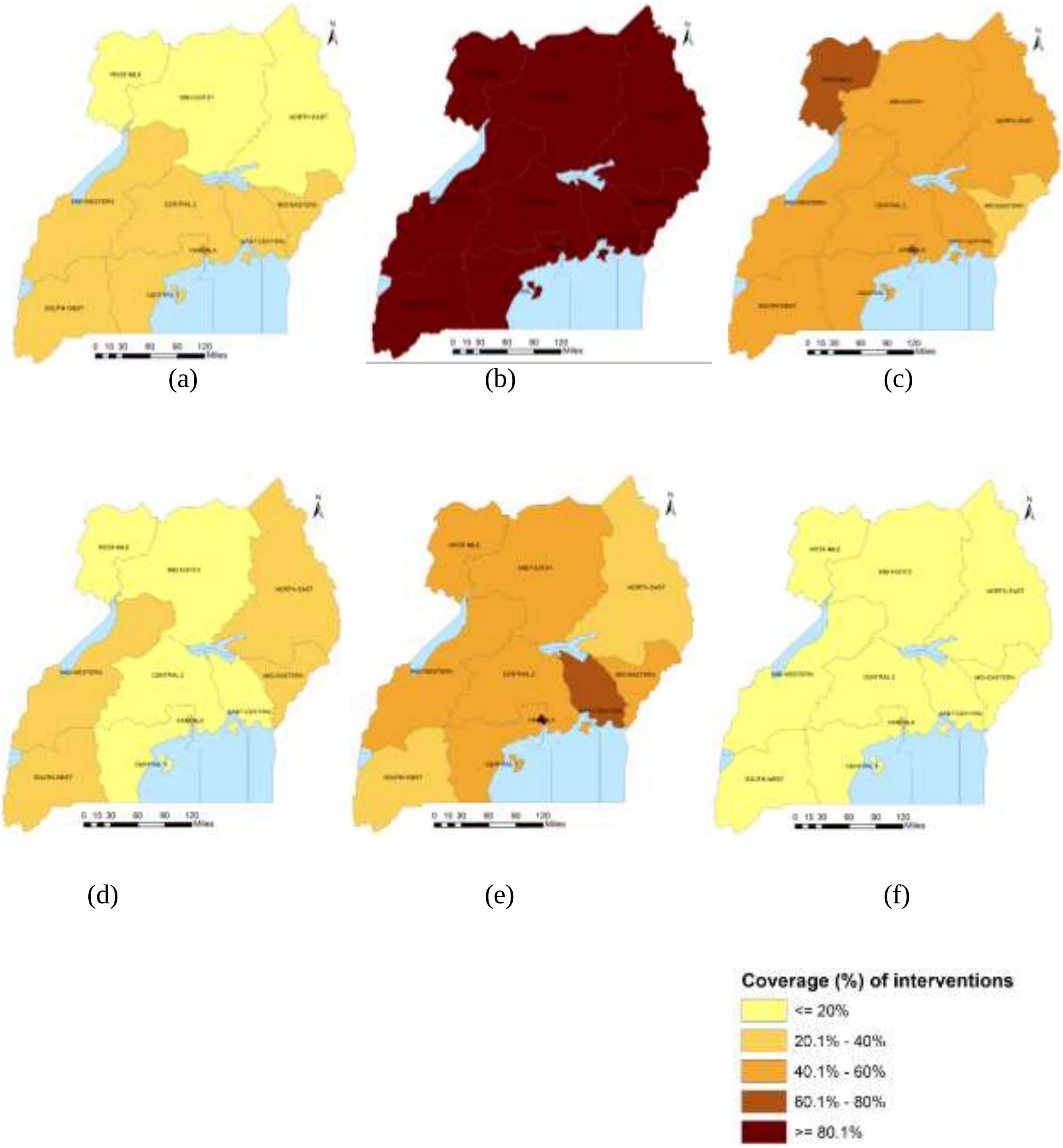
Supplementary Figure 3. 1: Geographical distribution of U5MR by region, Uganda DHS 2011



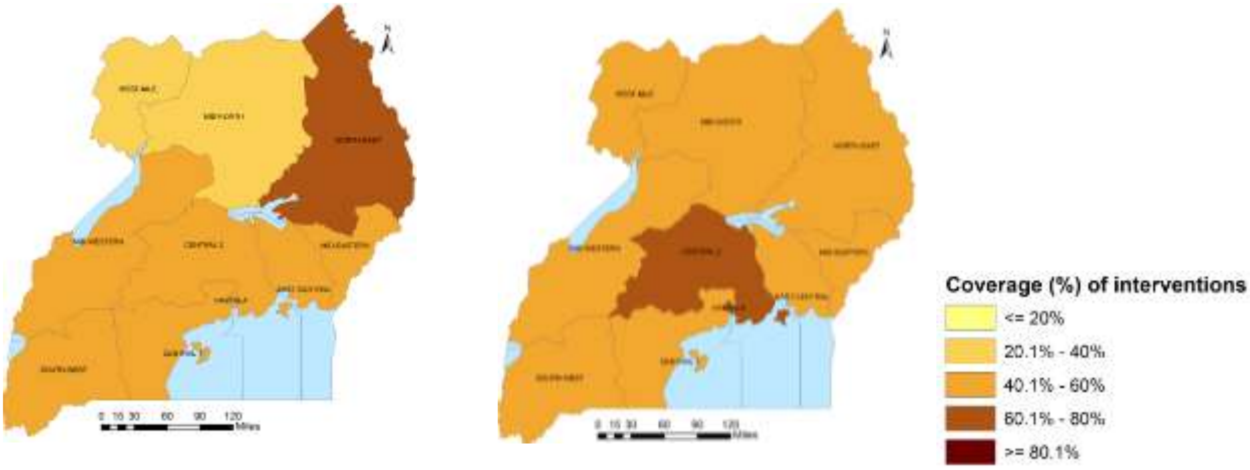
Supplementary Figure 3. 2: Coverage of malaria interventions by region, Uganda DHS 2011; (a) Percentage of households sprayed with Indoor Residual Spraying (IRS) in the past 12 months, (b) Percentage of households with atleast one ITN, (c) Percentage of households with atleast one ITN for every two people, (d) Percentage of population with access to an ITN within their household, (e) Percentage of the population in a household that slept under an ITN the previous night of the survey, (f) Percentage of children under 5 years in a household who slept under an ITN the previous night of the survey, (g) Percentage of existing ITNs used by the population in a household the previous night of the survey.



Supplementary Figure 3. 3: Coverage of Water, Sanitation and Hygiene practices by region, Uganda DHS 2011; (a) Percentage of households with improved source of drinking water, (b) Percentage of households using improved sanitation facilities, (c) Percentage of households having soap or detergent and water at hand washing places.

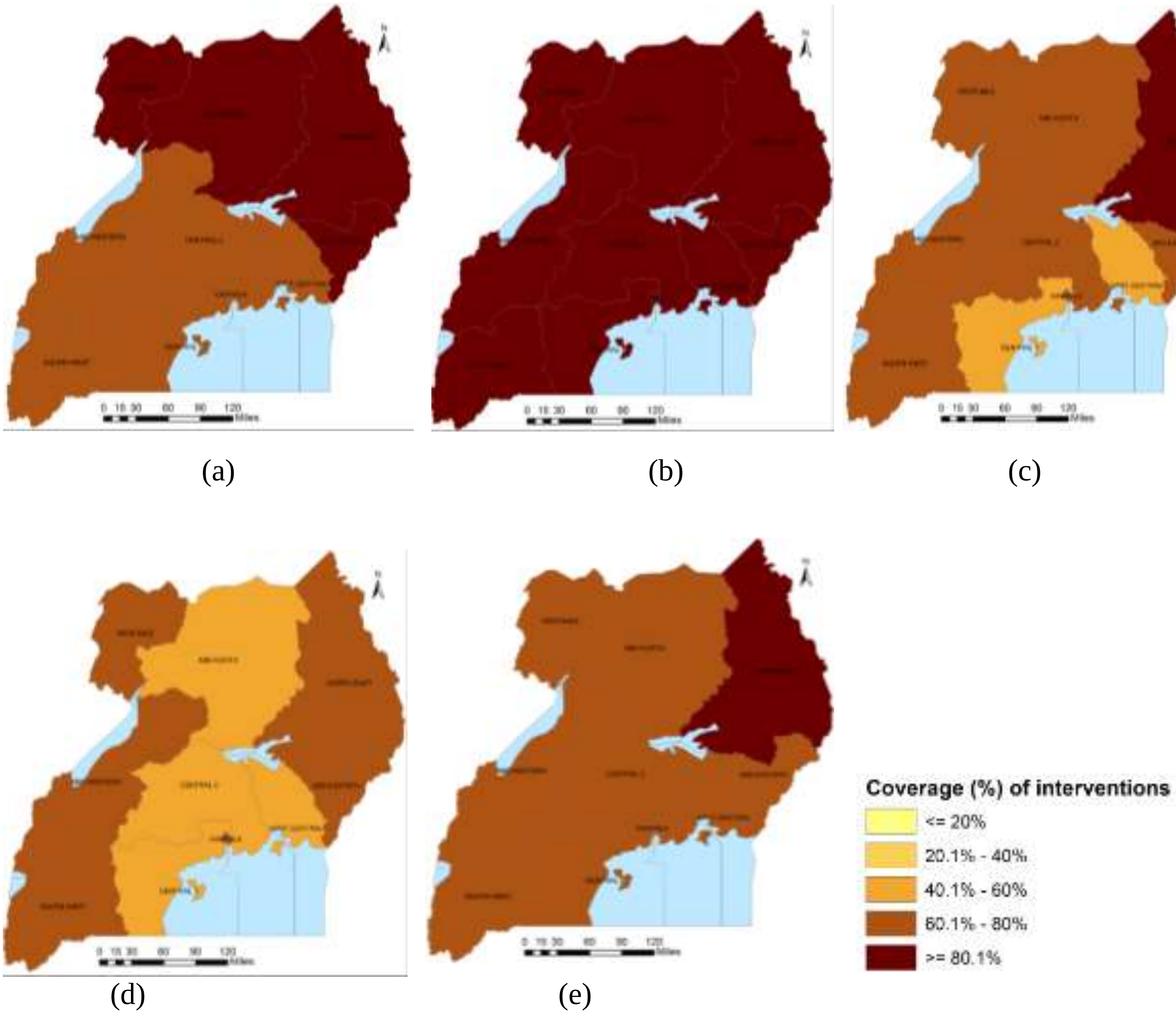


Supplementary Figure 3. 4: Coverage of reproductive health interventions by region, Uganda DHS 2011; (a) Percentage of married women using any family planning method, (b) Percentage of pregnant mothers receiving ANC from a skilled provider, (c) Percentage of pregnant women making four or more ANC visits during their entire pregnancy, (d) Percentage of women who received intermittent preventive treatment for malaria during pregnancy, (e) Percentage of births that took place with the assistance of a skilled provider, (f) Percentage of newborns receiving first postnatal checkup from a skilled provider within two days after delivery.

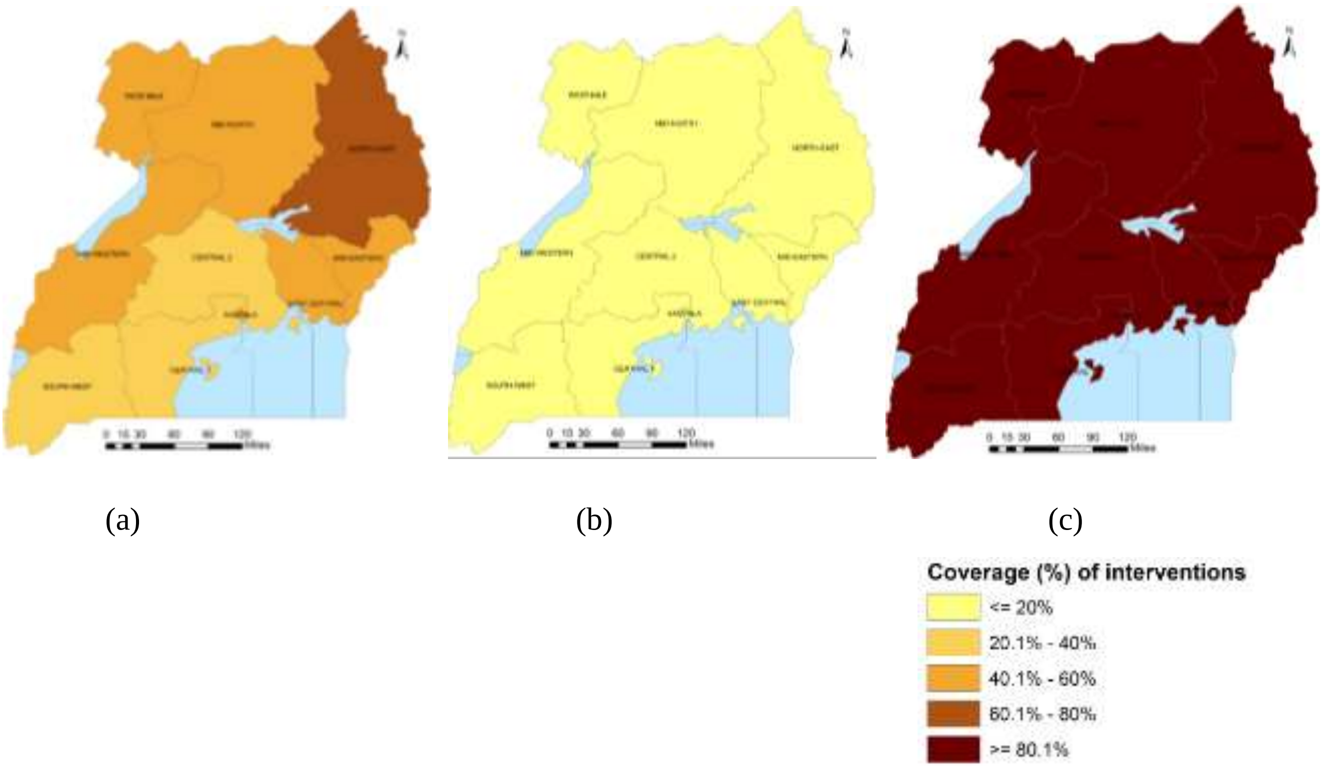


(a) (b)

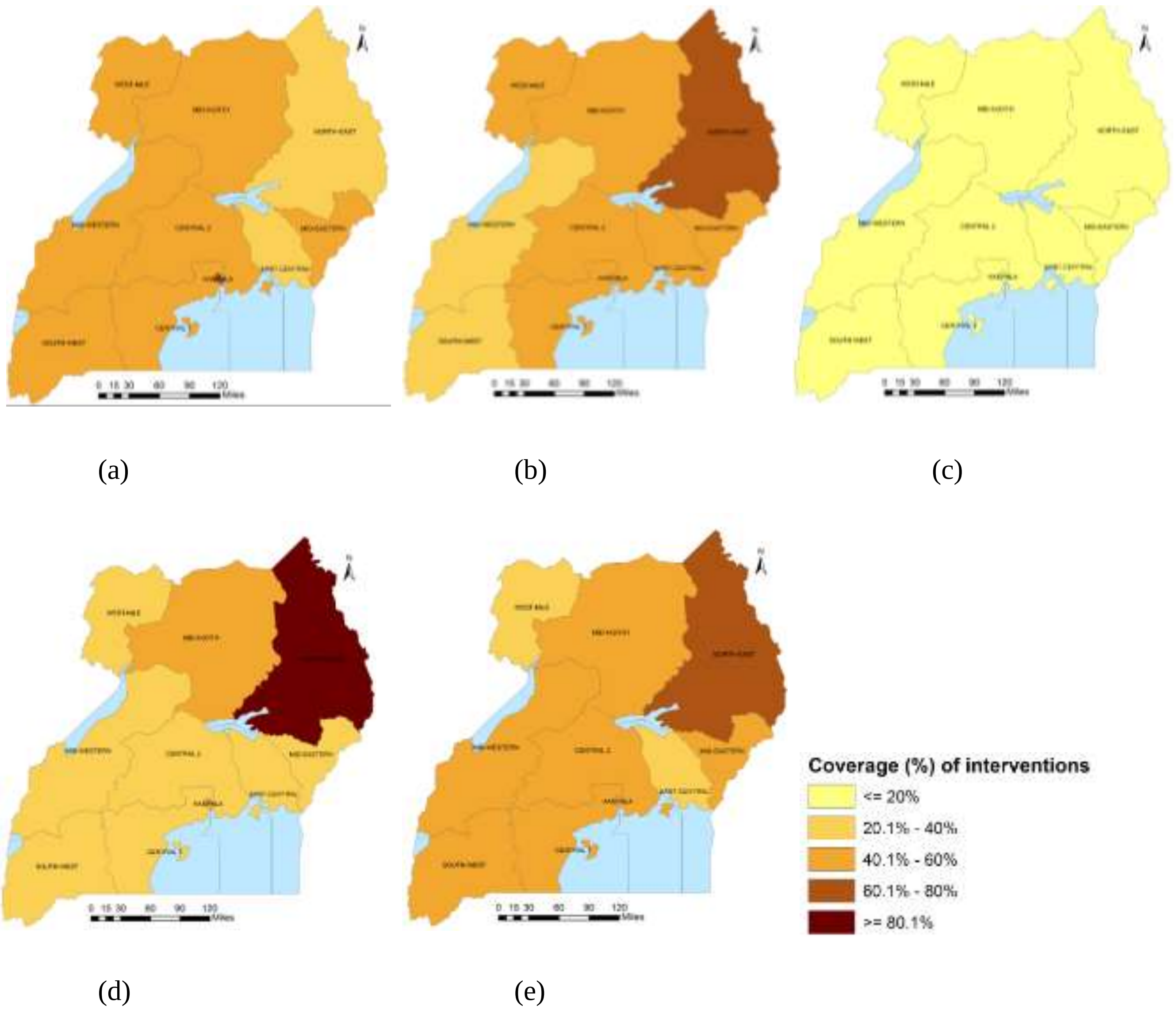
Supplementary Figure 3. 5: Coverage of breastfeeding by region, Uganda DHS 2011; (a) Percentage of infants who started breastfeeding within one hour of birth, (b) Percentage of infants exclusively breastfed during the first six months after birth



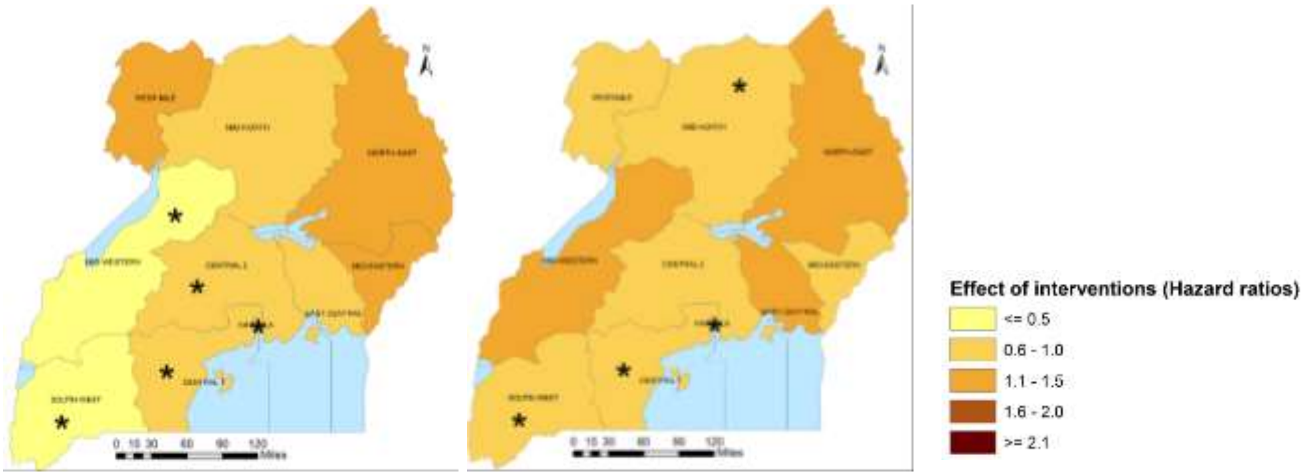
Supplementary Figure 3. 6: Coverage of vaccinations by region, Uganda DHS 2011; (a) Percentage of last-born child fully protected against neonatal tetanus, (b) Percentage of children vaccinated against BCG, (c) Percentage of children with complete vaccination of DPT, (d) Percentage of children with complete vaccination of polio, (e) Percentage of children vaccinated against measles.



Supplementary Figure 3. 7: Coverage of micronutrients intake by region, Uganda DHS 2011; (a) Percentage of children receiving vitamin A supplements in the past 6 months, (b) Percentage of children receiving iron supplements in the past 7 days, (c) Percentage of children living in households with iodized of salt.

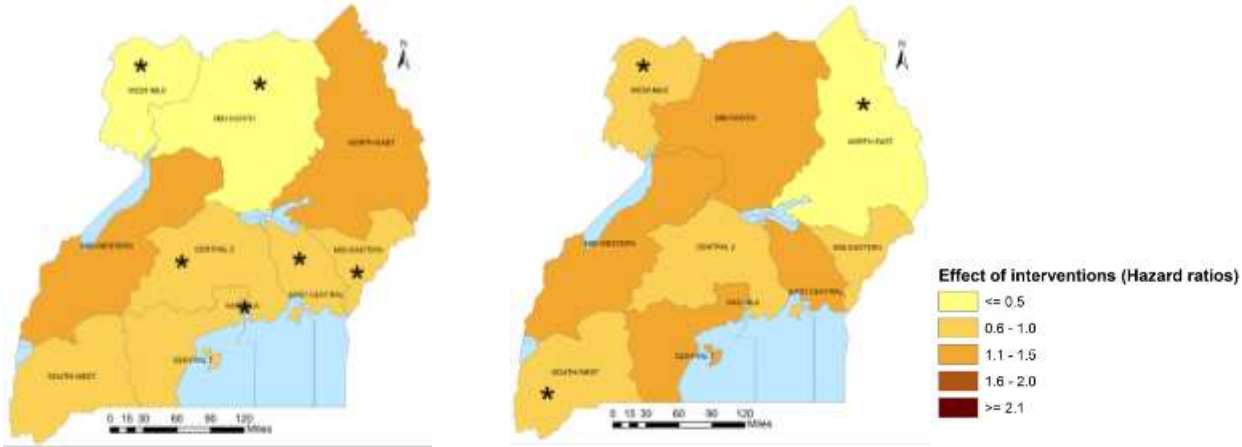


Supplementary Figure 3. 8: Coverage of treatments by region, Uganda DHS 2011; (a) Percentage of children with ARIs symptoms who took antibiotics, (b) Percentage of children with diarrhoea given fluid from oral rehydration solution sachets or recommended home fluids, (c) Percentage of children with diarrhoea given zinc sulphates, (d) Percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy, (e) Percentage of children given deworming medication in the past 6 months.



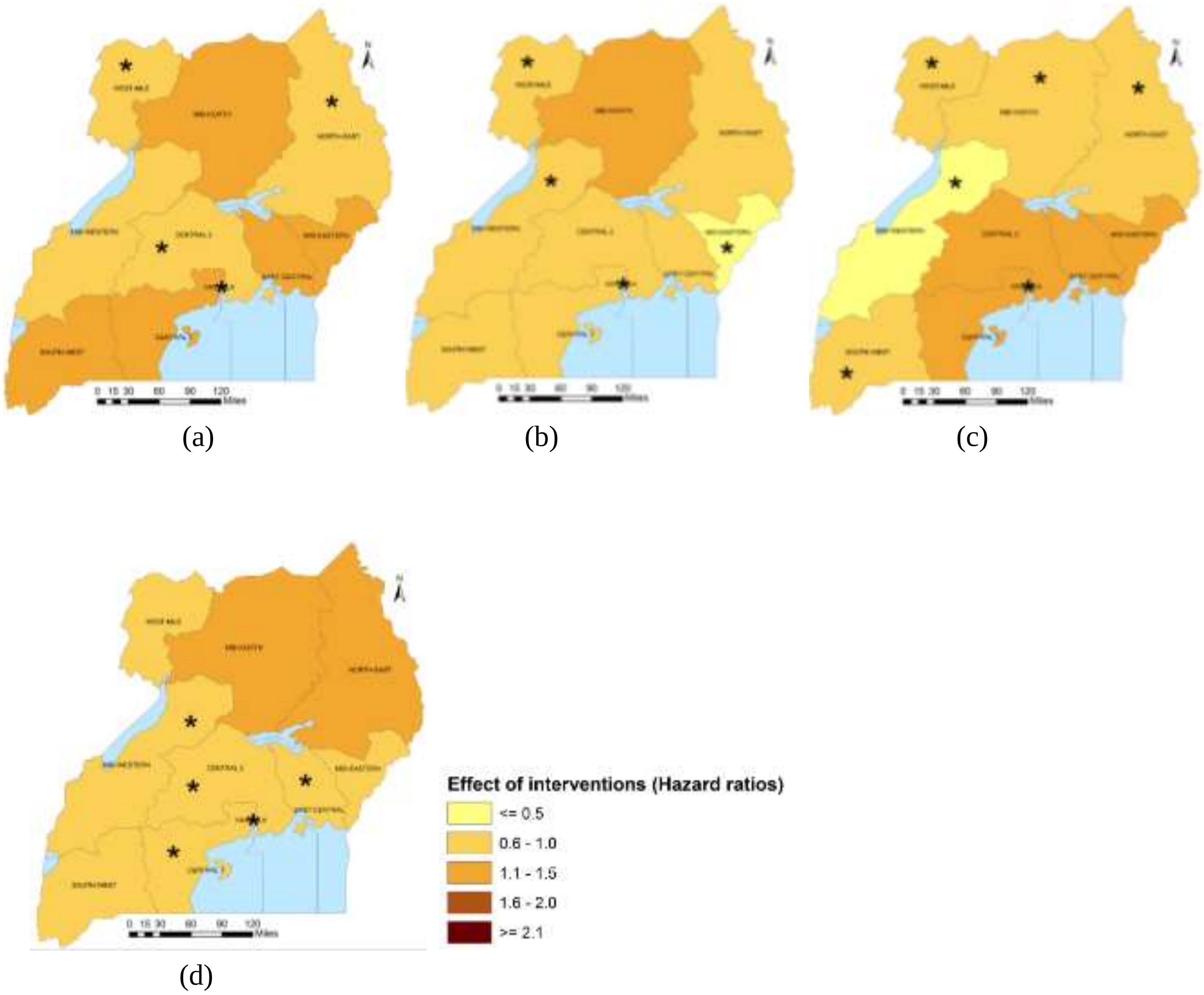
(a) (b)

Supplementary Figure 3. 9: Geographical distribution of the effects (Hazard ratios) of malaria interventions on U5MR; (a) Percentage of population with access to an ITN within their household, (b) Percentage of existing ITNs used by the population in a household the previous night of the survey.

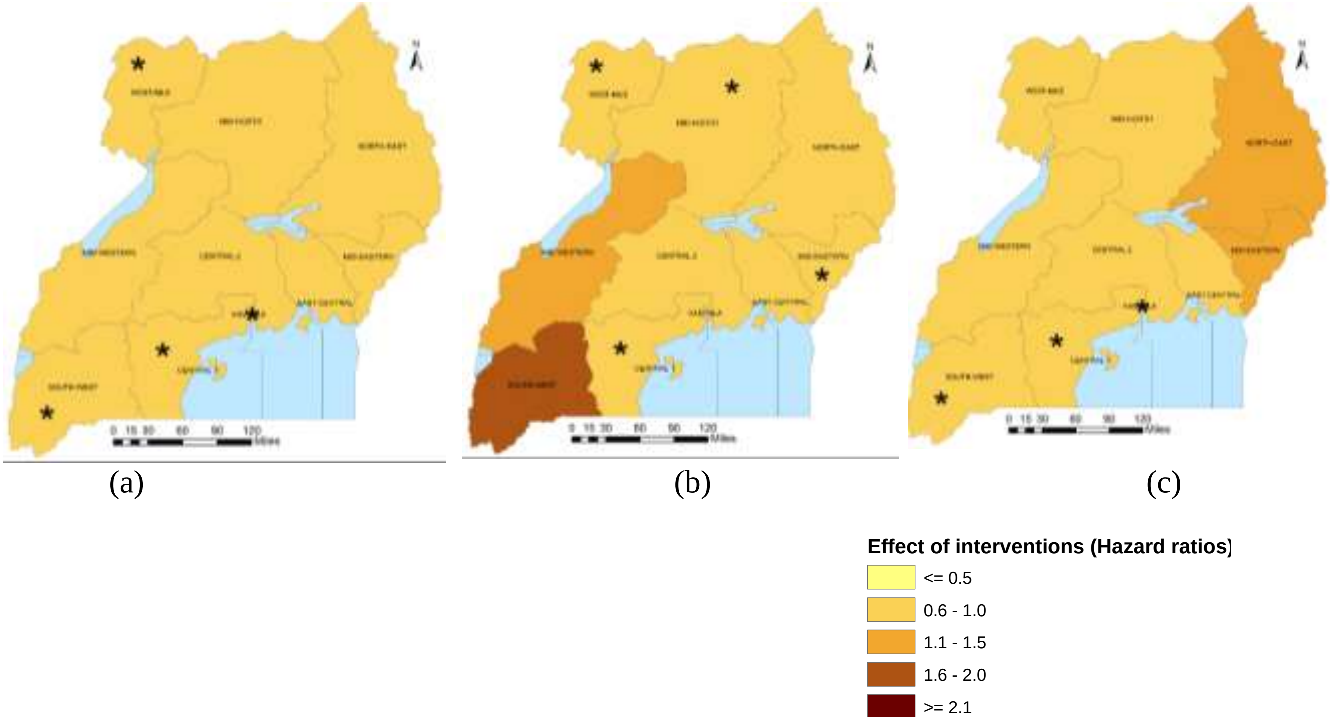


(a) (b)

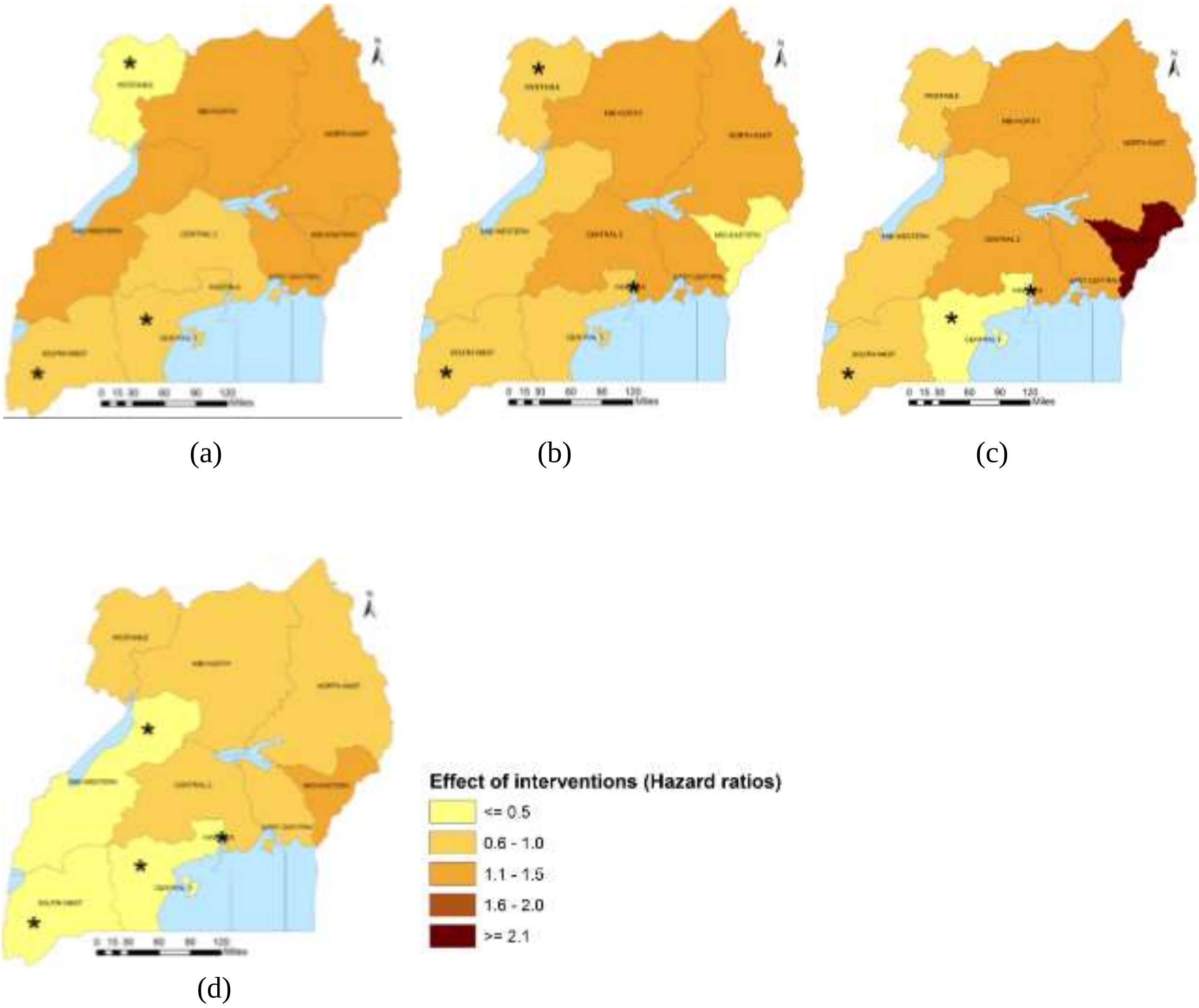
Supplementary Figure 3. 10: Geographical distribution of the effects (Hazard ratios) of WASH practices on U5MR; (a) Percentage of households with improved source of drinking water, (b) Percentage of households using improved sanitation facilities.



Supplementary Figure 3. 11: Geographical distribution of the effects (Hazard ratios) of reproductive health interventions on U5MR; (a) Percentage of married women using any family planning method, (b) Percentage of women who received intermittent preventive treatment for malaria during pregnancy, (c) Percentage of births that took place with the assistance of a skilled provider, (d) Percentage of newborns receiving first postnatal checkup from a skilled provider within two days after delivery.



Supplementary Figure 3. 12: Geographical distribution of the effects (Hazard ratios) of breastfeeding and vaccinations on U5MR; (a) Percentage of infants who started breastfeeding within one hour of birth, (b) Percentage of children with complete vaccination of DPT, (c) Percentage of children vaccinated against measles.



Supplementary Figure 3. 13: Geographical distribution of the effects (Hazard ratios) of micronutrients intake and treatments on U5MR; (a) Percentage of children receiving vitamin A supplements in the past 6 months, (b) Percentage of children given deworming medication in the past 6 months, (c) Percentage of children with diarrhoea given fluid from oral rehydration solution sachets or recommended home fluids, (d) Percentage of children with fever during the two weeks prior to the survey and took artemisinin-combination therapy.

Chapter 4: The contribution of childhood diseases on the geographical distribution of fever risk among children less than five years in Uganda

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Abstract

Background: Despite massive investment in diseases responsible for fever among children less than five years in Uganda, the burden of the fever symptom remains high and disproportionately distributed across regions. In Uganda, studies assessing the relationship between fever prevalence and multiple childhood diseases, especially at a local scale are scanty. We analyse the 2016 DHS data to quantify the effects and contribution of childhood diseases to fever prevalence among children less than five years in Uganda at the national and regional level.

Methods: Bayesian geostatistical logistic regression models with spatially varying coefficients were fitted to determine the effects and contribution of childhood diseases on fever prevalence at the national and regional levels. Region-specific spatially varying coefficients were modeled by a conditional autoregressive distribution. Cluster-specific random effects were introduced into the model to take into account spatial dependence in fever prevalence. Bayesian geostatistical stochastic search variable selection was applied to determine the most important predictors in explaining variation in fever prevalence. The contribution of childhood diseases to fever prevalence was estimated using population attributable fractions.

Results: The prevalence of fever was highest in Busoga and Teso regions and lowest in Bunyoro region. At the national level, the population attribution fraction of diarrhoea, ARI and malaria to the prevalence of fever in the under-five was 38.12 (95% BCI: 25.15, 41.59), 30.99 (95% BCI: 9.82, 34.26) and 9.50 (95% BCI: 2.34, 25.15), respectively. The attribution of diarrhoea was common in all regions except Bunyoro, while ARI was more common in Bugisu, Karamoja and West Nile, and malaria was commonest in Bunyoro. In Lango, the attribution of diarrhoea and ARI was similar.

Conclusion: Majority of fevers among the under-five are due to diarrhoea, followed by ARI. Hand washing with soap and water/detergent should be strengthened in all regions. Vaccination against ARI should be encouraged, in the regions of Central 2, Bugisu, Teso, Karamoja, Lango, West-Nile and Tooro. The health system should be reinforced to treat diarrhoea and ARI.

Key words: DHS, Children under five years, fever, malaria, ARI, diarrhoea, Population attributable fractions, Bayesian geostatistical inference, regions, Uganda.

4.1 Introduction

Fever is one of the leading causes of medical consultations in children under five years old (Nnedu et al., 2010; Royal College of Obstetricians and Gynaecologists, 2013; Serwint et al., 2006). Globally, over a third of all childhood deaths are caused by fever-related diseases (Liu et al., 2016). Similarly, in sub-Saharan Africa, fever-related diseases are the leading causes of under-five deaths (Liu et al., 2016). In Uganda, malaria, diarrhoea and pneumonia have been identified as the top causes of under-five deaths (Ministry of Health, 2015b; Nabongo et al., 2014). These diseases present with fever as an indication of illness in the early stages (Armon et al., 2001; Finkelstein et al., 2000). Furthermore, childhood fever is the most common clinical sign of infectious diseases. It is used as a measure of the disease public health burden, and of the effectiveness of programs aimed at preventing and treating diseases (Olotu et al., 2010).

The Uganda Demographic and Health Survey (DHS) is a nationally representative survey conducted every five years, to estimate among others the prevalence of fever and childhood diseases i.e. symptoms of acute respiratory infections (ARI), diarrhoea and malaria (Uganda Bureau of Statistics (UBOS) and ICF, 2018) in children under five years. The most recent DHS 2016 in Uganda showed that the national prevalence of fever in this age group was 33% (Uganda Bureau of Statistics (UBOS) and ICF, 2018). However, there were wide variations in regional fever prevalence, ranging from less than 20% in Kampala, Bugisu, Bunyoro, Kigezi and Ankole to over 50% in Eastern regions of Teso and Busoga (Uganda Bureau of Statistics (UBOS) and ICF, 2018). However, it is not clear to what extent the disparities in the fever prevalence are due to variations in interventions, treatments, health care seeking behaviors, socio-demographic, environmental/climatic factors or as a result of variations of childhood diseases in space.

Several studies have evaluated the causes of fever among children less than five years and the causes vary considerably in various countries. A systematic review (Stein and Marostica, 2007) and studies in America (Lutfiyya et al., 2006) reported pneumonia as the main cause of fever in children under five years. In Vietnam (Nguyen et al., 2004), gastrointestinal infections was found to be the main cause of fever in the same age group. In Uganda, malaria was reported as one of the causes of fever episodes in this age group (Lubanga et al., 1997). In Tanzania (Crump et al., 2013; D'Acremont et al., 2014; Hertz et al., 2013) and Zanzibar (Elfving et al., 2016), ARI, malaria and gastroenteritis were reported as the most frequent causes of fever episodes in children under five years. Similarly, malaria in Nigeria (Uzochukwu et al., 2008) and gastrointestinal infections in Burkina Faso (Nitiema et al., 2011) are well-known causes of fever episodes among children under five years.

Although previous studies broadly investigated the causes of fever, the majority are based on sub-national and hospital or laboratory data. Extrapolating these findings to other areas is not feasible considering that a large proportion of children may not seek treatment from health facilities, thus creating self-selection for good health seeking behaviors (Uganda Bureau of Statistics (UBOS) and ICF, 2018). In addition, most of these studies are rather descriptive and did not quantify the contribution of different diseases to the fever burden. Very few studies (El-Radhi et al., 1999; Okiro and Snow, 2010; Ssenyonga et al., 2009)have used analytical techniques to assess the relationship between fever and childhood diseases. They mainly focused on one disease such as fever with malaria (Okiro and Snow, 2010), diarrhoea (Ssenyonga et al., 2009) or bronchitis (El-Radhi et al., 1999) prevalence. However, they did not consider exposure to multiple childhood diseases or confounding effects of socio-economic, interventions, health care seeking behaviour and environmental/climatic factors. Environmental factors that influence fever risk are spatially structured introducing geographical dependence on the fever burden (Siraj et al., 2014; Ssempiira et al., 2017). Studies assessing geographical variation in the relation between fever and childhood diseases are limited.

In the current study, we determine the effects of multiple childhood diseases on fever prevalence in children less than five years in Uganda at country and regional levels, and identify childhood diseases that contribute to fever by region analyzing the 2016 DHS data and using Bayesian geostatistical models. The analysis was adjusted for spatial correlation in fever and potential confounding effects of socio-demographic characteristics, interventions (such as insecticide treated nets (ITN) use and ownership, vaccinations, treatments, health care seeking behaviour) and environmental/climatic factors. Findings of this study can aid in the planning and implementation of preventive and treatment measures, particularly at the regional scale to address fever-related diseases among the under-five children in Uganda.

4.2 Methods

4.2.1 Country profile

Uganda is a land locked country located in East Africa, and shares borders with South Sudan to the north, Kenya to the east, Democratic Republic of Congo to the west, and Tanzania and Rwanda to the south. The country lies between latitudes 1^0 south and 4^0 north of the equator, with altitude ranging from 620 meters to 5 111 meters above sea level, and mean annual temperatures between 14℃ and 32℃. It has two rainfall seasons in a year, one during March to May and a longer season crossing from September to December. The country is divided into 116 districts grouped into 15 regions and covers an area of about 241,039 square kilometres. Uganda has a population of about 40 million people (Uganda Bureau of Statistics, 2016). It is characterized by high fertility rates (Total Fertility Rate = 5.4) and a moderate life expectancy (63 years). Half of the population is younger than 15 years old while the proportion of pre-school children (aged less than 5 years) is approximately 20% (Uganda Bureau of Statistics, 2016).

4.2.2 Ethics approval and consent to participate

In this research article, secondary data that was made available to us by the Uganda Bureau of Statistics (UBOS) and the DHS Program (www.dhsprogram.com) was used. According to survey reports, ethical approval and consent to participate was obtained by the above bodies from the Institutional Review Board of International Consulting Firm (ICF) of Calverton, Maryland, USA, and from Makerere University School of Biomedical Sciences Higher Degrees Research and Ethics committee (SBS-HDREC) and the Uganda National Council for Science and Technology (UNCST). An interview was administered only if respondents assented verbally to an informed consent statement read to them by interviewers. Verbal informed consent for each malaria test was provided by the child's parent or care-giver before the test was performed. Information on ethical approval and consent to participate is published in the 2016 DHS (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

4.2.3 Study setting

The study analysed data from the 2016 DHS which was carried out from June through December (Uganda Bureau of Statistics (UBOS) and ICF, 2018). A representative sample of 20 880 households was selected according to a stratified two-stage cluster design (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Eligible women for the interview were aged between 15 – 49 years and were either usual residents or visitors present in the selected household on the night before the survey. Out of the 19 088 eligible women, the Woman's Questionnaire was successfully administered to 18 506 (97%) individuals. Disease and intervention data were collected on 15 522 children under five years old.

4.2.4 Data

4.2.4.1 Fever and childhood diseases

Fever, ARI and diarrhoea data were available from the 2016 DHS questionnaires, by asking mothers whether any of their children under the age of five years had fever, cough accompanied by short, rapid breathing or had diarrhoea at any time during the two-week period preceding the survey. The presence of malaria was determined by a rapid diagnostic test (RDT) for children aged 6-59 months.

4.2.4.2 Interventions and health care seeking behaviour

The percentages of children who received Bacillus Calmette Guerin (BCG), measles, complete Diphtheria, pertussis and tetanus (DPT) and complete polio vaccines were used as measures of vaccination coverage against the respective fever-related diseases.

ITN use and ownership were defined according to the standard guidelines of the Roll Back Malaria (World Health Organisation, 2013b). In particular, ITN use included the percentage of people in a household that slept under an ITN, the percentage of children under 5 years in a household who slept under an ITN and the percentage of existing ITN used by the people in the household the previous night of the survey. ITN ownership comprised the percentage of households with at least one ITN, the percentage of households with at least one ITN for every two people and the percentage of the population with access to an ITN within their household.

Water, Sanitation and Hygiene (WASH) practices, specifically, the percentage of households with improved source of drinking water, improved sanitation facilities and, soap/detergent and water at hand washing places were used as preventive interventions for diarrhoea and ARI.

Health care seeking behavior was measured by the percentage of children with fever, ARI and diarrhoea for whom advice or treatment was sought from a health provider, a health facility, or a pharmacy and by the percentage of children with fever who had blood taken from a finger or heel for malaria testing. Treatments included artemisinin-based combination therapy among those who took any antimalarial drugs for fever, antibiotics in the fever cases and fluids (made from a special packet of oral rehydration salts, or government-recommended home made) among children with diarrhoea. A list of interventions, health care seeking and treatments measures included in the analysis is provided in Supplementary Table 4.1.

4.2.4.3 Socio-demographic factors

Socio-demographic characteristics included household (e.g. wealth index, stool disposal, type of fuel used for cooking), maternal (e.g. age, education, marital status, occupation) and child (e.g. residence, age, sex) characteristics.

4.2.4.4 Environmental/climatic factors

Environmental and climatic predictors were extracted from remote sensing sources. Land Surface Temperature, rainfall and Normalized Difference Vegetation Index were averaged during January to December 2016. Four land cover types were provided according to the International Global Biosphere Programme classification scheme, that is, the percentage of surface covered by forests, water and crops within a 5km buffer, and area of residence (rural or urban). Distance to forests, water bodies, crops and savanna were calculated based on Moderate Resolution Imaging Spectroradiometer (MODIS) land cover satellite data of 2013. Supplementary Table 4.2 provides a list of environmental/climatic data together with their spatio-temporal resolution and data source.

4.2.5 Bayesian geostatistical modelling

A Bayesian geostatistical Bernoulli regression model (Banerjee et al., 2015) was fitted to quantify the effects of childhood diseases on the presence of fever. The model included spatially varying covariate effects for each childhood disease adjusted for interventions, health care seeking, treatments, socio-demographic and climatic/environmental factors. Spatially varying effects (Giardina et al., 2014) were modelled at regional level using a conditional autoregressive (CAR) prior distribution (Banerjee et al., 2015). Spatial correlation was taken into account in the fever outcome by cluster-specific random effects with a multivariate normal prior distribution capturing a stationary spatial process with exponential correlation function of distance between any pair of locations.

Bayesian variable selection with stochastic search (George and McCulloch, 1993) was performed to identify the most important predictors i.e. diseases, intervention coverage indicators, socio-economic and climatic factors related to the presence of fever and their functional form (linear or categorical). Continuous predictors were categorized according to their quartiles. Variable selection was also used to select one or none among the four ITN use and ITN ownership indicators. For each predictor, an indicator parameter was introduced estimating the probability of inclusion of the corresponding predictor into the model. Predictors with an inclusion probability of more than 50% were considered in the final model (Giardina et al., 2014). Bayesian geostatistical modelling details are provided in Supplementary file 4.1. Parameter estimates were summarized by posterior medians and the corresponding 95% Bayesian Credible Intervals (95% BCI). Odds ratios were obtained by exponentiation of parameter estimates and they were considered statistically important if their 95% BCI did not include one.

The contribution of childhood diseases to the fever burden was quantified through estimating the population attributable fractions (PAF). PAF measures the percentage of all fever cases attributable to a particular disease among children less than five years. PAF can also be interpreted as the proportional reduction in fever prevalence among children less than five years that would occur if exposure to a specific disease was reduced to an alternative ideal exposure scenario. The definition of PAF was used in terms of known prevalence of the disease in the population, p, and the adjusted odds ratio, aOR, (Leviton, 1973) as $PAF = p\,(aOR - 1)/(1 + p(aOR - 1))$. The PAFs were calculated for the whole country and for each region separately following the formula presented above. Markov Chain Monte Carlo simulation drawing samples from the posterior distribution of the OR, that is, $OR^1, OR^2, \dots OR^N \sim p(OR|data)$ were used to obtain confidence intervals for PAFs, with N being the number of simulations. The overall mean and variance of simulated samples are estimates of the posterior mean and variance and were thus used to estimate the 95% BCI for PAFs.

Descriptive data analysis was carried out in STATA version 14.0 (Stata Corporation, College Station, TX, USA). OpenBUGS version 3.2.3 (Imperial College and Medical Research Council, London, UK) was used to perform variable selection and model fit. Maps were produced in ArcGIS version 10.5 (ArcGIS version 10.5, Esri, Redlands, CA, USA).

4.3 Results

4.3.1 Descriptive data analysis

One-third (33%) of children under the age of five (15 522) had a fever in the 2 weeks preceding the survey. Of these, 47% tested positive for malaria, 34% and 18% were reported as having diarrhoea and ARI respectively. Results in Table 4.1 indicate that the prevalence of fever was highest among children in Busoga (66%) and Teso (59%) regions and lowest in Bunyoro region (11%). Three in 10 (30%) of under-five children tested positive for malaria according to the RDT results. The prevalence of malaria among children varies by region, from 1% in Kampala and 3% in Kigezi regions to 69% in Karamoja, 63% in Acholi, and 62%

in Lango regions. Mothers reported that 20% of children under 5 years old had a diarrhoeal episode in the 2 weeks preceding the survey. As with symptoms of fever, the percentage of children with diarrhoea was highest in Teso (29%) and Busoga (27%) regions and lowest in Bunyoro region (10%). The prevalence of reported ARI symptoms was 9%; highest among children in Karamoja region (27%) and lowest in Bunyoro region (1%). The varying childhood disease burden within the country may be responsible for inequalities in fever prevalence across regions in Uganda.

Table 4. 1: The prevalence of fever and childhood diseases at the national and regional levels, Uganda DHS 2016

	Fever and childhood disease prevalence n (%)			
Geographical scale	**Fever**	**Malaria**	**Diarrhoea**	**ARI**
National	4 824 (33)	4 725 (30)	2 832 (20)	1 354 (9)
Regions				
Kampala	78 (14)	1 (1)	86 (16)	27 (5)
Central 1	459 (25)	93 (16)	359 (20)	147 (8)
Central 2	420 (27)	110 (21)	256 (17)	131 (9)
Busoga	939 (66)	265 (53)	390 (27)	175 (12)
Bukedi	345 (34)	90 (27)	182 (18)	50 (5)
Bugisu	139 (19)	47 (20)	105 (14)	68 (9)
Teso	541 (59)	141 (52)	266 (29)	131 (14)
Karamoja	170 (43)	76 (69)	94 (24)	105 (27)
Lango	337 (44)	170 (62)	157 (21)	135 (18)
Acholi	350 (49)	154 (63)	174 (24)	65 (9)
West Nile	423 (42)	79 (25)	159 (16)	78 (8)
Bunyoro	96 (11)	87 (32)	85 (10)	8 (1)
Tooro	273 (24)	77 (18)	250 (22)	150 (13)
Ankole	182 (16)	41 (11)	192 (17)	54 (5)
Kigezi	71 (15)	4 (3)	76 (16)	31 (6)

ARI: Symptoms of acute respiratory infections

Supplementary Table 4.3 indicates that, among the malaria interventions, the percentage of households with at least one ITN has the highest coverage reaching 78% and ranges from 55% in Karamoja to 92% in West-Nile. The percentage of households with at least one ITN for every two people is the malaria intervention with the lowest coverage of 51% varying from 23% in Karamoja to 68% in the Kigezi. Amongst vaccinations, BCG had the highest coverage (96%) with almost all children vaccinated in all regions. The polio vaccine had the lowest coverage of 70% nationally varying from 57% in Busoga to 80% in Acholi. Overall, nearly eight out of every ten households had an improved source of drinking water, but the percentage of households having improved sanitation facilities was lower (19%) and varied from 2% in Karamoja to 33% in Central 1.

Table 4.2 shows that only 29% of fever children received antibiotics in Uganda. The coverage of antibiotic treatment in fever cases was highest Kampala (46%) and in Bukedi (43%). Countrywide, 88% of children with fever took artemisinin-combination therapy with regional variations ranging from 59% in Kigezi to 93% in Karamoja. Amongst the health care seeking behavior, the percentage of children having fever and ARI for whom advice or treatment was sought was highest (about 80%). There were no outstanding regional differences in the coverage of both treatments.

Table 4. 2: Coverage of treatments and health care seeking at national and regional levels, Uganda DHS 2016

Geographical scale	Treatments coverage (%)				Health care seeking coverage (%)		
	Antibiotics	ORS or RHF	ACT	RDT	Fever advice	ARI advice	Diarrhoea advice
National	29	49	88	49	81	80	71
Regions							
Kampala	46	45	72	55	92	88	71
Central 1	19	53	81	59	88	80	66
Central 2	28	48	90	43	89	85	68
Busoga	37	53	91	43	78	81	72
Bukedi	43	56	89	34	79	81	73
Bugisu	18	40	86	36	91	76	69
Teso	36	31	89	44	64	70	61
Karamoja	26	81	93	68	90	84	85
Lango	20	36	87	49	82	83	86
Acholi	26	55	91	67	85	95	78
West Nile	24	56	90	57	90	93	80
Bunyoro	13	55	90	48	73	93	75
Tooro	16	59	86	57	74	69	65
Ankole	32	30	71	47	80	81	64
Kigezi	21	59	59	37	80	74	71

ORS or RHF; oral rehydration solution sachets or recommended home fluids, ACT; artemisinin-based combination therapy, RDT; Rapid diagnostic test, ARI; symptoms of acute respiratory infections

4.3.2 Bayesian geostatistical variable selection

Supplementary Table 4.4 contains all variables that were included in the final model with posterior inclusion probabilities of at least 50%. The inclusion probabilities of malaria, diarrhoea and ARI risks were 100%, an indication of a strong relationship between fever prevalence and childhood diseases. Among preventive interventions, BCG vaccination (83%) and the hand washing with soap/detergent and water were selected (93%). None of the ITN interventions indicators was included in the final model due to low probabilities of inclusion, which could imply a weak relationship between ITN and fever prevalence. Socio-demographic factors including age of the child, area of residence, mothers' marital status and occupation, improved source of drinking water and household wealth index score were included in the final model with inclusion probabilities exceeding 80%.

4.3.3 Effects of childhood diseases on fever prevalence

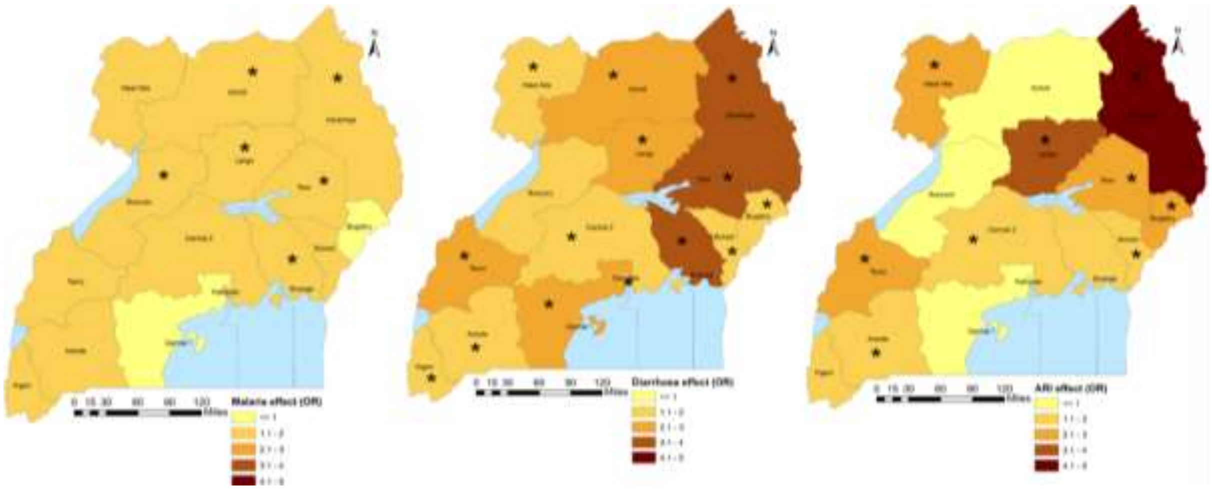
Table 4.3 shows the effects of childhood diseases on the prevalence of fever adjusted for interventions, socio-demographic and environmental/climatic factors. At the national level, the prevalence of malaria, diarrhoea and ARI were associated with increased odds of fever among children less than five years. In particular, the odd of fever was 35% higher among children with malaria than children without malaria (adjusted odds ratio, aOR = 1.35; 95% BCI: 1.08 – 2.12). Children who experienced diarrhoeal episodes had almost four times higher odds of fever compared to children without diarrhoea (aOR = 4.08; 95% BCI: 2.68 – 4.56). Furthermore, the odds of fever were almost six times higher for children with ARI relative to those without ARI (aOR = 5.99; 95% BCI: 2.21 – 6.79).

Table 4. 3: Posterior estimates for the effects of childhood diseases on fever prevalence adjusted for vaccinations, socio-demographic and climatic/environmental factors

	Malaria	Diarrhoea	ARI
Geographical scale	**aOR (95% BCI)**	**aOR (95% BCI)**	**aOR (95% BCI)**
National	1.35 (1.08, 2.12)*	4.08 (2.68, 4.56)*	5.99 (2.21, 6.79)*
Regions			
Kampala	1.14 (0.08, 3.21)	1.93 (1.63, 2.00)*	0.74 (0.25, 2.13)
Central 1	0.68 (0.19, 2.83)	2.72 (1.88, 3.74)*	0.96 (0.13, 2.21)
Central 2	1.48 (0.69, 2.43)	1.78 (1.17, 1.93)*	1.64 (1.22, 3.01)*
Busoga	1.38 (1.10, 2.86)*	3.21 (1.18, 3.77)*	1.19 (0.17, 3.57)
Bukedi	1.49 (0.74, 3.58)	1.74 (1.14, 2.54)*	1.38 (1.16, 1.98)*
Bugisu	0.16 (0.03, 1.16)	1.29 (1.03, 1.64)*	2.03 (1.79, 2.44)*
Teso	1.35 (1.06, 2.45)*	3.96 (1.41, 5.25)*	2.58 (1.08, 3.51)*
Karamoja	1.62 (1.06, 4.17)*	3.61 (2.06, 4.51)*	4.75 (1.64, 5.55)*
Lango	1.32 (1.05, 3.03)*	2.81 (2.48, 3.83)*	3.26 (1.07, 4.68)*
Acholi	1.36 (1.03, 3.30)*	2.82 (2.30, 3.79)*	0.62 (0.08, 1.95)
West Nile	1.62 (0.57, 2.87)	1.71 (1.09, 2.40)*	2.94 (1.96, 3.43)*
Bunyoro	1.10 (1.05, 2.49)*	1.55 (0.77, 4.49)	0.89 (0.23, 1.56)
Tooro	1.13 (0.42, 4.19)	2.38 (1.55, 3.33)*	2.09 (1.44, 2.24)*
Ankole	1.03 (0.14, 2.37)	1.74 (1.03, 2.64)*	1.84 (1.79, 2.06)*
Kigezi	1.01 (0.02, 2.31)	1.45 (1.01, 1.56)*	1.28 (0.04, 1.64)
Spatial parameters	**Median (95% BCI)**	**Median (95% BCI)**	**Median (95% BCI)**
Regional variance of disease effect[a]	2.27 (1.32, 3.71)	1.34 (0.77, 2.25)	3.11 (1.92, 5.38)
Range(km)[b]	2.60 (1.14, 7.32)		
Spatial variance in fever	3.16 (2.91, 3.47)		

*Statistically important effect; aOR: adjusted odds ratio, [a]Variance of conditional autoregressive process; ARI: Symptoms of acute respiratory infections, [b]Distance after which spatial correlation in fever becomes < 5%

Results of spatially varying geostatistical regression (Table 4.3) indicate that disease effects varied by region. Figure 4.1 illustrates the corresponding geographical distribution. The effect of malaria was statistically associated with higher odds of fever in Busoga, Teso, Karamoja, Lango, Acholi and Bunyoro whereas diarrhoea increased the odds of fever in all regions except Bunyoro. ARI was associated with increased odds of fever in Central 2, Bukedi, Bugisu, Teso, Karamoja, Lango, West Nile, Tooro and Ankole regions. Spatial correlation in fever risk was rather moderate extending up to 2.60km (Range: 1.14, 7.32).



(a) (b) (c)

Figure 4. 1: Geographical distribution of spatially varying disease effects (adjusted odds ratios) on fever prevalence; the (*) indicates a statistically significant disease effect, (a) malaria prevalence, (b) diarrhoea prevalence, (c) ARI prevalence.

Figure 4.2 displays the corresponding 2.5th, 50th and the 97.5th percentiles of the posterior distribution of the odds ratio.

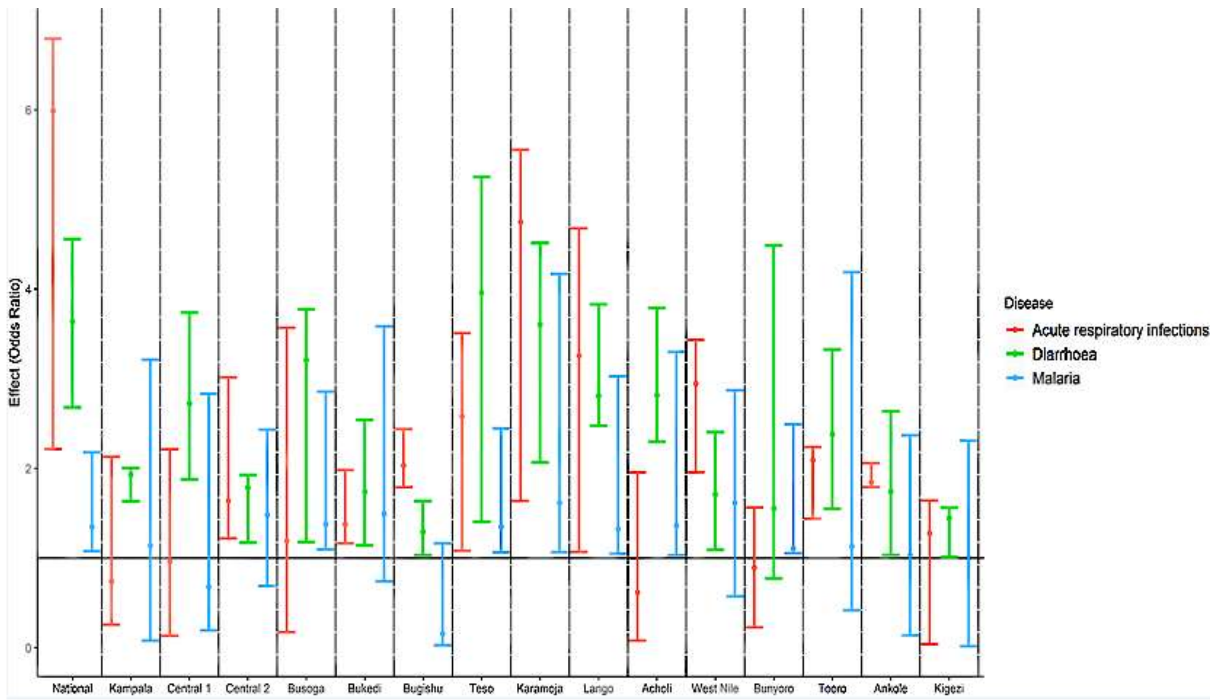


Figure 4. 2: Posterior estimates of disease effects with their corresponding 95% BCI at national and regional scales estimated from the Bayesian geostatistical logistic regression model. Points on the lines indicate the 2.5%, 50% and 97.5% quantiles of the posterior distribution of the odds ratio. Lines that do not cross one indicate a statistically important effect.

Table 4.4 shows a declining trend of risk of fever with increasing coverage of vaccination. A 1% increase in the coverage of BCG vaccine was associated with a 6% reduction in the odds of fever (aOR = 0.94; 95% BCI: 0.91 – 0.97). Children aged 12 months and older had higher odds of fever compared to those that were younger than 7 months old. The highest odds were estimated in the age of 12 – 23 months old (aOR = 2.49; 95% BCI: 2.09 – 3.22). The odds of fever was lower in urban areas (aOR = 0.53; 95% BCI: 0.35 – 0.94), in children born to married women (aOR = 0.33; 95% BCI: 0.25 – 0.45), in children from higher socio-economic status (aOR = 0.74; 95%BCI: 0.66 – 0.91 for the richest socio-economic status compared to the poorest one) and, in children living in households having both water and soap/detergent at hand washing places (aOR = 0.96; 95% BCI: 0.93 – 0.98). However, the odds of fever among children less than five years increase with increasing night LST (aOR = 1.30; 95% BCI: 1.23, 1.47).

Table 4. 4: Posterior estimates for the effects of interventions, socio-demographic and environmental/climatic factors on fever prevalence

Variable	OR (95% BCI)
Vaccinations	
BCG	0.94 (0.91, 0.97)*
WASH practices	
Water: No	1.0
Yes	0.99 (0.71, 1.53)
Soap/detergent and water: No	1.0
Yes	0.96 (0.93, 0.98)*
Socio-demographic factors	
Child factors	
Age (months): 0-6	1.0
7-11	1.19 (0.92, 1.54)
12-23	2.49 (2.09, 3.22)*
24-35	2.06 (1.89, 2.62)*
36-47	1.62 (1.22, 1.91)*
>=48	1.22 (1.08, 1.42)*
Residence: Rural	1.0
Urban	0.53 (0.35, 0.94)*
Maternal factors	
Marital status: Not married	1.0
Married	0.33 (0.25, 0.45)*
Occupation: No	1.0
Yes	1.14 (0.83, 1.79)
Household factors	
Wealth index: Poorest	1.0
Poorer	0.83 (0.67, 0.93)*
Middle	0.73 (0.53, 0.86)*
Richer	0.67 (0.43, 0.82)*
Richest	0.74 (0.66, 0.91)*
Type of cooking fuel: No wood	1.0
Wood	1.06 (0.43, 1.23)
Climatic/environmental factors	
% surface covered by water within a 5km buffer	0.94 (0.06, 1.47)
LST night	1.30 (1.23, 1.47)*
Distance to savanna	0.90 (0.72, 1.09)

*Statistically important effect

4.3.4 Contribution of childhood diseases on fever prevalence

National population attributable fraction (PAF) estimates (Table 4.5) indicate that 38% (PAF = 38.12; 95%BCI: 25.15, 41.59), 31% (PAF = 30.99; 95%BCI: 9.82, 34.26) and 10% (PAF =

9.50; 95%BCI: 2.34, 25.15) of the fever burden among children less than five years in Uganda is attributable to diarrhoea, ARI and malaria respectively. Most cases of fever in Kampala, Central 1, Central 2, Busoga, Bukedi, Teso, Acholi, Tooro, Ankole and Kigezi regions are attributable to diarrhoea. In Bugisu, Karamoja and West Nile, the highest percentage of fevers can be attributed to ARI whereas in Bunyoro region, majority of the fever cases are due to malaria. In Lango, diarrhoea and ARI are equally responsible for a bigger percentage of fever cases in these regions.

Table 4. 5: Population attributable fraction (PAF) estimates (%) for malaria, diarrhoea and ARI at the national and regional scale relative to fever

	Malaria	Diarrhoea	ARI
Geographical scale	**PAF (95% CI)**	**PAF (95% CI)**	**PAF (95% CI)**
National	[a]9.50 (2.34, 25.15)*	38.12 (25.15, 41.59)*	30.99 (9.82, 34.26)*
Regions			
Kampala	0.14 (-0.93, 2.16)	12.95 (9.16, 13.79)*	-1.32 (-3.90, 5.35)
Central 1	-5.40 (-14.89, 22.65)	25.60 (14.97, 35.40)*	-0.32 (-7.48, 8.83)
Central 2	9.16 (-6.96, 23.09)	11.71 (2.81, 13.65)*	5.45 (1.94, 15.32)*
Busoga	16.76 (5.03, 49.64)*	37.37 (4.63, 42.79)*	2.23 (-11.06, 23.57)
Bukedi	11.68 (-7.55, 41.06)	11.75 (2.46, 21.70)*	1.86 (0.79, 4.67)*
Bugisu	-20.19 (-24.07, 3.10)	3.90 (0.42, 8.22)*	8.48 (6.64, 11.47)*
Teso	15.40 (3.03, 42.99)*	46.19 (10.63, 55.21)*	18.11 (1.11, 26.00)*
Karamoja	29.96 (3.98, 68.63)*	38.51 (20.28, 45.729*	50.31 (14.73, 55.13)*
Lango	16.56 (3.01, 55.72)*	27.54 (23.71, 37.28)*	28.92 (1.24, 39.85)*
Acholi	18.49 (1.85, 59.17)*	30.40 (23.78, 40.11)*	-3.54 (-9.03, 7.88)
West Nile	13.42 (-12.04, 31.86)	10.20 (1.42, 18.30)*	13.43 (7.13, 16.28)*
Bunyoro	3.10 (1.57, 32.29)*	5.21 (-2.35, 25.87)	-0.11 (-0.78, 0.56)
Tooro	2.29 (-11.66, 36.48)	23.29 (10.79, 33.89)*	12.41 (5.41, 13.88)*
Ankole	0.33 (-10.45, 13.10)	11.17 (0.51, 21.80)*	4.03 (3.80, 5.03)*
Kigezi	0.03 (-3.03, 3.78)	6.72 (0.16, 8.22)*	1.65 (-6.11, 3.70)

*Percentage of fever cases attributable to a disease, [a]9.50% (PAF = 9.50; 95%CI: 2.34, 25.15) of fever cases among children less than five years in Uganda are attributed to malaria, ARI: Symptoms of acute respiratory infections

4.4 Discussion

This study quantified the contribution of childhood diseases to the risk of fever in children below 5 years old in Uganda at the national and sub-national scale. The analysis adjusted for the confounding effects of health interventions, health care seeking behaviour, socio-demographic and environmental/climatic factors. Study findings indicated that most fevers among children under five years are due to diarrhoea, followed by ARI. Also, there were strong geographical variations in the effects of malaria, diarrhoea and ARI on the distribution of fever risk among children less than five years in Uganda. Previous studies assessed the relationship between fever risk and a single childhood disease (either malaria, diarrhoea or ARI) (El-Radhi et al., 1999; Okiro and Snow, 2010; Ssenyonga et al., 2009)and did not quantify the disease contribution to fever. The current work takes into account exposure of children to multiple diseases as well as determining their contribution to fever prevalence.

Results at the national level indicated that children having malaria, diarrhoea or ARI were at a higher risk of fever compared to those without the diseases. The significant association between malaria and fever prevalence could be due to the inadequately developed immune system through the initial five years of life (Okiro and Snow, 2010). Analysis of MIS of six African countries (Djibouti, Kenya, Namibia, Angola, Liberia and Senegal) undertaken between 2007 and 2009 found a similar result (Okiro and Snow, 2010).

Despite the satisfactory coverage of ITN use and ownership in Uganda (Uganda Bureau of Statistics (UBOS) and ICF, 2018), the association between fever prevalence and ITN was not significant. This may be because the majority of fever cases are explained by diarrhoea and not malaria yet ITN target malaria-related fever. According to Atieli et al (Atieli et al., 2011), Lengeler (Lengeler, 2004) and Lengeler and Snow (Lengeler and Snow, 1996), households owning ITN and using them effectively, are protected from mosquito bites, thus decreasing episodes of fever or malaria infection. The least fever cases attributed to malaria may be a result of the high ITN coverage in Uganda.

The significant national effect of diarrhoea on fever can be tagged to the low coverage of poor WASH practices in the country, in particular, the presence of soap/detergent and water at hand washing places, which this study has found protective against fever. In Uganda, more than half of households lacked soap/detergent and water at hand washing places (Uganda Bureau of Statistics (UBOS) and ICF, 2018). In addition, only two in ten households in the country use improved toilet facilities (Uganda Bureau of Statistics (UBOS) and ICF, 2018). The effect of diarrhoea on fever is distinguished. For example, Ssenyonga et al (Ssenyonga et al., 2009) analysed the 2000/2001 Uganda DHS data and found diarrhoea to be associated with an increased risk of fever.

National estimates showed an important association between ARI and fever prevalence despite the low ARI prevalence. A similar relationship among vulnerable age groups has been observed in other investigations such as El-Radhi et al (El-Radhi et al., 1999). The low ARI prevalence could be attributed to the high coverage of vaccines targeting ARI conditions, particularly the pentavalent and pneumococcal vaccines (Gavi Full Country Evaluations Tea, 2016). However, not all ARI-related fevers can be prevented through vaccination due to the presence of non-vaccine ARI serotypes (Schaad, 2005), which calls for further efforts beyond vaccination. In order to fully address ARI in all settings, a balanced and comprehensive approach that emphasizes other preventive strategies as well as vaccination should be implemented. Uganda and other resource limited countries still have a challenge of addressing other drivers of ARI. According to Uganda’s 2016 DHS, nearly thirty percent of the under-fives are stunted due to poor nutrition, which falls within the World Health Organization category of public health problems. Further, under five mortality rates are higher in rural areas, where almost 100 percent of households use solid type of fuel for cooking and lighting which causes air pollution and health services are severely under facilitated (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

Apart from preventive measures, the poor health system in Uganda (Ssempiira et al., (in press)) seems to contribute to the enormous disease burden in the country. Health care seeking from health facilities is high throughout the country and within regions. However, coverage of treatments is low, especially of antibiotics and ORS or RHF. Only twenty nine percent and less than half of the under-five children in Uganda having ARI and diarrhoea, respectively received treatment (Uganda Bureau of Statistics (UBOS) and ICF, 2018). A similar pattern prevails within regions. This may imply a weak health system in the country with lack or shortage of treatments in health facilities.

Sub-national findings showed that effects of childhood diseases on fever vary by region. This could explain the large disparities in the geographical distribution of fever prevalences within the country. The effects of malaria and ARI were highest in Karamoja while that of diarrhoea was among the strongest in this region. The malaria effect can be attributed to the high malaria prevalence in Karamoja in which almost three quarters of children in the region tested positive with malaria (Uganda Bureau of Statistics (UBOS) and ICF, 2018). The high malaria burden in Karamoja has also been reported by Ssempiira et al, who analysed the Uganda MIS data 2014–15 (Ssempiira et al., 2017). The high prevalence of diarrhoea in Karamoja may be due to the deficiency of preventive interventions in this region (Uganda Bureau of Statistics (UBOS) and ICF, 2018). In this region, less than two in ten households had soap/detergent and water at hand washing places and only two percent of households in the region used improved sanitation facilities (Uganda Bureau of Statistics (UBOS) and ICF, 2018). This can explain the significant effect of diarrhoea on fever in Karamoja. The high prevalence of ARI in Karamoja region (Uganda Bureau of Statistics (UBOS) and ICF, 2018) could be responsible for the high effect of ARI on fever. Besides, the high levels of poverty in this region are a contributing factor to high malaria, ARI and diarrhoea morbidity. Over eighty percent of households in Karamoja are in the lowest wealth quintile, in contrast to less than one percent in the highest quintile. The extreme poverty in this region hinders access to quality preventive health services (Yeka et al., 2012). Despite the high poverty levels in Karamoja, health care seeking is satisfactory for all diseases. Treatment coverage for malaria and diarrhoea in the region is also sufficient. However, treatment for ARI in Karamoja is poor with only twenty six percent of children having ARI receiving treatment yet most fever cases in this region are attributable to ARI.

Diarrhoea risk was associated with fever prevalence in all regions except Bunyoro. This can be a result of the low implementation of WASH practices in most regions. About thirty percent of households had soap/detergent and water at handwashing places in ten out of the fifteen studied regions (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Coverage of improved sanitation was also poor in all regions, ranging from fifteen percent to thirty three percent (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

The study revealed that ARI had an important effect on fever prevalence in the regions of Central 2, Bukedi, Bugisu, Teso, Karamoja, Lango, West Nile, Tooro and Ankole. The smaller percentage of households having soap/detergent and water at hand washing places may be responsible for the statistically important effects of ARI on fever in these areas, since hand washing has been reported to lower the risk of respiratory infections (Rabie and Curtis, 2006). Only three out of ten households in over two thirds of the regions (Bugisu, Teso, Karamoja, Lango and West Nile) in which ARI had a significant association with fever had soap/detergent and water at hand washing places (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

Estimates of the population attributable fractions indicate that the highest burden of fever among children less than five years in Uganda is attributable to diarrhoea, followed by ARI and malaria had the least contribution. At the sub-national scale, most cases of fever in Kampala, Central 1, Central 2, Busoga, Bukedi, Teso, Acholi, Tooro, Ankole and Kigezi regions are attributable to diarrhoea. In Bugisu, Karamoja and West Nile, the highest percentage of fevers can be attributed to ARI whereas in Bunyoro region, majority of the fever cases are due to malaria. In Lango, diarrhoea and ARI are equally responsible for a bigger percentage of fever cases.

BCG vaccination was protective against fever. BCG is a vaccine against Tuberclosis (TB) which is known to be a fever-related disease. This relationship does not come as a surprise as vaccination against TB has been universally implemented in Uganda. Similar results have been observed in other countries. For example, an analysis of DHS data in Ghana, Nigeria, Kenya and Sierra Leon (Novignon and Nonvignon, 2012) and a study on the global burden of fever (Kothari et al., 2008) reported a positive effect of vaccination on fever prevalence.

Children in households with higher socio-economic status had a reduced risk of fever relative to children in households with a lower status. This relationship has been found in other settings. For instance, studies by Yusuf et al. in Nigeria (Yusuf et al., 2010), Njau in Tanzania (Njau et al., 2006) and, Novignon and Nonvignon in Ghana, Nigeria, Kenya and Sierra Leon (Novignon and Nonvignon, 2012) found that individuals in households with better socio-economic status were less likely to report fever than those in poorer households. Wealthier households are in a better position to provide preventive and curative measures to household members including children less than five years. Rich children are less exposed to disease risk factors such as poor water, sanitation and hygiene (WASH) practices and undernutrition, because wealth people can afford such services which enhances body defenses of rich children (Victora et al., 2003). Moreover, in the case of a fever event, financial related access to right, prompt and quality health care services is easier among affluent families. In developing countries where health care costs are high, poverty could be a key hindrance to looking for early and effective treatment (Novignon and Nonvignon, 2012).

Children born to single mothers were at a higher risk of fever compared to those whose mothers were in union. Marital status of a woman in Africa is a proxy of improved socio-economic status, as marriage may come with advantages such as pooling of resources to support better health services and provide improved nutrition to children (Kanmiki et al., 2014). DHS studies in Cameroon and Democratic Republic of Congo have already indicated single motherhood to be a risk factor for health outcomes of children less than five years (Ntoimo and Odimegwu, 2014).

The risk of fever was higher in rural than urban areas. This may be linked to higher levels of poverty in rural areas in Uganda (Yeka et al., 2012) and the poorer health system where facilities often run short of medical supplies and lack skilled healthcare workers (Victora et al., 2003). Rural areas have also inadequate transport systems which constrain access to curative (e.g. artemisinin-combination therapy and antibiotics) and preventive measures of fever-related diseases (e.g. insecticide treated nets and vaccinations) (Victora et al., 2003). Yusuf et al. found a similar association between the risk of fever and the area of residence among children less than five years in Nigeria (Yusuf et al., 2010).

The presence of soap/detergent and water at hand washing places was protective against the fever risk. Hand washing with a soap/detergent ensures that the transmission of germs is restricted, which substantially reduces the risk of diarrhoeal diseases among children (Ejemot-Nwadiaro et al., 2008). In a systematic review (Curtis and Cairncross, 2003) and a study in Britain (Burton et al., 2011), handwashing with soap/detergent and water was found effective for the removal of bacteria from hands. Despite its significant effect, the percentage of households with soap/detergent and water at hand washing places was low in the country with the exception of Kampala region (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

Furthermore, children aged two years and older were at a higher risk of fever compared to younger ones. This result can be attributed to the preventive effect of breastfeeding on infections in the younger group. Breastfeeding contains antibodies which reduce the risk of fever-diseases including gastroenteritis and respiratory illnesses

(Anatolitou, 2012). Yusuf et al., (2010) (Yusuf et al., 2010) also found older children to have a higher risk of fever when they analysed the Nigeria DHS 2008 data.

Environmental/climatic factors were significant predictors of fever prevalence. Increasing night LST was associated with high fever prevalence. Higher temperatures increase the rate of development of mosquitoes from one immature stage to the next (Machault et al., 2011). This accelerates vector distribution, shortens parasite life cycle, increases mosquito longevity and hence increased malaria transmission, a disease we found to be an important driver of the fever symptom. Elevated temperatures have been reported as a risk factor of fever in other countries, for example, Thailand (Nitatpattana et al., 2007).

The analysis comes with various constraints. Caretakers reported the presence of illness among under-five children in the two weeks prior to the survey. The data might have been subjected to recall bias as guardians were made to remember whether the child had illness in the previous two weeks. However, studies based on the Swedish registry data and a public health survey found high percentages of correctly self-reported data for recall periods of one month (99%), three months (98%), six months (96%) and twelve months (94%) (Kjellsson et al., 2014). Thus, a recall period of two weeks may not result into over or under estimation of results especially when events are memorable like child health.

4.5 Conclusion

In Uganda, the majority of fevers among children under five years are due to diarrhoea, followed by ARI. Therefore, improved coverage of diarrhoea and ARI interventions in the country while prioritizing the affected regions may be essential in minimizing fever-related morbidity. In particular, hand washing with soap/detergent and water should be strengthened in all regions except Bunyoro. Vaccination against ARI should be encouraged, especially, in the regions of Central 2, Bukedi, Bugisu, Teso, Karamoja, Lango, West-Nile, Tooro and

Ankole. The health system should be reinforced to treat diarrhoea and ARI mainly in the affected areas.

Declarations

Acknowledgements

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Availability of data and materials

The datasets supporting conclusions in this article are available at the DHS MEASURE website (www.dhsprogram.com) with request for access and following instructions at https://dhsprogram.com/data/Access-Instructions.cfm.

Authors' contributions

All authors take responsibility for the structure and content of the paper. BBN conceptualized the research, managed and analyzed the data, developed the methodology and implemented it in software, interpreted results and wrote the first draft of the manuscript. Author JS participated in data management. Authors FEM and SK formulated research goals and objectives, participated in the process of acquisition of project financial support and edited the manuscript. PV was the lead author who conceived the research, formulated research goals and objectives, acquired project financial support, led methodology development, model fitting and result interpretation and manuscript writing.

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Consent for publication

Not applicable.

Competing risks

The authors declare that they have no competing interests.

4.6 Supplementary files

Supplementary Table 4. 1: Description of interventions, health care seeking and treatment coverage measures

Variable	
ITN ownership	**Description**
%hh1itn	Percentage of households with at least one ITN
%hh1itn4two	Percentage of households with at least one ITN for every two people
%pp1itn	Percentage of people with access to an ITN within their household
ITN use	
%ppslept	Percentage of people in the household that slept under an ITN the previous night of the survey
%chslept	Percentage of children under 5 years in the household, who slept under an ITN the previous night
%itnused	Percentage of existing ITNs used by the people in the household the previous night
Vaccinations	
BCG	Percentage of children vaccinated with BCG
DPT	Percentage of children with complete vaccination of DPT
Polio	Percentage of children with complete vaccination of polio
Measles	Percentage of children vaccinated against measles
WASH practices	
Water	Percentage of households with improved source of drinking water
Sanitation	Percentage of households using improved sanitation facilities
Soap/detergent and water	Percentage of households with soap/detergent and water at hand washing place
Treatments	
ACT	Percentage of children receiving artemisinin-based combination therapy (ACT) among those with a fever who took any antimalarial drugs (during the 2 weeks period before the survey)
Antibiotics	Percentage of fever children receiving antibiotics
ORS or RHF	Percentage of children with diarrhea receiving fluid from oral rehydration solution (ORS) sachets or recommended home fluids (RHF)
Health care seeking	
Rapid diagnostic test	Percentage of fever children who had blood taken from a finger or heel for malaria testing
Fever advice	Percentage of fever children for whom advice or treatment was sought from health provider, a health facility, or a pharmacy
ARI advice	Percentage of children with symptoms of ARI for whom advice or treatment was sought from health provider, a health facility, or a pharmacy
Diarrhoea advice	Percentage of children with diarrhea for whom advice or treatment was sought from health provider, a health facility, or a pharmacy

Supplementary Table 4. 2: Remote sensing data sources[a]

Source	Data type	Temporal resolution	Spatial resolution
MODIS/Terra[b]	LST[l]	8 days	1km
MODIS/Terra[b]	NDVI[m]	16 days	1km
U.S. Geological Survey-Earth Resources Observation Systems (USGSS)	Rainfall	10 days	8x8km^2
Shuttle Radar Topographic Mission (SRTM)	Altitude	NA	1x1km^2
MODIS,IBGD type	Land cover Water bodies	NA	0.5x0.5km^2
Global Rural and Urban Mapping project	Urban Rural extent	NA	1x1km^2

NA: Not applicable; Land cover groups (forest, crops, urban); [a]Land cover data accessed in June 2016 and other data accessed in November 2013; [b]Moderate Resolution Imaging Spectroradiometer (MODIS)/Terra, available at: http://modis.gsfc.nasa.gov/; [l]Land surface temperature (LST) day and night; [m]Normalized difference vegetation index

Supplementary file 4. 1: Bayesian geostatistical modeling

Bayesian geostatistical variable selection

A Bayesian geostatistical logistic regression model, adopting a stochastic search variable selection approach, was used to determine the most important predictors of fever prevalence and their functional form (George and McCulloch, 1993). ITN coverage measures were grouped into use and ownership. Only one (or none) ITN measure among those defining ownership and one (or none) ITN measure among those defining use (Giardina et al., 2014) was selected. For each ITN coverage measure X_p in the ownership group, a categorical indicator I_p , was introduced to represent exclusion of the variable from the model ($I_p = 1$), or inclusion of one of the ITN ownership measure i.e. %hh1itn ($I_p = 2$), %hh1itn4two ($I_p = 3$) and %pp1itn $\left(I_p = 4\right)$. A similar definition was adopted for the ITN use coverage measure i.e. exclusion of the variable from the model ($I_p = 1$), inclusion of %ppslept ($I_p = 2$), %chslept ($I_p = 3$) and %itnused $\left(I_p = 4\right)$. The ITN measure with the highest probability of inclusion in each category was included in the final model.

For the environmental/climatic variables except of land cover types, variable selection compared their linear and categorical forms and selected the one that had the highest probability of inclusion or neither of the two forms. The categorical forms were generated based on the quartiles of variables. We introduced an indicator I_p for each environmental/climatic covariate X_p which defines exclusion of the variable from the model ($I_p = 1$), inclusion in a categorical ($I_p = 2$) or linear ($I_p = 3$) form.

For childhood diseases, vaccinations, treatments, health care seeking characteristics, socio-demographics and land cover types, a binary indicator parameter I_p suggesting presence ($I_p = 1$) or absence ($I_p = 0$) of the predictor from the model was introduced. I_p has a probability mass function $\prod_{j=1}^{p} \pi_j^{\delta_j(I_p)}$, where π_j denotes the inclusion probabilities, $j =$

(1,2,3,4), e.g. for ITN coverage measures so that $\sum_{j=1}^{p} \pi_j = 1$ and $\delta_j(.)$ is the Dirac function,

$$\delta_j(I_p) = f(x) = \begin{cases} 1, if\ I_p = j \\ 0, if\ I_p \neq j \end{cases}.$$

For inclusion probabilities of ITN use and ownership, a non-informative Dirichlet distribution was adopted with hyper parameters $\alpha = (1,1,1,1)^T$, that is, $\boldsymbol{\pi} = (\pi_1, \pi_2, \pi_{3,} \pi_4)^T \sim Dirichlet(4, \alpha)$. A similar distribution was adopted for the inclusion probabilities of environmental/climatic factors. For childhood diseases, vaccinations, treatments, health care seeking characteristics, socio-demographics and land cover types, a Bernoulli prior with an equal inclusion or exclusion probability was assumed for the indicator i.e. $I_p \sim bern(0.5)$. Also, inverse Gamma priors with parameters (2.01, 1.01) were assumed for the precision hyper parameters τ_p^2. The predictors identified as important are those with posterior inclusion probability greater than or equal to 50% (Ssempiira et al., 2017).

We assumed a spike and slab prior for regression coefficient β_p corresponding to the corresponding covariate, X_p i.e. for the coefficient β_p of the predictor in linear form we take $\beta_p \sim (1 - \delta_1(I_p))N(0, u_0\tau_p^2) + \delta_1(I_p)N(0, \tau_p^2)$ proposing a non-informative prior for β_p in case X_p is included in the model in a linear form (slab) and an informative normal prior with variance close to zero (i.e. $u_0 = 10^{-3}$) shrinking β_p to zero (spike) if X_p is excluded from the model. Similarly, for the coefficient $\{\beta_{p,l}\}_{l=1,..,L}$ corresponding to the categorical form of $\underline{X}_p$ with L categories, we assume that $\beta_{p,l} \sim \delta_2(I_p)N(0, \tau_{p,l}^2) + (1 - \delta_2(I_p))N(0, \vartheta_0\tau_{p,l}^2)$.

Bayesian geostatistical logistic regression model with spatially varying effects of childhood diseases

A Bayesian geostatistical logistic regression model (Banerjee et al., 2015) was fitted to quantify the effects of childhood diseases on the fever prevalence. The model included spatially varying coefficients for childhood diseases adjusted for socio-demographic factors, vaccinations, health care seeking characteristics, treatments, ITN use and ownership and climatic/environmental factors. The model assesses the effects of childhood diseases at a regional level using spatially varying coefficients (Giardina et al., 2014) and is formulated assuming a conditional autoregressive (CAR) prior distribution (Cressie, 2015). The CAR introduces a neighbour-based spatial structure for the regression coefficients for each childhood disease effect (Bivand et al., 2013). Neighbours were defined as the adjacent areas for each region. To adjust for spatial correlation present in the fever prevalence due to similar exposure effect in neighbouring clusters, cluster-specific random effects were introduced into the model. The cluster random effects were assumed to arise from a Gaussian stationary process with a covariance matrix capturing correlation between any pair of cluster locations as a function of their interlocation distances.

Let Y_{ij} be the binary outcome for child i at location s_j taking values 1 and 0 when fever is present or absent respectively, $\boldsymbol{X_j}(s_j)$ be the vector of socio-demographic factors, vaccinations, health care seeking characteristics, treatments, ITN use and ownership and climatic/environmental factors and $Z_d(s_j)$ be the prevalence of disease d at location s_j.

Y_{ij} is assumed to follow a Bernoulli distribution $Y_{ij} \sim Ber(p_{ij})$ and is related to its predictors using a logistic regression model as follows;

$logit(p_{ij}) = \beta_0 + \boldsymbol{\beta}^T \boldsymbol{X_j}(s_j) + \sum_{d=1}^{D} \left(b_d + \varepsilon_{dk(j)}\right)^T Z_d(s_j) + W(s_j) + v_j$ where p_{ij} is the presence or absence of fever of child i at location s_j, $\boldsymbol{\beta}^T = \left(\beta_1, \ldots, \beta_p\right)$ is the vector of regression coefficients with $\exp(\beta_l), l = 1, \ldots p$, corresponding to the odds ratio. $W(s_j)$ is a cluster-specific random frailty which captures spatial correlation in the fever prevalence due to similar exposure effect in neighbouring clusters. We modeled $\boldsymbol{W}(s) = (W(s_1), W(s_2), \ldots, W(s_m))^T$ by a Gaussian process, i.e. $\boldsymbol{W}(s) \sim N(0, \Sigma)$, where Σ is the variance-covariance matrix and each element is defined by an exponential correlation function of the distance d_{kl} between locations s_k and s_l, that is $\Sigma_{kl} = \sigma^2 \exp(-d_{kl}\rho)$ (Banerjee et al., 2015). The parameter σ^2 gives the variance of the spatial process and ρ is a smoothing parameter that controls the rate of correlation decay with distance. For the exponential correlation function, $\frac{-\log(0.05)}{\rho}$ determines the distance at which the correlation drops to 0.05 (i.e. effective range of spatial process). Non-spatial variation is estimated by the random effects v_j, assumed independent and normally distributed with mean 0 and variance σ_v^2 .

Our model assumed that the relation between childhood diseases and fever prevalence varied across regions by including disease specific spatially varying coefficients, $b_d + \varepsilon_{kd}$, where b_d is the effect of the disease $d = 1, \dots D$ on fever prevalence at country (national) level and $\boldsymbol{\varepsilon_d} = (\varepsilon_{d1}, \dots, \varepsilon_{dk})^{\boldsymbol{T}}$ are the varying effects at regional (sub-national) levels $k = 1, \dots K$ with $k(j)$ indicating the region k corresponding to the location s_j.We introduced spatial dependence among the regions via a conditional autoregressive (CAR) prior for $\boldsymbol{\varepsilon_d}$, that is $\boldsymbol{\varepsilon_d} \sim N(\mathbf{0}, \Omega_d)$ with $\Omega_d = \sigma_d^2 (I - \gamma C)^{-1} \Delta$. σ_d^2 is the variance of spatially varying disease effects, Δ is a diagonal matrix with entries $\Delta_{kk} = {g_k}^{-1}$where g_k is the number of neighbours of region k, γ measures overall spatial dependence and C is the adjacency matrix with normalized entries that is $C_{kl} = \omega_{kl}/g_k$, ω_{kl} is 1 if region k neighbors l and 0 otherwise (Banerjee et al., 2015).

Model specification was completed by assigning prior distributions to model parameters. We assumed inverse gamma priors for all spatial variances with known parameters, i.e. $\sigma^2, \sigma_d^2 \sim IG(2.01, 1.01)$, a uniform prior distribution for $\rho \sim U(a, b)$, where a and b chosen such that the effective range is within the maximum and minimum distances of the observed locations (Thomas et al., 2004) and a uniform prior for $\gamma \sim U(\lambda_1^{-1}, \lambda_2^{-1})$ where λ_1, λ_2 are the smallest and largest eigenvalue of $\Delta^{-1/2} \mathrm{C} \Delta^{1/2}$ (Banerjee et al., 2015). Non-informative normal priors were adopted for the regression coefficients $\beta_l, b_d \sim N(0, 10^3)$ for $l = 1, \dots p$ and $d = 1, \dots D$. The joint posterior distribution of the model is given by

$$\prod_{\boldsymbol{j}} [\, Y_i(s_j) \,|\boldsymbol{\beta}, b_d, W(s_j)\, \varepsilon_{dk}, \boldsymbol{X_j}(s_i), \boldsymbol{Z_d}(s_j)][\, \boldsymbol{W}(s)|\sigma^2, \rho][\boldsymbol{\varepsilon_d}|\, \sigma_d^2, \gamma][\boldsymbol{\beta}, b_d, \sigma^2, \sigma_d^2, \gamma, \rho]$$

Model parameters were estimated using Markov Chain Monte Carlo simulation (George and McCulloch, 1993). A two chain algorithm of 400 000 iterations with an initial burn-in of 20 000 iterations was run. Convergence was assessed by the Gelman and Rubin diagnostic (Rubin and Gelman, 1992).

Supplementary Table 4. 3: Coverage of interventions at national and regional levels, Uganda DHS 2016

	INT coverage (%)						Vaccination coverage (%)				WASH practices coverage (%)		
Geographical scale	**%hh1itn**	**%hh1itn4two**	**%pp1itn**	**%ppslept**	**%chslept**	**%itnused**	**BCG**	**DPT**	**Polio**	**Measles**	**Water**	**Sanitation**	**Soap/detergent water**
National	78	51	65	55	62	74	96	80	70	80	78	19	44
Regions													
Kampala	75	58	66	60	69	81	99	82	59	83	94	24	71
Central 1	79	59	70	59	67	77	93	76	64	76	70	33	58
Central 2	75	50	65	53	63	73	95	78	59	73	72	31	57
Busoga	75	48	61	52	58	77	97	72	57	70	90	29	22
Bukedi	74	41	54	42	49	69	98	78	62	77	94	15	54
Bugisu	72	39	55	52	60	85	99	73	58	80	84	7	27
Teso	84	48	64	62	72	87	99	92	78	87	95	16	16
Karamoja	55	23	36	33	47	68	99	86	78	91	87	2	15
Lango	79	47	63	53	66	77	96	79	65	75	85	9	23
Acholi	81	41	58	59	68	83	99	85	80	85	81	9	22
West Nile	92	61	77	71	77	73	96	83	74	82	85	4	37
Bunyoro	76	49	62	57	60	77	98	79	75	84	77	15	38
Tooro	77	49	63	50	53	67	96	76	62	87	63	11	57
Ankole	85	58	74	55	58	65	97	84	76	82	53	15	37
Kigezi	89	68	79	55	60	57	98	89	78	96	64	15	31

Supplementary Table 4. 4: Posterior inclusion probabilities for diseases, interventions, treatments, health care seeking, socio-demographic and environmental/climatic factors

Variable	Inclusion probability (%)	Variable	Inclusion probability (%)
Diseases		**Household factors**	
Malaria	100.0*	Stool disposal	2.0
All ARI	100.0*	**Climatic/environmental factors**	
Diarrhoea	100.0*	**Land cover**	
ITN ownership		% surface covered by forest within a 5km buffer	38.3
None	95.1	% surface covered by water within a 5km buffer	88.5*
%hh1itn	1.0	% surface covered by crop within a 5km buffer	34.0
%hh1itn4two	1.8	Rural or urban	47.8
%pp1itn	2.1	**LST day**	
ITN use		None	100.0
None	92.4	Linear	0.0
%ppslept	0.8	Categorical	0.0
%chslept	0.6	**LST night**	
%itnused	6.2	None	0.0
Vaccinations		Linear	100.0*
BCG	83.0*	Categorical	0.0
DPT	1.0	**NDVI**	
Polio	1.0	None	70.8
Measles	2.0	Linear	29.2
Treatments		Categorical	0.0
ACT	6.0	**Rainfall**	
Antibiotics	1.4	None	91.8
ORS or RHF	1.2	Linear	8.2
WASH practices		Categorical	0.0
Water	98.0*	**Altitude**	
Sanitation	28.0	None	59.0
Soap/detergent and water	93.0*	Linear	41.0
Health care seeking		Categorical	0.0
Rapid diagnostic test	2.0	**Distance to forest**	
Fever advice	2.0	None	98.0
ARI advice	0.0	Linear	2.0
Diarrhoea advice	1.0	Categorical	0.0
Socio-demographic factors		**Distance to water**	
Child factors		None	89.2
Sex	3.4	Linear	10.8
Age of child		Categorical	0.0
None	0.0	**Distance to savanna**	
Linear	0.0	None	49.8
Categorical	100.0*	Linear	50.2*
Residence	88.3*	Categorical	0.0
Maternal factors		**Distance to crops**	
Education level	18.0	None	67.2
Marital status	100.0*	Linear	32.8
Occupation	100.0*	Categorical	0.0
Household factors			
Wealth index	100.0*		
Type of cooking fuel	55.0*		

*Included in the final model with a probability ≥ 50%

Chapter 5: The effect of the presence of soap and water at handwashing places on the risk of diarrhoea and respiratory infections among children under-five years in Uganda: A spatial analysis

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Abstract

Background: Worldwide, diarrhoea and acute respiratory infections (ARI) especially pneumonia are the leading causes of under-five deaths and morbidity. In Uganda, pneumonia is second to malaria while diarrhoea ranks number six among the principal causes of under-five deaths. Handwashing with soap and water is recommended as one of the most cost-effective interventions to prevent diarrhoea and respiratory infections. However, there is paucity of literature on studies assessing the effect of handwashing with soap and water on the risk of diarrhoea and ARI among the under-five in Uganda. This study quantifies the effect of the presence of soap and water at handwashing places in households on the risk of diarrhoea and ARI among children less than five years old.

Methods: Data was obtained from the 2016 Uganda Demographic and Health Survey (DHS). Bayesian geostatistical logistic regression models were fitted to determine the effects of handwashing with soap and water on the risk of diarrhoea and ARI. Cluster-specific random effects were introduced into the model to take into account spatial correlation in the risk of diarrhoea and ARI. Bayesian geostatistical stochastic search variable selection was applied to determine the most important predictors in explaining variation in the risk diarrhoea and ARI.

Results: Nine percent (9%) and 20% of children under age five (15 522) had ARI and diarrhoea respectively in the two weeks before the survey. About half (44%) of households had water and soap at hand washing places. One-third (33%) and 40% of children having ARI and diarrhoea respectively lived in households having water and soap at hand washing places. Results show that the odds of diarrhoea and ARI in children who lived in households having soap and water at handwashing places were 14% and 24% less than those living in households without the intervention (adjusted odds ratio, aOR = 0.86; 95% BCI: 0.77 – 0.96) and (aOR = 0.76; 95% BCI: 0.65 – 0.88) respectively.

Conclusion: The presence of soap and water at handwashing places in households is associated with a reduction in the risk of diarrhoea and ARI among the under-five. However, coverage of the intervention is low and should be scaled up.

Key words: DHS, Diarrhoea, symptoms of acute respiratory infections, handwashing with soap and water, under-five, Uganda

5.1 Introduction

Globally, diarrhoea and acute respiratory infections (ARI) especially pneumonia are the leading causes of mortality and morbidity among children less than five years (Liu et al., 2016), which certainly decelerates the achievement of Sustainable Development Goal 3 (World Health Organization, 2015b). Diarrhoea is caused by a host of bacterial, viral and parasitic organisms, most of which are spread through water contaminated by human-faeces or animals, poor personal hygiene such as dirt under nails and food prepared or stored in unhygienic conditions (The United Nations Children's Fund (UNICEF)/World Health Organization (WHO) and World Health Organization, 2009). Respiratory infections are caused by viruses, fungi, or bacteria and can be passed from one person to another by breathing in respiratory droplets from a person coughing or sneezing, by touching the nose, mouth or eyes after being in contact with someone who has a respiratory infection, or by touching another object exposed to the virus (Ferkol and Schraufnagel, 2014).

Globally, diarrhoea and pneumonia accounted for 9% and 13% of the 5.94 million deaths that occurred in 2015 respectively (Liu et al., 2016). Compared to other diseases worldwide, each of the major killers caused more child deaths compared to malaria (5%), HIV/AIDS (1%) and measles (1%) combined (Liu et al., 2016). In sub-Saharan Africa, pneumonia (17%) and diarrhoea (10%) caused more child deaths than malaria (10%), HIV/AIDS (less than 1%) and measles (less than 1%) combined (Liu et al., 2016). In Uganda, pneumonia is second to malaria while diarrhoea ranks number six among the principal causes and were responsible for 11% and 5% of the under-five deaths respectively in 2015/2016 (Ministry of Health, 2015b). Uganda conducts the Demographic and Health Survey (DHS) every five years, to estimate among others the prevalence of diseases and evaluate the impact of health programmes (Uganda Bureau of Statistics (UBOS) and ICF, 2018). The most recent DHS 2016 in Uganda showed that the national prevalence of ARI and diarrhoea among the under-five was 9% and 20% respectively. These prevalences are indicators of diarrhoea and ARI role in causing under-five deaths and thus the need to prevent the diseases. Handwashing with soap and water is recommended as one of the most cost-effective interventions to prevent diarrhoea and respiratory infections (Jamison et al., 2006). Despite its benefits, coverage of the intervention is low (44%) in Uganda yet prevalences of diseases targeted by this intervention are high (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

Reviews of epidemiological studies suggest that handwashing with soap could reduce the risk of severe diarrhoea by 48% and the risk of any diarrhoea by 47% (Curtis and Cairncross, 2003). A further review (Rabie and Curtis, 2006), concluded that handwashing with soap reduces the risk of lower respiratory tract infections such as pneumonia by up to 23%. A meta-analysis assessing the health impact of promoting handwashing with soap in resource-poor settings reported a 31% reduction in the risk of acute gastrointestinal disease and 21% reduction in risk of acute respiratory illness (Aiello et al., 2008). A study in rural Kenya based on a population-based infectious diseases surveillance system found that children in households with soap at handwashing places were at a lower risk of diarrhoea (Kamm et al., 2014). Other studies in Burkina Faso (Curtis et al., 2001), in Ghana (Scott et al., 2007) and in Tanzania (Pickering et al., 2010) showed that handwashing with soap reduced diarrhoea and respiratory infections. Further, a systematic review on hand hygiene intervention strategies to reduce diarrhoea and respiratory infections among school children in developing countries, reported that handwashing with soap reduced the incidence of diarrhoea and respiratory infections (Mbakaya et al., 2017).

In Uganda, a few studies have assessed the effect of handwashing with soap and water on the risk of diarrhoea (Zhang et al., 2013). However, the former study was school-based and included children aged 7 – 13 years excluding the under-five. Other studies used DHS data and evaluated the determinants of diarrhoea (Bbaale, 2011; Ssenyonga et al., 2009) without examining the effect of handwashing with soap and water. Another study reported higher WASH (Water, Sanitation and Hygiene) quintiles to significantly reduce the prevalence of diarrhoea (Hirai et al., 2016). However, WASH quintiles were constructed using the main source of drinking water for a household, types of household sanitation facilities, practice of sharing sanitation facilities, handwashing materials in the household and water collection time. This study did not quantify the effect of handwashing with soap and water on the risk of diarrhoea. Limited studies have assessed the determinants of ARI in Uganda (Bbaale, 2011) but little is known about the effect of handwashing with soap on the risk of ARI. In addition, previous studies on diarrhoea and ARI did not consider the spatial structure of environmental/climatic factors that drive the spread of diarrhoea and ARI risk (Siraj et al., 2014). Further, former studies focused on controlling for socio-demographic factors and interventions, in particular, breastfeeding and WASH practices.

The objective of this study is to estimate the effects of handwashing with soap and water on the risk of diarrhoea and ARI using Bayesian geostatistical methods, while adjusting for spatial correlation in disease outcomes and potential confounding effects of socio-demographic characteristics, interventions (i.e. vaccinations, WASH and breastfeeding), health care seeking behaviour and environmental/climatic factors. Results of this study will be vital for policy formulation and advocacy to programmes that aim to reduce the burden of diarrhoea and ARI among the under-five in Uganda. In addition, although the effect of the presence of handwashing with soap in households has been broadly studied in other countries, studies in Uganda assessing the intervention among the under-five as well as using nationally representative data are scarce. Therefore, this study adds to the existing evidence that the presence of soap and water at handwashing places in households can reduce the risk of diarrhoea and ARI among the under-five.

5.2 Methods

5.2.1 Country profile

Uganda is located in eastern Africa, west of Kenya, south of South Sudan, east of the Democratic Republic of the Congo, and north of Rwanda and Tanzania. It is in the heart of the Great Lakes region, and is surrounded by three of them, Lake Edward, Lake Albert, and Lake Victoria. The country is mostly plateau with a rim of mountains ("Uganda, The World Fact book, United States Central Intelligence Agency," 2015). The climate is tropical and generally rainy with two dry seasons (December to February, June to August) ("Uganda, The World Fact book, United States Central Intelligence Agency," 2015). Uganda has an area of 241 039 km^2 and a population of about 40 million of which 20% are under-five years of age (Uganda Bureau of Statistics (UBOS) and ICF International Inc, 2012). Diarrhoea and acute respiratory infections are among the leading causes of child morbidity in Uganda and accounted for 20% and 9% respectively of children under age five in 2016 (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

5.2.2 Ethical approval and consent to participate

In this research article, secondary data that was made available to us by the Uganda Bureau of Statistics and the DHS Program (www.dhsprogram.com) was analysed. According to survey reports, ethical approval and consent to participate was obtained by the above bodies from the Institutional Review Board of International Consulting Firm of Calverton, Maryland, USA, and from Makerere University School of Biomedical Sciences Higher Degrees Research and Ethics committee and the Uganda National Council for Science and Technology. An interview was administered only if respondents assented verbally to an informed consent statement read to them by interviewers. Details on ethical approval and consent to participate is published in the 2016 DHS (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

5.2.3 Study setting

Data analysed in this study were obtained from the 2016 DHS which was carried out from June through December (Uganda Bureau of Statistics (UBOS) and ICF, 2018). The DHS is a nationally representative survey which employs a stratified two-stage cluster design. In the first stage, 697 clusters were selected from the 2014 Uganda National Population and Housing Census sampling frame. Households constituted the second stage of sampling. A representative sample of 20,880 households was randomly selected for the 2016 UDHS. Eligible women for the interview were aged between 15 – 49 years and were either permanent residents of the selected households or visitors who stayed in the household the night before the survey. The response rate to the Woman's Questionnaire was 97%. Mothers reported data on diarrhoea and symptoms of acute respiratory infections (ARI) on 15 522 children under five years old. Data on handwashing with water and soap were collected at household level.

5.2.4 Data

5.2.4.1 Diarrhoea, ARI and handwashing with water and soap

Diarrhoea and ARI data were available from the 2016 DHS questionnaires, by asking mothers whether any of their children under the age of five years had cough accompanied by short, rapid breathing or had diarrhoea at any time during the two-week period preceding the survey. The presence of water and soap at hand washing places was determined by interviewers asking and observing the place where household members most often wash their hands.

5.2.4.2 Interventions and health care seeking behaviour

The percentages of children who received measles and complete Diphtheria, pertussis and tetanus (DPT) vaccines were used as prevention measures against ARI. WASH practices, specifically, the percentage of households with improved source of drinking water and improved sanitation facilities were used as preventive interventions for diarrhoea. The percentage of infants who started breastfeeding within one hour of birth and the percentage of infants exclusively breastfed during the first six months after birth were assessed as interventions against childhood diseases.

Health care seeking behavior was measured by the percentage of children with ARI or diarrhoea for whom advice or treatment was sought from a health provider, a health facility, or a pharmacy. Treatments included the percentage of fever cases who received antibiotics and fluids (made from a special packet of oral rehydration salts, or government-recommended home made) among children with diarrhoea. Table 5.1 presents a list of interventions, health care seeking and treatments measures.

Table 5. 1: Description of interventions, health care seeking and treatment coverage measures

Vaccinations	**Description**
DPT	Percentage of children with complete vaccination of DPT
Measles	Percentage of children vaccinated against measles
Breastfeeding	
Breastfeed_1hr	Percentage of infants who started breastfeeding within one hour of birth
Exclusive	percentage of infants exclusively breastfed during the first six months after birth
WASH practices	
Water	Percentage of households with improved source of drinking water
Sanitation	Percentage of households using improved sanitation facilities
Treatments	
Antibiotics	Percentage of fever children receiving antibiotics
ORS or RHF	Percentage of children with diarrhea receiving fluid from oral rehydration solution (ORS) sachets or recommended home fluids (RHF)
Health care seeking	
ARI advice	Percentage of children with symptoms of ARI for whom advice or treatment was sought from health provider, a health facility, or a pharmacy
Diarrhoea advice	Percentage of children with diarrhea for whom advice or treatment was sought from health provider, a health facility, or a pharmacy

5.2.4.3 Socio-demographic factors

Socio-demographic characteristics included household (e.g. wealth index, type of fuel used for cooking), maternal (e.g. age, education, marital status, occupation) and child (e.g. malnutrition, residence, age, birth size, birth order) characteristics.

5.2.4.4 Environmental/climatic factors

The environmental/climatic factors such as seasonality affect the distribution of diarrhoea and ARI. Environmental and climatic predictors were extracted from remote sensing sources. Land Surface Temperature, rainfall and Normalized Difference Vegetation Index were averaged during January to December 2016. Four land cover types were provided according to the International Global Biosphere Programme classification scheme, that is, the percentage of surface covered by forests, water and crops within a 5km buffer, and area of residence (rural or urban). Distance to forests, water bodies, crops and savanna were calculated based on Moderate Resolution Imaging Spectroradiometer (MODIS) land cover satellite data of 2013. Supplementary Table 5.1 provides a list of environmental/climatic data together with their spatio-temporal resolution and data source.

5.2.5 Bayesian geostatistical modelling

Two Bayesian geostatistical Bernoulli regression models (Banerjee et al., 2015) were fitted. The first model quantified the effects of hand washing with water and soap on the presence of ARI while the second one quantified the effects of hand washing with water and soap on the presence of diarrhoea. The models adjusted for interventions, health care seeking, treatments, socio-demographic and climatic/environmental factors. Spatial correlation was taken into account in the ARI or diarrhoea outcome by cluster-specific random effects with a multivariate normal prior distribution capturing a stationary spatial process with exponential correlation function of distance between any pair of locations.

A spike and slab geostatistical Bayesian variable selection procedure was applied to select the most important predictors related to the presence of ARI or diarrhoea and their functional form (linear or categorical) (Chammartin et al., 2013). Predictors with an inclusion probability of more than 50% were considered in the final model (Giardina et al., 2014).

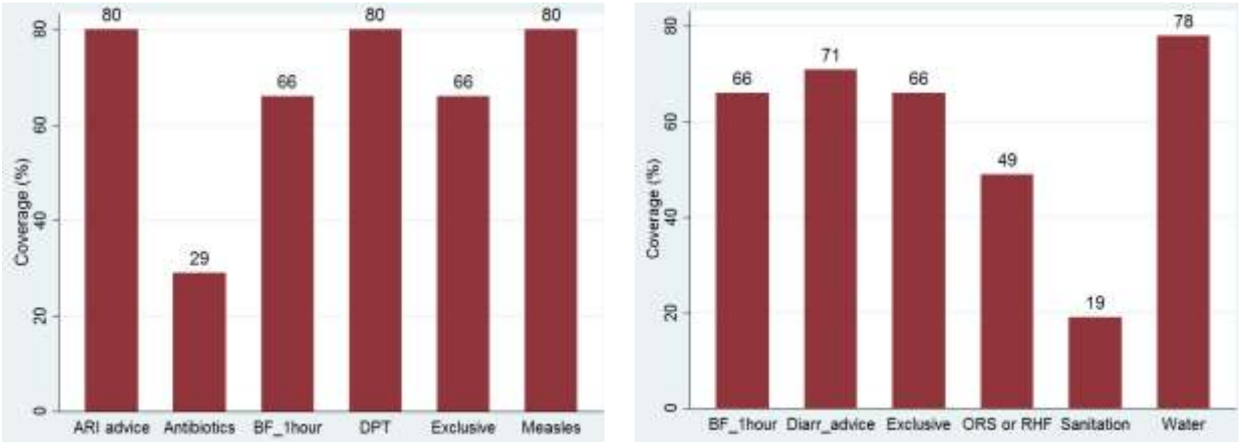
Descriptive data analysis was carried out in STATA version 14.0 (Stata Corporation, College Station, TX, USA). OpenBUGS version 3.2.3 (Imperial College and Medical Research Council, London, UK) was used to perform variable selection and model fit.

Parameter estimates were summarized by posterior medians and the corresponding 95% Bayesian Credible Intervals (95% BCI). Odds ratios were obtained by exponentiation of parameter estimates and they were considered statistically important if their 95% BCI did not include one. Detailed explanations of the fitted statistical models are presented in Supplementary file 5.1.

5.3 Results

5.3.1 Descriptive data analysis

Nine percent (9%) and 20% of children under age five (15 522) had ARI and diarrhoea respectively in the two weeks before the survey. About half (44%) of households had water and soap at hand washing places. One-third (33%) and 40% of children having ARI and diarrhoea respectively lived in households having water and soap at hand washing places. Figure 5.1 summarizes the coverage of interventions, health care seeking and treatments. The coverage of ARI advice, complete DPT and measles vaccines was similar (80%) among children (Panel (a)). Despite a high level of health care seeking for ARI, fever children receiving antibiotics were less (29%). Among diarrhoea interventions and health care seeking characteristics, improved source of drinking water had the highest coverage (78%) (Panel (b)). The percentage of households using improved sanitation facilities was the lowest (19%).



(a) (b)

Figure 5. 1: Coverage of interventions, health care seeking and treatments, Uganda DHS 2016; (a) ARI interventions, health care seeking and treatments (b) diarrhoea interventions, health care seeking and treatments.

5.3.2 Model results

Table 5.2 presents results obtained from Bayesian geostatistical variable selection. Handwashing with soap and water was selected with high inclusion probabilities (>85%) which suggests a strong association with the risk of diarrhoea and ARI. Among the preventive interventions for ARI, breastfeeding (57.3%) and DPT (52.0%) were selected. LST day on a linear scale was the environmental/climatic factor (100.0%) that explained maximum variation in the risk of ARI. Wealth index (100.0%) and age of the child (100.0%) had the highest probabilities of inclusion in the ARI model among the socio-demographic characteristics. Results of the diarrhoea model indicate a high probability of inclusion for improved sanitation facilities (79.0%), LST night linear (87.0%), rainfall categorical (81.3%), age of the child (100%), mother's highest level of education (100.0%) and wealth index (100.0%). All variables selected with inclusion probability of at least 50% were included in the final models.

Table 5. 2: Posterior inclusion probabilities of handwashing, interventions, treatments, health care seeking, environmental/climatic factors and socio-demographic factors

ARI model		**Diarrhoea model**	
Variable	**Inclusion probability (%)**	**Variable**	**Inclusion probability (%)**
Handwashing	86.2*	Handwashing	90.5*
Interventions		**Interventions**	
Breastfeed_1hr	57.3*	Water	10.0
Exclusive	33.1	Sanitation	79.0*
DPT	52.0*	Breastfeed_1hr	31.0
Measles	40.0	Exclusive	28.4
Treatments		**Treatments**	
Antibiotics	18.0	ORS or RHF	42.0
Health care seeking		**Health care seeking**	
ARI advice	61.0*	Diarrhoea advice	37.0
Environmental/climatic		**Environmental/climatic**	
% surface covered by forest within a 5km buffer	46.0	% surface covered by forest within a 5km buffer	14.5
% surface covered by water within a 5km buffer	41.6	% surface covered by water within a 5km buffer	42.5
% surface covered by crop within a 5km buffer	42.2	% surface covered by crop within a 5km buffer	6.0
LST day linear	100*	LST day linear	43.0
LST night linear	1.6	LST night linear	87.0*
NDVI linear	47.6	NDVI linear	17.0
Rainfall linear	8.8	Rainfall categorical	81.3*
Altitude linear	34.2	Altitude linear	17.5
Distance to forest linear	1.2	Distance to forest categorical	0.3
Distance to water linear	0.8	Distance to water linear	0.5
Distance to savanna linear	36.8	Distance to savanna linear	2.5
Distance to crops categorical	22.4	Distance to crops categorical	15.0
Socio-demographics		**Socio-demographics**	
Sex of child	13.0	Sex of child	10.3
Birth order	57.3*	Birth order	42.0
Birth size	66.2*	Birth size	80.5*
Age of child	100.0*	Age of child	100.0*
Malnutrition	73.0*	Malnutrition	39.8
Maternal age	0.0	Maternal age	100.0*
Maternal Education level	71.3*	Maternal education level	59.3*
Marital status	40.4	Marital status	7.5
Maternal occupation	21.2	Maternal occupation	1.8
Wealth index	100.0*	Wealth index	100.0*
Residence	61.2*	Residence	68.0*
Type of cooking fuel	72.8*		

*Included in the final model with probability ≥50%

Table 5.3 presents results from Bayesian geostatistical models. The ARI model results show that the odds of ARI in children who lived in households having soap and water at handwashing places were 24% less than those living in households without the intervention (adjusted odds ratio, aOR = 0.76; 95% BCI: 0.65 – 0.88). Similarly, results of the diarrhoea model indicate that the presence of soap and water at handwashing places is associated with a reduced risk of diarrhoea among the under-five of 14% (aOR = 0.86; 95% BCI: 0.77 – 0.96).

Children aged 7 months and older had higher odds of ARI compared to those that were younger than 7 months old; (aOR = 1.55; 95% BCI: 1.18 – 2.02) and (aOR = 1.51; 95% BCI: 1.16 – 1.98) among those aged 7 – 11 months and 12 – 23 months respectively. The risk of diarrhoea was higher at the age of 12 – 23 months old (aOR = 1.32; 95% BCI: 1.10 – 1.58) compared to children younger than 7 months. Children who were reported as average size or larger at birth were at a lower risk of diarrhoea (aOR = 0.85; 95% BCI: 0.75 – 0.96) and ARI (aOR = 0.78; 95% BCI: 0.66 – 0.93). Also, living in urban areas was found protective of childhood ARI by 43% (aOR = 0.57; 95% BCI: 0.47 – 0.70) and diarrhoea by 16% (aOR = 0.84; 95% BCI: 0.74 – 0.95). The odds of ARI and diarrhoea were lower in children born to educated women (ARI aOR = 0.44; 95% BCI: 0.34 – 0.55) and (diarrhoea aOR = 0.60; 95% BCI: 0.53 – 0.68) for women who attained secondary education or higher compared to women with no education) and in children from higher socio-economic status (ARI aOR = 0.40; 95%BCI: 0.51 – 0.61) and (diarrhoea aOR = 0.74; 95%BCI: 0.60 – 0.91) for the richest socio-economic status compared to the poorest one). The odds of diarrhoea were lower in children living in households having improved sanitation facilities aOR = 0.72; 95% BCI: 0.58 – 0.89). The odds of ARI increased in households that used wood as a source of cooking fuel aOR = 1.30; 95% BCI: 1.09 – 1.56) and with higher day LST (aOR = 1.06; 95% BCI: 1.03, 1.09). Higher maternal ages were associated with reduced odds of diarrhoea aOR = 0.45; 95% BCI: 0.38 – 0.53) compared to young mothers (15 – 24 years old). However, the risk of diarrhoea increased with higher amounts of rainfall (aOR = 1.18; 95% BCI: 1.02, 1.37) and increasing night LST (aOR = 1.05; 95% BCI: 1.02, 1.09). Spatial correlation in ARI risk was strong extending up to 25.0km (Range: 11, 48) but was rather moderate in the risk of diarrhoea reaching 0.5km (Range: 0.2, 2.0).

Table 5. 3: Posterior estimates for the effects of handwashing, interventions, health care seeking, treatments and environmental/climatic factors

ARI model		Diarrhoea model	
Variable	**aOR (95% BCI)**	**Variable**	**aOR (95% BCI)**
Handwashing: No	1.0	Handwashing: No	1.0
Yes	0.76 (0.65, 0.88)*	Yes	0.86 (0.77, 0.96)*
Child age (months): 0-6	1.0	Child age (months): 0-6	1.0
7-11	1.55 (1.18, 2.02)*	7-11	1.21 (0.97, 1.50)
12-23	1.51 (1.16, 1.98)*	12-23	1.32 (1.10, 1.58)*
24-35	1.43 (0.91, 1.87)	24-35	1.19 (0.99, 1.42)
36-47	1.32 (0.74, 1.75)	36-47	1.23 (0.89, 1.48)
>=48	1.14 (0.81, 1.62)	>=48	1.05 (0.87, 1.26)
Birth size: < average	1.0	Birth size: < average	1.0
≥ average	0.78 (0.66, 0.93)*	≥ average	0.85 (0.75, 0.96)*
Residence: Rural	1.0	Residence: Rural	1.0
Urban	0.57 (0.47, 0.70)*	Urban	0.84 (0.74, 0.95)*
Maternal Education: None	1.0	Maternal Education: None	1.0
Primary	0.61 (0.50, 0.75)*	Primary	0.88 (0.73, 1.05)
Secondary+	0.44 (0.34, 0.55)*	Secondary+	0.60 (0.53, 0.68)*
Wealth index: Poorest	1.0	Wealth index: Poorest	1.0
Poorer	0.66 (0. 35, 0.83)*	Poorer	0.90 (0.75, 1.06)
Middle	0.59 (0.47, 0.74)*	Middle	0.84 (0.70, 1.01)
Richer	0.59 (0.47, 0.74)*	Richer	0.88 (0.74, 1.05)
Richest	0.40 (0.51, 0.61)*	Richest	0.74 (0.60, 0.91)*
Type of cooking fuel: No wood	1.0	Sanitation: No	1.0
Wood	1.30 (1.09, 1.56)*	Yes	0.72 (0.58, 0.89)*
DPT	0.96 (0.92, 1.12)	Maternal age group: 15-24	1.0
Breastfeed_1hr	0.99 (0.96, 1.09)	25-29	0.76 (0.66, 0.87)*
ARI advice	0.88 (0.81, 1.36)	30-34	0.62 (0.53, 0.72)*
LST day linear	1.06 (1.03, 1.09)*	35-49	0.45 (0.38, 0.53)*
Malnutrition: No	1.0	Maternal occupation: No	1.0
Yes	0.67 (0.51.0, 1.28)	Yes	0.87 (0.76, 1.00)
Birth order: 1-5	1.0	LST night linear	1.05 (1.02, 1.09)*
>5	1.26 (0.94, 2.13)	Rain (mm): 8.00 - 15.99	1.0
Range (km)	25.0 (11.0, 48.0)	15.20 - 16.81	0.92 (0.80, 1.07)
Variance in ARI risk	0.63 (0.48, 0.78)	16.82 - 18.30	1.18 (1.02, 1.37)*
		18.31 - 29.67	0.94 (0.81, 1.08)
		Range (km)	0.5 (0.2, 2.0)
		Variance in diarrhoea risk	1.31 (1.06, 1.59)

*Statistically significant, aOR: adjusted odds ratio

5.4 Discussion

This study analysed the 2016 DHS data and quantified the effect of the presence of soap and water at handwashing places on the risk of diarrhoea and ARI among the under-five in Uganda. The analysis adjusted for spatial correlation in disease outcomes and the confounding effects of socio-demographic characteristics, interventions, health care seeking behaviour and environmental/climatic factors. The study showed that the presence of soap and water at handwashing places reduced the risk of diarrhoea and ARI. Unlike the effect of the presence of soap and water at handwashing places on the risk of diarrhoea, that has been previously documented among school children (Zhang et al., 2013), scanty evidence on the effect of the intervention on the risk of diarrhoea and ARI among the under-five exists in Uganda. The present study quantifies the effect of the intervention on the risk of diarrhoea and ARI in children less than five years in Uganda. Spatial correlation in disease outcomes was strong particularly in the ARI risk, suggesting the need to adjust for spatial dependence in the analysis.

The protective effect of handwashing with soap and water on the risk of diarrhoea and ARI among the under-five could mainly be because washing hands with soap and water decontaminates the hands and interrupt the transmission of the pathogens that cause diarrhoea and pneumonia (Liu et al., 2016). These findings agree with those of studies in Western Kenya (Kamm et al., 2014), California (Nicas and Best, 2008) and in a systematic review (Jefferson et al., 2011). Despite its benefits, coverage of handwashing with soap and water is low in the country (Uganda Bureau of Statistics (UBOS) and ICF, 2018) yet prevalences of diseases targeted by this intervention are high.

Children aged 12-23 months were significantly associated with increased diarrhoea risk compared to children aged below 7 months. In Uganda, this is the age at which almost all children are weaned off and mothers start introducing other feeds to children. It is during this period of mixed feeding that diarrhoea is most prevalent due to multiple factors including contaminated feeds, unclean water and environment. Similar relationships between age and diarrhoea have been documented. For example, in Uganda (Bbaale, 2011; Ssenyonga et al., 2009), in Ethiopia (Sinmegn Mihrete et al., 2014) and Eritrea (Woldemicael, 2001). A significant inverse relationship between age and ARI found in this study may be due to the behaviour of young children such as, lack of awareness of hand hygiene which might increase their exposure to pathogens through person-to-person contact. This finding is similar to those of other studies in Australia (Chen et al., 2014), in Canada (Alharbi et al., 2012) and in China (Zhang et al., 2012). Although our study found a significant effect of age on the risk of ARI, a meta-analysis by Jackson et al. (Jackson et al., 2013) reported an inconsistency in this effect. Four of the studies reviewed in this meta-analysis found a significant association with age while three did not.

Children born with less than average sizes were at a higher risk of diarrhoea and ARI. Low birth weight is inversely related to many factors such as socio-economic status and maternal age (Madden, 2014) which we have found to be protective of diarrhoea and ARI in this study. The increased risk of ARI may also be explained by poor lung development among low birth weight children (Stern et al., 2007). Walter et al. also reported low birth weight as a risk factor of ARI (Walter et al., 2009) while Lira et al. found low birth weight to increase the risk of diarrhoea (Lira et al., 1996).

Our study found a lower risk of diarrhoea and ARI for children residing in urban areas than those living in rural settings. This can be explained by several factors. For example, the higher poverty levels in rural areas (only 9% in the wealthiest quintile), more exposure to smoke in houses as almost all households (82%) in rural areas are not electrified and the poor sanitation facilities in rural areas where seven out of every ten households use unimproved sanitation facilities (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Our study has found all these factors to be inversely associated with ARI. This finding is in line with those of Kumi et al. (Kumi-Kyereme and Amo-Adjei, 2016) and Ujunwa and Ezeonu (Ujunwa and Ezeonu, 2014). However, inconsistent findings on the effect of residence on the risk of diarrhoea have been reported. According to Siziya et al. (Siziya et al., 2009), children from urban areas were more likely to have diarrhoea compared to children from rural areas.

The study found that children whose mothers had some level of education were at reduced risk of diarrhoea and ARI than those whose mothers had no formal education. This is probably because children spend more time with their mothers, and mothers' educational level determines the quality of care and many social and environmental factors that the child will be exposed to. The findings on diarrhoea corroborate those of studies by Ssenyonga et al. (Ssenyonga et al., 2009) and Bbaale (Bbaale, 2011) in Uganda. Ujunwa and Ezeonu (Ujunwa and Ezeonu, 2014) and Tazinya et al. (Tazinya et al., 2018) also found a positive association between ARI and poor maternal education.

Being in a higher wealth status compared to the lowest (poorest), was associated with lower risks of diarrhoea and ARI. An analysis of the Multiple Indicator Survey data by Siziya et al. (Siziya et al., 2009), indicated that higher socio-economic status was associated with a lower risk of diarrhoea and ARI. Improved sanitation facilities were associated with a lower risk of diarrhoea. The type of toilet facility might shade light on the level of household sanitary conditions and as such on the possibility of the transmission of diarrheal pathogens through fecal contamination (Shamebo et al., 1993). These results are similar to those of Sinmegn et al.(Sinmegn Mihrete et al., 2014).

The use of wood as fuel for cooking increased the risk of ARI. This is not surprising since the use of solid fuel in Uganda is almost universal, with 95 percent of households using solid fuel for cooking (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Cooking and heating with solid fuels can lead to high levels of indoor smoke, which consists of a complex mix of pollutants such as particulate matter; carbon monoxide; nitrogen oxides; formaldehyde; benzene; hydrocarbons and many other toxic compounds (Larson and Rosen, 2002). Exposure to these pollutants in developing countries is reported to be higher in women and children (Albalak et al., 1999). It has been shown that exposure to such fuel smoke is responsible for a number of respiratory diseases including ARI (Bruce et al., 2000). Other studies also found a significant association between wood fuel and ARI (Mathew et al., 2011).

Our findings revealed that children born to older women compared to those in the 15-24 year group had a lower risk of diarrhoea and ARI. This can be attributed to the knowledge and experience concerning childcare accumulated by older women over time which gives them an advantage over younger women. A study by Bbaale in Uganda (Bbaale, 2011) found a similar result.

The effect of increasing temperature on the risk of diarrhoea observed in our study may be due to the fact that high temperatures lead to increased exposure to bacterial and other parasites causing diarrhoea, meaning that the bacteria-related gastrointestinal diseases are more likely to occur in high temperatures because bacteria that contaminate food are more prevalent in high temperatures (Xu et al., 2012). This might relate to the theory that a wide number of diarrhoea causing pathogens propagate faster and survive more easily in higher temperatures, thereby increasing the risk of being exposed to contaminated food and water (Rose et al., 2001). Bandyopadhyaya et al.'s examination of temperature and childhood diarrhea in 14 sub-Saharan African countries found a one degree Celsius increase in the average maximum temperature to increase diarrhea prevalence by one percent (Bandyopadhyay et al., 2012). Other studies in South Africa (Musengimana et al., 2016), in Brisbane in Queensland (Z. Xu et al., 2014) and in Ethiopia (Azage et al., 2017) observed a similar relationship.

The effect of higher temperatures on ARI can be related to the dry season in Uganda. In Uganda, high temperatures usually occur during the dry season which is characterized by dusty winds. This accelerates the spread of the ARI virus and thus increases infections. Xu et al. (Zhiwei Xu et al., 2014), also found a similar finding when they investigated the impact of temperature on childhood pneumonia estimated from satellite remote sensing.

The increased effect heavier rainfall on the risk of diarrhoea compared to light rain observed in this study can partly be explained by the poor WASH practices in Uganda. About twenty percent of households in the country do not use improved sanitation facilities. Nearly, a quarter of the households in Uganda collect drinking water from unimproved sources. Rainfall runoff and flooding can lead to human exposure to pathogens by flushing pathogens from environmental reservoirs or fecal matter into freshwater supplies (Alexander and Blackburn, 2013).

The main limitation of this study is that all other variables were self-reported except the presence of soap and water at handwashing places which was observed by interviewers. These may suffer from recall biases. However, previous studies (Bhandari and Wagner, 2006) showed that the level of agreement between self-reported and registered data remains high (almost 100%) in a shorter recall periods not exceeding 6 months, thus minimizing over- or under-estimation of results. Moreover, data collection was cross sectional. Thus, we cannot infer causation between explanatory variables and, the risk of diarrhoea or ARI other than associations. Limitations aside, results of this study will be vital for policy formulation and advocacy to programmes that aim to reduce the burden of diarrhoea and ARI among the under-five in Uganda. Also, this study adds to the body of literature on the effects of the presence of soap and water at handwashing places on the risk of diarrhoea and ARI among the under-five.

5.5 Conclusion

The presence of soap and water at handwashing places in households is associated with a reduction in the risk of diarrhoea and ARI. However, coverage of the intervention is low and should be scaled up. For example, through training and educating individuals about hygiene, disease transmission and increase access to resources which support handwashing with soap and water.

Declarations

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Availability of data and materials

The datasets supporting conclusions in this article are available at the DHS MEASURE website (www.dhsprogram.com) with request for access and following instructions at https://dhsprogram.com/data/Access-Instructions.cfm.

Authors' contributions

BBN conceptualized the research, managed and analyzed the data, developed the methodology and implemented it in software, interpreted results and wrote the first draft of the manuscript. Author JS participated in data management and manuscript editing. Authors FEM and SK formulated research goals and objectives, participated in the process of acquisition of project financial support and edited the manuscript. PV was the lead author who conceived the research, formulated research goals and objectives, acquired project financial support, led methodology development, model fitting and result interpretation and manuscript writing. All authors approved the final draft of the manuscript.

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Consent for publication

Not applicable.

Competing risks

The authors declare that they have no competing interests.

5.6 Supplementary files

Supplementary Table 5. 1: Remote sensing data sources[a]

Source	Data type	Temporal resolution	Spatial resolution
MODIS/Terra[b]	LST[l]	8 days	1km
MODIS/Terra[b]	NDVI[m]	16 days	1km
U.S. Geological Survey-Earth Resources Observation Systems (USGSS)	Rainfall	10 days	8x8km^2
Shuttle Radar Topographic Mission (SRTM)	Altitude	NA	1x1km^2
MODIS,IBGD type	Land cover Water bodies	NA	0.5x0.5km^2
Global Rural and Urban Mapping project	Urban Rural extent	NA	1x1km^2

NA: Not applicable; Land cover groups (forest, crops, urban); [a]Land cover data accessed in June 2016 and other data accessed in November 2013; [b]Moderate Resolution Imaging Spectroradiometer (MODIS)/Terra, available at: http://modis.gsfc.nasa.gov/; [l]Land surface temperature (LST) day and night; [m]Normalized difference vegetation index

Supplementary file 5. 1: Bayesian geostatistical modeling

Bayesian geostatistical variable selection

A Bayesian geostatistical logistic regression model, adopting a stochastic search variable selection approach, was used to determine the most important predictors of the presence of ARI or diarrhoea and their functional form (George and McCulloch, 1993).

For the environmental/climatic variables except of land cover types, variable selection compared their linear and categorical forms and selected the one that had the highest probability of inclusion or neither of the two forms. The categorical forms were generated based on the quartiles of variables. We introduced an indicator I_p for each environmental/climatic covariate X_p which defines exclusion of the variable from the model ($I_p = 1$), inclusion in a categorical ($I_p = 2$) or linear ($I_p = 3$) form.

For hand washing with water and soap, interventions, treatments, health care seeking characteristics, socio-demographics and land cover types, a binary indicator parameter I_p suggesting presence ($I_p = 1$) or absence ($I_p = 0$) of the predictor from the model was introduced. I_p has a probability mass function $\prod_{j=1}^{p} \pi_j^{\delta_j(I_p)}$, where π_j denotes the inclusion probabilities, $j = (1,2,3)$, e.g. for environmental/climatic factors so that $\sum_{j=1}^{p} \pi_j = 1$ and $\delta_j(.)$ is the Dirac function, $\delta_j(I_p) = f(x) = \begin{cases} 1, if\ I_p = j \\ 0, if\ I_p \neq j \end{cases}$.

For inclusion probabilities of environmental/climatic factors, a non-informative Dirichlet distribution was adopted with hyper parameters $\alpha = (1,1,1)^T$, that is, $\boldsymbol{\pi} = (\pi_1, \pi_2, \pi_3)^T \sim Dirichlet(3, \alpha)$. For hand washing with water and soap, interventions, treatments, health care seeking characteristics, socio-demographics and land cover types, a Bernoulli prior with an equal inclusion or exclusion probability was assumed for the indicator i.e. $I_p \sim bern(0.5)$. Also, inverse Gamma priors with parameters (2.01, 1.01) were assumed for the precision hyper parameters τ_p^2. The predictors identified as important are those with posterior inclusion probability greater than or equal to 50% (Ssempiira et al., 2017).

We assumed a spike and slab prior for regression coefficient β_p corresponding to the corresponding covariate, X_p i.e. for the coefficient β_p of the predictor in linear form we take $\beta_p \sim \left(1 - \delta_1(I_p)\right) N\left(0, u_0 \tau_p^2\right) + \delta_1(I_p) N(0, \tau_p^2)$ proposing a non-informative prior for β_p in case X_p is included in the model in a linear form (slab) and an informative normal prior with variance close to zero (i.e. $u_0 = 10^{-3}$) shrinking β_p to zero (spike) if X_p is excluded from the model. Similarly, for the coefficient $\{\beta_{p,l}\}_{l=1,..,L}$ corresponding to the categorical form of $\underline{X}_p$ with L categories, we assume that $\beta_{p,l} \sim \delta_2(I_p) N\left(0, \tau_{p,l}^2\right) + \left(1 - \delta_2(I_p)\right) N\left(0, \vartheta_0 \tau_{p,l}^2\right)$

Bayesian geostatistical logistic regression model

Two Bayesian geostatistical logistic regression models (Banerjee et al., 2015) were fitted. The first model quantified the effects of hand washing with water and soap on the presence of ARI while the second one quantified the effects of hand washing with water and soap on the presence of diarrhoea. The models adjusted for interventions, health care seeking, treatments, socio-demographic and climatic/environmental factors. To adjust for spatial correlation present in the presence of ARI or diarrhoea due to similar exposure effect in neighbouring clusters, cluster-specific random effects were introduced into the model. The cluster random effects were assumed to arise from a Gaussian stationary process with a covariance matrix capturing correlation between any pair of cluster locations as a function of their interlocation distances.

Let Y_{ij} be the binary outcome for child i at location s_j taking values 1 and 0 when ARI or diarrhoea is present or absent respectively, $\boldsymbol{X_j}(s_j)$ be the vector of socio-demographic factors, interventions, health care seeking, treatments, socio-demographic and climatic/environmental factors.

Y_{ij} is assumed to follow a Bernoulli distribution $Y_{ij} \sim Ber(p_{ij})$ and is related to its predictors using a logistic regression model as follows;

$logit(p_{ij}) = \beta_0 + \boldsymbol{\beta}^T \boldsymbol{X_j}(s_j) + W(s_j) + v_j$ where p_{ij} is the presence or absence of ARI or diarrhoea in child i at location s_j, $\boldsymbol{\beta}^T = (\beta_1, \ldots, \beta_p)$ is the vector of regression coefficients with $\exp(\beta_l), l = 1, \ldots p$, corresponding to the odds ratio. $W(s_j)$ is a cluster-specific random frailty which captures spatial correlation in the presence of ARI or diarrhoea due to similar exposure effect in neighbouring clusters. We modeled $\boldsymbol{W}(s) = (W(s_1), W(s_2), \ldots, W(s_m))^T$ by a Gaussian process, i.e. $\boldsymbol{W}(s) \sim N(0, \Sigma)$, where Σ is the variance-covariance matrix and each element is defined by an exponential correlation function of the distance d_{kl} between locations s_k and s_l, that is $\Sigma_{kl} = \sigma^2 \exp(-d_{kl}\rho)$ (Banerjee et al., 2015). The parameter σ^2 gives the variance of the spatial process and ρ is a smoothing parameter that controls the rate of correlation decay with distance. For the exponential correlation function, $\frac{-\log(0.05)}{\rho}$ determines the distance at which the correlation drops to 0.05 (i.e. effective range of spatial process). Non-spatial variation is estimated by the random effects v_j, assumed independent and normally distributed with mean 0 and variance σ_v^2 .

Model specification was completed by assigning prior distributions to model parameters. We assumed inverse gamma priors for spatial variance with known parameters, i.e. $\sigma^2 \sim IG(2.01, 1.01)$, a uniform prior distribution for $\rho \sim U(a, b)$, where a and b chosen such that the effective range is within the maximum and minimum distances of the observed locations (Thomas et al., 2004). Non-informative normal priors were adopted for the regression coefficients $\beta_l \sim N(0, 10^3)$ for $l = 1, \ldots p$. The joint posterior distribution of the model is given by

$$\prod_{\boldsymbol{j}} [\, Y_i(s_j) \,|\boldsymbol{\beta}, \boldsymbol{X_j}(s_i)][\, \boldsymbol{W}(s)|\sigma^2, \rho][\boldsymbol{\beta}, \sigma^2, \rho].$$

Model parameters were estimated using Markov Chain Monte Carlo simulation (George and McCulloch, 1993). A two chain algorithm of 100 000 iterations with an initial burn-in of 5 000 iterations was run. Convergence was assessed by the Gelman and Rubin diagnostic (Rubin and Gelman, 1992).

Chapter 6: Assessing the effects of maternal health interventions on all-cause maternal mortality in Uganda

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Abstract

Background: To improve maternal mortality in Uganda, it is essential to identify interventions associated with maternal mortality reduction so that, intervention policies aimed at improving maternal health can be designed and implemented. However, more reliable estimates of the intervention-mortality relationship are lacking in the country because limited studies have examined this relationship using nationally representative data. In the present research article, we assess the effects of health interventions on maternal mortality in Uganda using Demographic and Health Survey (DHS) and the National Population and Housing Census data (NPHC).

Methods: Maternal mortality and live births data aggregated at regions were obtained from the 2014 NPHC. Data on maternal interventions and socio-economic factors were extracted from the 2016 DHS. Data on health facility assessment readiness indicators were obtained from the 2013 Uganda Service Delivery Indicators Survey. To determine important predictors of mortality, we applied a Bayesian stochastic search approach. A Bayesian negative binomial model was employed to estimate the effects of health interventions on maternal mortality. To model spatial dependence in mortality across regions, we introduced regional-specific random effects into the model via a conditional autoregressive (CAR) prior distribution. The analysis adjusted for confounding effects of health facility assessment readiness indicators and characteristics. The effects of covariates on mortality were summarized by posterior medians of their mortality rate ratios (MRRs) and the corresponding 95% Bayesian Credible Intervals (95% BCI).

Results: We found that declines in maternal mortality rates were associated with increasing coverage of intermittent preventive treatment (MRR = 88%; 95% BCI: 86%, 91%), iron supplements (MRR = 95%; 95% BCI: 93%, 98%), skilled birth attendance (MRR = 96%; 95% BCI: 94%, 98%) and family planning (MRR = 95%; 95% BCI: 92%, 98%).

Conclusion: We have used country-level data and obtained more reliable and informed estimates of the effects of health interventions on maternal mortality in Uganda. We have demonstrated that intermittent preventive treatment, iron supplements, skilled birth attendance and family planning are associated with reduction in maternal mortality. However, coverage of intermittent preventive treatment and family planning is low in the country. Therefore, scaling up coverage of important interventions may improve maternal mortality in Uganda.

Key words: Maternal mortality, DHS, NPHC, interventions, Bayesian negative binomial models, Uganda

6.1 Introduction

Maternal mortality, commonly measured by the maternal mortality ratio (MMR) indicator (World Health Organization, 2013), is a measure of the quality of the health system. Also MMR is essential for monitoring progress towards the achievement of Sustainable Development Goals (SDGs) (World Health Organization, 2015b). Additionally, the indicator reflects inequality between the rich and the poor, urban and rural areas, and between and within countries (World Health Organization, 2015a). Maternal mortality results in vulnerable families and increases the chances of infant mortality before reaching their second birthday. Further, it is estimated that for each maternal death, twenty and more women will live with lasting sequelae (World Health Organization, 2015a). Globally, MMR has declined from the 1990 level (385) to 216 deaths per 100 000 live births in 2015. Similarly, MMR decreased in sub-Saharan Africa from 987 to 546 deaths per 100 000 live births during the same period (World Health Organization, 2015a). Uganda experienced a reduction in MMR as well from 687 in 1990 to 336 deaths per 100 000 live births in 2016 (Uganda Bureau of Statistics (UBOS) and ICF, 2018; World Health Organization, 2015a). This decline can partly be attributed to the improvement in the coverage of maternal health interventions (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Despite the substantial improvements, the burden of MMR in Uganda is still huge and far higher than the SDG target of 140 deaths per 100 000 livebirths by 2030 (United Nations, 2015b).

Maternal deaths result from direct or indirect causes. Worldwide, the major direct causes include haemorrhage, hypertensive disorders of pregnancy, postpartum infections, obstructed labour (GBD 2013 Mortality and Causes of Death Collaborators, 2015) and complications from unsafe abortion (Haddad and Nawal, 2009). Indirect causes such as malaria, anaemia and malnutrition which constitute pre-existing conditions or concurrent diseases result into the least deaths (Say et al., 2014). As regards to the timing of maternal deaths, majority occur in the postpartum period and a reasonable proportion happens during child birth (Li et al., 1996). Thus, it is important to determine the most optimal prenatal and postnatal interventions to alleviate maternal mortality and its consequences.

In Uganda, a few studies have assessed the relation between health interventions and maternal mortality (Mbonye, 2001; Mbonye et al., 2007b, 2007a) but there is limited literature of studies examining this relation using nationally representative data. Most studies that evaluated the above relation have largely been undertaken among health facility attending populations, which only include information on mothers with access to health facilities. Such studies are likely to under-estimate MMR as mothers who experience a higher mortality burden (e.g. the poor, those in remote areas) are less likely to deliver babies in health facilities (Uganda Bureau of Statistics (UBOS) and ICF, 2018; World Health Organization, 2015a). Therefore, the generalizability of such estimates to the country is uncertain and there is need to provide more reliable estimates of the intervention-mortality relationship. National studies only assessed a single category of maternal interventions i.e. number of antenatal care visits (Atuhaire and Kaberuka, 2016).

The use of nationally representative data is one way to obtain reliable estimates of the intervention-mortality relationship. However, sources of dependable data to estimate maternal mortality accurately are sparse (Yazbeck, 2007). Despite the scarcity of data sources, efforts have been made to improve the quality of information about maternal mortality. These include the integration of sibling history modules in the Demographic and Health Survey (DHS) and related surveys (Stanton et al., 2000), the incorporation of questions whether deaths in a household were pregnancy-related in censuses (Hill K et al., 2009) and the use of vital registration systems to categorize maternal deaths (Schuitemaker et al., 1997). The current study makes use of the National Population and Housing Census (NPHC) data, 2014 (Uganda Bureau of Statistics, 2016) to estimate maternal deaths.

Maternal deaths are estimated by asking respondents if a maternal death occurred in a household in the past 12 months. The Uganda Bureau of Statistics (UBOS) undertakes the NPHC and estimates the total population count as well as several statistics at sub-national scales. Regional estimates are among the most reliable sub-national data UBOS collects (Uganda Bureau of Statistics, 2016). In this paper, we used maternal deaths aggregated at regions and evaluated the mortality-intervention relationship. The DHS data are not appropriate to estimate maternal mortality at local scales. This is because the sisterhood method (Graham et al., 1989) used in the DHS to determine maternal deaths does not specify the location of the dead. Thus, if disaggregated at sub-national levels, the obtained estimates may not represent the true MMR in the sub-national units. The civil registration systems, considered the gold standard source for all-cause mortality (Setel et al., 2007), are absent, under-developed or incomplete in most developing countries (Mathers et al., 2005). The MMR regional estimates computed from the NPHC are nationally representative and also fill the vacuum for reliable sub-national estimates of maternal mortality (Uganda Bureau of Statistics, 2016).

The current study uses national-level data to investigate the effects of maternal health interventions on maternal mortality, taking into account the geographical variation of socio-economic factors, health facility assessment readiness indicators and characteristics. A Bayesian negative binomial model was employed to analyse the data while adjusting for the effect of neighbouring regions on mortality. Regional-specific random effects were used to capture dependence in mortality across regions via a conditional autoregressive (CAR) prior distribution. The study provides reliable estimates of health interventions for policy formulation aimed at improving maternal health in Uganda.

6.2 Methods

6.2.1 Study setting

Uganda is located on the Eastern side of Africa and lies astride the Equator. The country is landlocked, bordering Kenya in the East, South Sudan in the North, the Democratic Republic of Congo in the West, Tanzania in the South; and Rwanda in South-West. In 2014, Uganda was divided administratively into 112 districts, which were grouped into 15 regions. The 15 regions will be referred to as the sub-national scale in this paper. Uganda has a population of about 40 million of which approximately 42% are women of reproductive age (15-49 years) (Uganda Bureau of Statistics, 2016). Adult mortality is higher among men (6 deaths per 1 000 population) than among women (4 deaths per 1 000 population) and maternal deaths represent 18% of all deaths among women age 15-49 (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

6.2.2 Data

6.2.2.1 Maternal mortality and live births data

The outcome variable, the number of maternal deaths, and the number of livebirths were obtained from the 2014 NPHC (Uganda Bureau of Statistics, 2016). Respondents were asked if a maternal death occurred in the household in the past 12 months preceeding the survey. Maternal deaths and the corresponding number of live births were aggregated at the regional level, and MMR was computed as the number of maternal deaths divided by the number of live births multiplied by 100 000.

6.2.2.2 Intervention coverage indicators and socio-economic factors

Data on interventions and socio-economic factors were obtained from the Uganda demographic and health survey (DHS) which was carried out from June through December, 2016 (Uganda Bureau of Statistics (UBOS) and ICF, 2018).

Maternal interventions comprise malaria, antenatal care (ANC), skilled birth attendance and postnatal care. Malaria indicators (ITNs) were defined using standard guidelines of the Roll Back Malaria (World Health Organisation, 2013b). All intervention coverage indicators were aggregated at the region to take into account their geographical heterogeneity. Interventions with coverage exceeding 95% (i.e. ANC provider; 97%) at the national level were excluded from the analysis due to lack of variation in estimating their relation with mortality. The key indicators in each category of interventions are presented in Table 6.1.

Socio-economic factors included wealth index score, the percentage of households having improved sanitation facility and improved source of drinking water. All factors were aggregated at the regional level.

Table 6. 1: Maternal health interventions, Uganda DHS 2016

Intervention	Description
Malaria	
%P_ITNS	Percentage of pregnant women who slept under an ITN the night before the survey
Antenatal care	
ANC provider	Percentage of pregnant mothers receiving ANC from a skilled provider
4+ ANC visits	Percentage of pregnant women making four or more ANC visits during their entire pregnancy
TT	Percentage of mothers whose most recent live birth was protected against neonatal tetanus
IPT	Percentage of women who received intermittent preventive treatment for malaria during pregnancy
Iron	Percentage of women who during the pregnancy of their most recent live birth took iron tablets or syrup
Deworming	Percentage of women who took deworming medication during pregnancy of last birth
Skilled birth assistance	
Skilled delivery	Percentage of births that took place with the assistance of a skilled provider
C_ section	Percentage of live births in the 5 years preceding the survey delivered by caesarean section
Postnatal care	
Post_check	Percentage of women with a postnatal check during the first 2 days after birth
Family_ planning	Percentage of married women using any family planning method

DHS: Uganda Demographic and Health Survey

6.2.2.3 Health facility assessment readiness indicators

Data on health facility assessment indicators and health facility characteristics were obtained from the Uganda Service Delivery Indicator (USDI) survey, 2013 (Wane, 2017). The indicators consist of the general service and specific-service facility readiness (World Health Organization, 2015c). General facility readiness indicators evaluate the total ability of health facilities to deliver general health services determined by the availability of tracer items in the five domains, that is, basic amenities, basic equipment, standard precautions for infection prevention, diagnostic capacity and essential medicines. Service-specific readiness refers to the capability of health facilities to provide services based on the availability of tracer items that are necessary for delivery of services of minimum standards. They include percentage of health facilities offering family planning services, ANC services, basic emergency obstetric care, comprehensive obstetric care, delivery services that have priority medicines for mothers, malaria services readiness, Human Immunodeficiency Virus (HIV) counselling and testing; and sexually transmitted infections services. Coverage of health facility indicators that were less than 5% were excluded from analysis. Readiness indicators were defined following standard definitions of the World Health Organization (World Health Organization, 2015c). Health facility characteristics included; whether facility was rural or urban, type of health facility, number of hours a facility offers outpatient consultation in a day, percentage of facilities open all week and distance to district headquarters (Km).

6.2.2.4 Uganda regional shape files

The regional shape files were downloaded from the spatial data repository of the DHS program (https://spatialdata.dhsprogram.com/boundaries/#view=table&countryId=UG) (Spatial Data Repository).

6.2.3 Statistical analysis

6.2.3.1 Bayesian variable selection

A Bayesian negative binomial model, adopting a spike and slab variable selection was used to determine the most important predictors of maternal mortality (George and McCulloch, 1993). The predictors identified as important are those with posterior inclusion probability of atleast 50% (Giardina et al., 2014).

6.2.3.2 Bayesian negative Binomial model

To assess the effect of maternal health interventions on maternal mortality, a Bayesian negative binomial model (Banerjee et al., 2015) was fitted. Random effects at a regional level were used to model spatial dependence in mortality across regions via a conditional autoregressive (CAR) prior distribution (Besag et al., 1991). Maternal deaths were aggregated at the regional level and were offset by the corresponding number of live births. The effects of interventions were adjusted for the geographical variation in socio-economic factors, health facility assessment readiness indicators and characteristics.

Data analysis was executed in STATA version 14.0 (Stata Corporation, College Station, TX, USA) and model fit was carried out in OpenBUGS 3.2.3 (Imperial College and Medical Research Council, London, UK). Maps were produced in ArcGIS version 10.5 (ArcGIS version 10.5, Esri, Redlands, CA, USA). The effects of covariates on mortality were summarized by posterior medians of their mortality rate ratios (MRRs) and the corresponding 95% Bayesian Credible Intervals (95% BCI). Effects were considered statistically important if their 95% BCI did not include one. Supplementary file 6.1 describes in details the Bayesian methods.

6.3 Results

6.3.1 Descriptive analysis

Table 6.2 summarizes health interventions coverage and the MMR estimates at regional and national levels. The percentage of pregnant women who slept under an ITN the night before the survey has a national coverage of 64% and ranges from 46% to 83% Bukedi and West-Nile regions respectively. Among the antenatal care components, the percentage of pregnant mothers receiving ANC from a skilled provider has the highest coverage of almost 100% with no outstanding regional differences. IPT was not widespread throughout the country with only 45% of the pregnant women receiving the treatment. The lowest coverage (27%) was observed in the Karamoja and the highest (53%) in each of Central 2 and Teso regions. Overall, nearly seven out of every ten births took place with the assistance of a skilled provider, but the assistance varied by region from 58% in each of region of Bugisu and Bunyoro to 96% in Kampala. Delivery by caesarean was the least implemented with 6% receiving the intervention within the country. The lowest coverage (3%) was observed in four regions, that is, Busoga, Bukedi, Bugisu and Karamoja and the highest (13%) in Kampala.

Among postnatal care interventions, family planning was the least effected with 39% nationally and varied from 7% in Karamoja to 47% in each of Central 1, Central 2 and Kigezi regions. Supplementary Figure 6.1 in illustrates the geographical distribution of maternal health intervention coverages at the regional level. The observed differences in interventions coverage across regions may contribute to the regional heterogeneities in MMR.

Table 6. 2: Health interventions coverage, number of live births and deaths and, MMR estimates at region and national levels, Uganda DHS 2016 and NPHC 2014

Variable	Coverage (%)														
Malaria	**Central1**	**Central2**	**Kampala**	**Busoga**	**Bukedi**	**Bugisu**	**Teso**	**Karamoja**	**Lango**	**Acholi**	**WN**	**Bunyoro**	**Tooro**	**Kigezi**	**Ankole**	**National**
%P_ITNS	70	59	75	64	46	69	70	51	68	68	83	64	60	68	61	**64**
Antenatal care	**Central1**	**Central2**	**Kampala**	**Busoga**	**Bukedi**	**Bugisu**	**Teso**	**Karamoja**	**Lango**	**Acholi**	**WN**	**Bunyoro**	**Tooro**	**Kigezi**	**Ankole**	**National**
ANC provider	96	99	98	98	97	97	99	97	97	97	99	92	98	100	97	**97**
4+ ANC visits	63	58	66	66	55	46	53	66	56	61	65	44	64	68	59	**60**
TT	73	83	81	79	86	72	81	92	86	84	94	71	79	87	77	**81**
IPT	46	53	49	49	47	41	53	27	45	38	48	43	45	44	41	**45**
Iron	88	90	94	85	91	86	92	97	83	94	92	84	87	95	85	**88**
Deworming	59	58	63	48	78	55	65	63	47	66	70	42	63	76	58	**60**
Skilled birth assistance	**Central1**	**Central2**	**Kampala**	**Busoga**	**Bukedi**	**Bugisu**	**Teso**	**Karamoja**	**Lango**	**Acholi**	**WN**	**Bunyoro**	**Tooro**	**Kigezi**	**Ankole**	**National**
Skilled delivery	82	77	96	75	67	58	75	73	68	81	78	58	76	71	71	**74**
C_section	11	7	13	3	3	3	5	3	5	5	6	4	10	8	6	**6**
Postnatal care	**Central1**	**Central2**	**Kampala**	**Busoga**	**Bukedi**	**Bugisu**	**Teso**	**Karamoja**	**Lango**	**Acholi**	**WN**	**Bunyoro**	**Tooro**	**Kigezi**	**Ankole**	**National**
Post_check	56	58	78	43	59	56	66	85	56	54	61	39	43	48	43	**54**
Family_planning	47	47	45	32	40	45	34	7	43	31	22	31	43	47	43	**39**
NPHC data	**Central1**	**Central2**	**Kampala**	**Busoga**	**Bukedi**	**Bugisu**	**Teso**	**Karamoja**	**Lango**	**Acholi**	**WN**	**Bunyoro**	**Tooro**	**Kigezi**	**Ankole**	**National**
Live births	168774	146523	59402	152289	78753	66220	74692	36083	80657	63731	106619	91153	110337	48604	106151	**1389988**
Maternal deaths	853	601	234	577	179	231	155	212	225	297	234	288	327	263	519	**5285**
MMR NPHC	505	410	394	379	227	349	208	588	279	466	304	316	296	541	489	**380**

DHS: Demographic and health survey; NPHC: National Population and Housing Census 2014; WN: West- Nile; MMR: Maternal Mortality Ratio

%P_ITNS: Percentage of pregnant women who slept under an ITN the night before the survey

ANC provider: Percentage of pregnant mothers receiving ANC from a skilled provider

4+ ANC visits: Percentage of pregnant women making four or more ANC visits during their entire pregnancy

TT: Percentage of mothers whose most recent live birth was protected against neonatal tetanus

IPT: Percentage of women who received intermittent preventive treatment for malaria during pregnancy

Iron: Percentage of women who during the pregnancy of their most recent live birth took iron tablets or syrup

C_section: Percentage of live births in the 5 years preceding the survey delivered by caesarean section

Post_check: Percentage of women with a postnatal check during the first 2 days after birth

The overall MMR was 380 deaths per 100 000 live births (Table 6.2). Large regional differentials in MMR per 100 000 live births were observed, highest in Karamoja (588) and lowest in Teso (208). Figure 6.1 presents the corresponding geographical distribution of MMR per 100 000 live births by region.

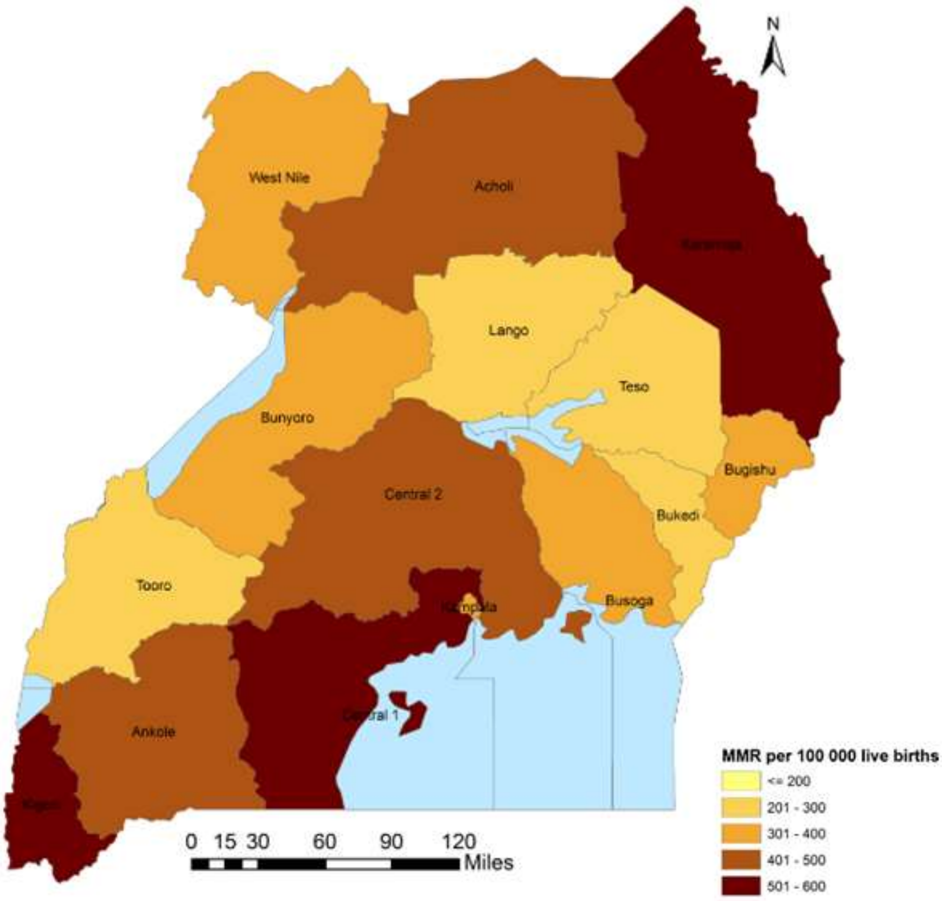

Figure 6. 1: Geographical distribution of maternal mortality ratio per 100 000 live births by region, Uganda NPHC 2014

Table 6.3 contains coverage of health facility assessment readiness indicators at the national level. Among the general service health facility readiness indicators, the percentage of health facilities with all basic amenities was the lowest (0.5%) while that of facilities with all basic equipment items was the highest (40.1%). Sexually transmitted infection services were the most frequent among service-specific readiness indicators, with about 42% of health facilities offering the service. The percentage of health facilities offering delivery services with priority medicines was the smallest (0.3%) among service specific readiness indicators

Table 6. 3: Coverage of health facility assessment readiness indicators at the national level, USDI 2013

Variable	Coverage (%)
General service facility readiness indicators	
Percentage of facilities with all basic amenities	0.5
Percentage of facilities with all basic equipment items	40.1
Percentage of facilities with all standard precaution items for infection prevention	19.0
Percentage of facilities with all diagnostic laboratory tests	15.6
Percentage of facilities with all essential medicines	1.8
Specific service facility readiness indicators	
Percentage of health facilities offering family planning services	3.9
Percentage of health facilities offering ANC services	6.3
Percentage of health facilities offering basic emergency obstetric care	10.7
Percentage of health facilities offering comprehensive obstetric care	3.9
Percentage of facilities offering delivery services that have priority medicines	0.3
Percentage of facilities offering malaria services readiness	20.3
Percentage of facilities offering HIV counselling and testing	39.3
Percentage of facilities offering sexually transmitted infections services	42.2

USDI: Uganda Service Delivery Indicators; HIV: Human Immunodeficiency Virus

6.3.2 Bayesian variable selection

Bayesian variable selection was applied on maternal health interventions, socio-economic factors, health facility assessment readiness indicators and characteristics to determine predictors that explain maximum variation (inclusion probability ≥50%) in maternal mortality. Results (Table 6.4) indicate that maximum variation in maternal mortality was explained by 4+ ANC visits, IPT, Iron, skilled delivery, postnatal care timing, family planning, percentage of facilities with all standard precaution items for infection prevention, all diagnostic laboratory tests, HIV counselling and testing services and, the percentage of households collecting drinking water from improved sources.

Table 6. 4: Posterior inclusion probabilities of health interventions, health facility assessment indicators and socio-demographic characteristics

Variable	Inclusion probability (%)
Malaria	
%P_ITNS	31.0
Antenatal care	
4+ ANC visits	84.0*
TT	0.0
IPT	94.0*
Iron	98.0*
Deworming	6.0
Skilled birth assistance	
Skilled delivery	100.0*
C_section	0.0
Postnatal care	
Post_check	73.0*
Family planning	61.0*
Health facility assessment indicators	
Basic equipment	17.0
Standard precautions	53.0*
Laboratory readiness	88.0*
ANC services	39.0
Basic emergency	4.0
Malaria services	45.0
HIV counselling and testing	82.0*
Sexually transmitted infections (STIs)	21.0
Socio-economic factors	
Improved sanitation facility	46.0
Improved source of drinking water	83.0*
Wealth index score	2.0

*Selected variables with ≥ 50% inclusion probability

Basic equipment: Percentage of health facilities with all basic equipment items, Standard precautions: Percentage of health facilities with all standard precautions items, Laboratory readiness: Percentage of health facilities with all laboratory tests, ANC services: Percentage of health facilities offering ANC services, Basic emergency: Percentage of health facilities offering basic emergency, Malaria services: Percentage of health facilities offering malaria services, HIV counselling and testing: Percentage of health facilities offering HIV counselling and testing, Sexually transmitted infections: Percentage of health facilities offering STI services.

6.3.3 Effect of health interventions on maternal mortality adjusted for health facility assessment readiness indicators and socio-economic factors

Table 6.5 shows adjusted mortality rate ratios (MRRs) and their Bayesian Confidence Intervals (BCI) for the effect of health interventions on maternal mortality. A 1% increase in the coverage of intermittent preventive treatment was associated with a reduction of 12% (MRR = 88%; 95% BCI: 86%, 91%) in the rate of maternal mortality. Similarly, the rate of maternal mortality declined by 5% (MRR = 95%; 95% BCI: 93%, 98%), 4% (MRR = 96%; 95% BCI: 94%, 98%) and 5% (MRR = 95%; 95% BCI: 92%, 98%) for 1% increase in the implementation of iron supplementation, skilled birth attendance and family planning respectively. Also, an increase in the percentage of health facilities with all standard precaution items for infection prevention and, with all diagnostic laboratory tests was associated with a 6% (MRR = 94%; 95% BCI: 90%, 96%) and, a 5% (MRR = 95%; 95% BCI: 92%, 98%) reduction in the rate of maternal mortality respectively. A 1% increase in the percentage of households collecting drinking water from an improved source was associated with a 7% reduction (MRR = 0.93, 95% BCI: 0.91, 0.98) in the rate of maternal mortality.

Table 6. 5: Posterior estimates for the effects of maternal health interventions on MMR adjusted for health facility assessment indicators and socio-economic characteristics

Variable	MRR (95% BCI)
Antenatal care	
4+ ANC visits	1.12 (0.41, 1.58)
IPT	0.88 (0.86, 0.91)*
Iron	0.95 (0.93, 0.98)*
Skilled birth assistance	
Skilled delivery	0.96 (0.94, 0.98)*
Postnatal care[a]	
Post_check	0.96 (0.81, 1.12)
Family planning	0.95 (0.92, 0.98)*
Health facility assessment indicators	
Standard precautions	0.94 (0.90, 0.96)*
Laboratory readiness	0.95 (0.92, 0.98)*
HIV counselling and testing	1.03 (0.99, 1.09)
Socio-economic factors	
Improved source of drinking water	0.93 (0.91, 0.98)*
Spatial parameters	**Median (95% BCI)**
Spatial variance in mortality rate	1.73 (0.42, 4.43)
Other parameters:	
Dispersion parameter[b]	1.26 (0.69, 2.91)

*Statistically significant effect; MRR: Mortality Rate Ratio; [a]Overdispersion parameter quantifying the amount of extra Poisson variation.

6.4 Discussion

We analyzed maternal mortality data, reported through the NPHC, to determine the effects of maternal health interventions on maternal mortality, taking into account the geographical variation of socio-economic factors, health facility assessment readiness indicators and characteristics. Data on interventions were obtained from the 2016 DHS whereas health facility data were collected during the 2013 USDI survey. We found that maternal mortality rate reduced with increasing coverage of health interventions. Also, health facility readiness to provide general services and access to improved water sources were associated with a decline in maternal mortality. The unique feature of the current study as opposed to former research which used health facility data to assess the relationship between all-cause maternal mortality and health interventions in Uganda (Mbonye, 2001; Mbonye et al., 2007b, 2007a), is that, the latter has used nationally representative data to evaluate the relation. Thus our findings are more reliable and can be generalizable to the national level.

Our study suggests that intermittent preventive treatment (IPT) had a protective effect on maternal mortality. This is because IPT prevents development of malaria and eliminates malaria parasites from the placenta during pregnancy (Rogerson et al., 2000; Shulman et al., 2001; Steketee et al., 1996, 2001). This reduces maternal malaria episodes, maternal parasiteamia and maternal anaemia (Mbonye et al., 2008; Wolfe et al., 2001; Salihu et al., 2002; Kayentao et al., 2005) which would result in adverse consequences of malaria on maternal outcomes. The protective effect of IPT on maternal mortality was also reported in an analysis of district health facility data to identify priority interventions to achieve the maternal mortality Millennium Development Goal in Uganda (Mbonye et al., 2007b).

It is known that IPT is one of the components of ANC, and according to the most recent DHS, almost all (ninety seven percent) pregnant mothers received ANC from a skilled provider (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Despite universal implementation of ANC services, poor utilization of IPT is reported. In Uganda, only forty five percent of pregnant women received the recommended two-dose regimen. Even across regions, coverage of the intervention was low with the highest of fifty three percent realized in each of Central 2 and Teso regions (Uganda Bureau of Statistics (UBOS) and ICF, 2018). The low coverage of IPT has also been reported in other settings despite the high awareness of the intervention by skilled providers. For example, in a systematic review which investigated the impact of malaria during pregnancy on low birth weight in sub-Saharan Africa (Guyatt and Snow, 2004) and in Kenya where IPT was implemented to control malaria during pregnancy (van Eijk et al., 2004). The low use and adherence to IPT can be attributed to late ANC attendance and failure to complete the recommended four ANC visits. About thirty percent of women made their first ANC visit at five months and only sixty percent attended atleast four visits (Uganda Bureau of Statistics (UBOS) and ICF, 2018). This implies that women start attending ANC almost halfway through the overall gestation period and not all of them complete the recommended ANC visits. This reduces the number of contacts between care givers and pregnant women and lessens the opportunities to expand IPT coverage. Therefore, other approaches to increase coverage of IPT need to be implemented in addition to ANC attendance. One way to increase contacts between care givers and pregnant women is through community-based approaches such as adolescent peer mobilisers, village health volunteers and traditional birth attendants. These have been found to increase access and adherence to IPT in Uganda (Mbonye et al., 2008, 2007b) and in Gambia (Greenwood et al., 1992).

The protective effect of iron supplements on maternal mortality indicated by our study can be attributed to the increasing haemoglobin levels resulting from improved iron supplementation coverage (Ndyomugyenyi and Magnussen, 2000). The intervention was sufficiently implemented country-wide (eighty eight percent) and at regional levels with the least coverage of eighty three percent in Lango region (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Higher haemoglobin concentration not only increases the oxygen-carrying capacity, but also provides a buffer against the blood loss that can occur during delivery (Hallberg L, 1988), hence decreasing maternal mortality (Stoltzfus RJ, 2003). A similar effect of iron supplements on maternal mortality was found in a systematic review of evidence-based practices to reduce maternal mortality in sub-Saharan Africa (Piane, 2008).

The study shows that skilled birth attendance was associated with lower maternal mortality rate. This is because delivering under the supervision health professionals ensures proper medical attention and hygienic conditions during delivery which can reduce the risk of complications and infections that may cause death or serious illness to either the mother or the baby (or both) (Snow et al., 2015). These results highlight the importance of skilled delivery in maternal health which would save more lives if increased to higher levels in the country. Similar relations were found in Uganda (Mbonye, 2001; Mbonye et al., 2007b, 2007a), sub-Saharan Africa (Alvarez et al., 2009; Buor and Bream, 2004) and at the global level (Robinson and Wharrad, 2001).

Results indicate that family planning was associated with reduced maternal mortality rate. Our results are consistent with those of Mbonye who examined risk factors associated with maternal deaths in health units in Uganda (Mbonye, 2001), Piane who carried out a systematic review on evidence-based practices to reduce maternal mortality in sub-Saharan Africa (Piane, 2008) and Alveraz et al who performed an ecological study and assessed risk factors associated with maternal mortality in Sub-Saharan Africa in (Alvarez et al., 2009). The lower mortality rate can be explained by the fact the family planning increases birth intervals and reduce the risk of unwanted pregnancies, thereby reducing the high levels of maternal deaths associated with risky pregnancies (Cleland J et al., 2006; Mbonye, 2001; Snow et al., 2015; United Nations Population Fund, 2017). This finding provides evidence that family planning plays a role in preventing some of the maternal deaths. However, family planning implementation is poor with only thirty nine percent of married women using any family planning method in Uganda (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Moreover, the utilization of the intervention at the sub-national scale is inadequate. The highest percentage of currently married women using any contraceptive method (forty seven percent) was observed in each region of Central 1, Central 2 and Kigezi and the lowest (seven percent) occurred in Karamoja. The low contraceptive prevalence rate in Karamoja could be one of the factors contributing to the high MMR in this region (588 deaths per 100 000 live births).

Our findings demonstrate that the availability of standard precautions to prevent infections and laboratory tests with reagents in health facilities were important predictors of maternal mortality. However, most health facilities in Uganda lack these indicators and therefore cannot provide quality care. Standard precautions to prevent infections and laboratory tests with reagents were present in only sixteen percent and fifteen percent of all health facilities respectively. This implies that unless resources are allocated to the development of the health system, Uganda is unlikely to experience improved maternal outcomes. Our findings are consistent with those of other studies who found the availability of antibiotics and laboratories with reagents to be protective of maternal mortality at health facilities (Mbonye, 2001; Mbonye et al., 2007b, 2007a).

Access to improved water sources was associated with a reduction in the rate of maternal mortality. This is because access to safe drinking water is a fundamental pillar for maternal health (Alvarez et al., 2009; Muldoon et al., 2011). Unhygienic birthing practices and facilities that are not properly equipped to provide a sterile environment for a post-partum mother commonly contribute to elevated rates of maternal mortality (Muldoon et al., 2011).

The strength of this study is that it uses country-level data which provides more reliable and informed estimates of the effects of health interventions on maternal mortality, and our results can be generalized to the entire country. Also, our findings are consistent with health facility based findings (Mbonye, 2001; Mbonye et al., 2007b, 2007a).

A restriction of this analysis is the lack of variables which are influential in the health of mothers; such as socio-economic status, education level, occupational status, number of live births, age at birth, number of pregnancy terminations and marital status (Mbonye, 2001). It would have been informative to establish the effect of these variables on maternal mortality.

Also, the cross-sectional nature of the census and survey data does not allow the inference of casual associations between maternal mortality and the investigated factors.

Another constraint of our study is the sparsity of maternal mortality data at a sub-national scale. This has hindered the estimation of the effects of health interventions on maternal mortality that may exist at a local-scale (Bustreo et al., 2013; Say et al., 2014). Although, MMR has considerably improved nationally, the burden is unevenly distributed at sub-national level. The highest MMR (588) occurred in Karamoja while Teso region experienced the lowest of 208 deaths per 100 000 live births (Uganda Bureau of Statistics, 2016). Coverage of maternal health interventions is also inequitably spread among regions. The region of Kampala experienced the highest skilled birth attendance (ninety six percent) whereas each of Bunyoro and Bugisu had the lowest (fifty eight percent). The lowest postnatal care (thirty nine percent percent) was reported in Bunyoro and the highest (eighty five percent) in Karamoja. Family planning was most prevalent (forty seven percent) in each of Central 1, Central 2 and Kigezi regions and least predominant in Karamoja (seven percent) (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Regional disparities in maternal mortality may partly be due to differing coverage of interventions across regions. This calls for the need to investigate the effect of interventions on maternal mortality at a local scale in order to guide region-specific interventions aimed at improving maternal health outcomes. Specifically, implementing targeted interventions at a local scale would reduce within country mortality disparities, and consequently improve Uganda’s national MMR target.

6.5 Conclusion

We have used country-level data and obtained more reliable and informed estimates of the effects of health interventions on maternal mortality in Uganda. We have demonstrated that intermittent preventive treatment, iron supplements, skilled birth attendance and family planning are associated with reduction in maternal mortality. However, coverage of intermittent preventive treatment and family planning is low in the country. Therefore, scaling up coverage of important interventions may improve maternal mortality in Uganda. Community-based approaches alongside early ANC attendance are some of the approaches which can improve IPT coverage since they increase contacts between care givers and pregnant women.

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Declarations

Availability of data and materials

The data regarding maternal health interventions and socio-economic factors are available at the DHS MEASURE website (www.dhsprogram.com) with request for access and following instructions at https://dhsprogram.com/data/Access-Instructions.cfm (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Maternal mortality and births data can be obtained from the Uganda Bureau of Statistics upon request (Uganda Bureau of Statistics, 2016). Health facility assessment data were collected and availed by the Uganda Service Delivery Indicator survey office (Wane, 2017).

Authors' contributions

All authors take responsibility for the structure and content of the paper. BBN conceptualized the research, managed and analyzed the data, developed the methodology and implemented it in software, interpreted results and wrote the first draft of the manuscript. Author JS participated in data management and analysis. Authors JG and IK provided the maternal mortality and live births, and health facility assessment data respectively. Authors FEM and SK formulated research goals and objectives, and also participated in the process of acquisition of project financial support. PV was the lead author who conceived the research, formulated research goals and objectives, acquired project financial support, lead methodology development, model fitting and result interpretation and manuscript writing. JU contributed to the review of the manuscript. All authors read and approved the submitted manuscript.

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Ethical approval and consent to participate

In this research article secondary data that was made available to us by the USDI, the Uganda Bureau of Statistics (UBOS) and the DHS Program (www.dhsprogram.com) was used. According to survey reports, ethical approval and consent to participate was obtained by the above bodies from the Institutional Review Board of International Consulting Firm (ICF) of Calverton, Maryland, USA, and from Makerere University School of Biomedical Sciences Higher Degrees Research and Ethics committee (SBS-HDREC) and the Uganda National Council for Science and Technology (UNCST). Information on ethical approval and consent to participate is published in the 2016 DHS (Uganda Bureau of Statistics (UBOS) and ICF, 2018), the 2014 NPHC (Uganda Bureau of Statistics, 2016) and the 2013 USDI (Wane, 2017).

Consent for publication

Not applicable.

Competing risks

The authors declare that they have no competing interests.

6.6 Supplementary files

Supplementary file 6. 1: Bayesian methods

Bayesian variable selection

A Bayesian negative binomial model, adopting a spike and slab variable selection was used to determine the most important predictors of maternal mortality (George and McCulloch, 1993). Specifically, for each predictor $\underset{\sim}{X}p$ we introduce a binary indicator parameter I_p suggesting presence ($I_p = 1$) or absence ($I_p = 0$) of the predictor from the model. I_p has a probability mass function $\prod_{j=0}^{1} \pi_j^{\sigma_j(I_p)}$ where π_j are the inclusion probabilities of functional form j (i.e. j=0, 1) such that $\sum_{j=0}^{1} \pi_j = 1$ and $\sigma_j(.)$ is the Dirac function, $\sigma_j(I_p) = \begin{cases} 1, & if\ I_p = j \\ 0, & if\ I_p \neq j \end{cases}$.

We assumed a spike and slab prior for regression coefficient β_p corresponding to the corresponding covariate, X_p i.e. for the coefficient β_p of the predictor in linear form we take $\beta_p \sim (1 - \delta_1(I_p))N(0, u_0\tau_p^2) + \delta_1(I_p)N(0, \tau_p^2)$ proposing a non-informative prior for β_p in case X_p is included in the model in a linear form (slab) and an informative normal prior with variance close to zero (i.e. $u_0 = 10^{-3}$) shrinking β_p to zero (spike) if X_p is excluded from the model. Similarly, for the coefficient $\{\beta_{p,l}\}_{l=1,..,L}$ corresponding to the categorical form of $\underline{X}_p$ with L categories, we assume that $\beta_{p,l} \sim \delta_2(I_p)N(0, \tau_{p,l}^2) + (1 - \delta_2(I_p))N(0, \vartheta_0\tau_{p,l}^2)$. A Bernoulli prior is assumed for the indicator, $I_p \sim Be(0.5)$. The predictors identified as important are those with posterior inclusion probability of atleast 50% (Ssempiira et al., 2017).

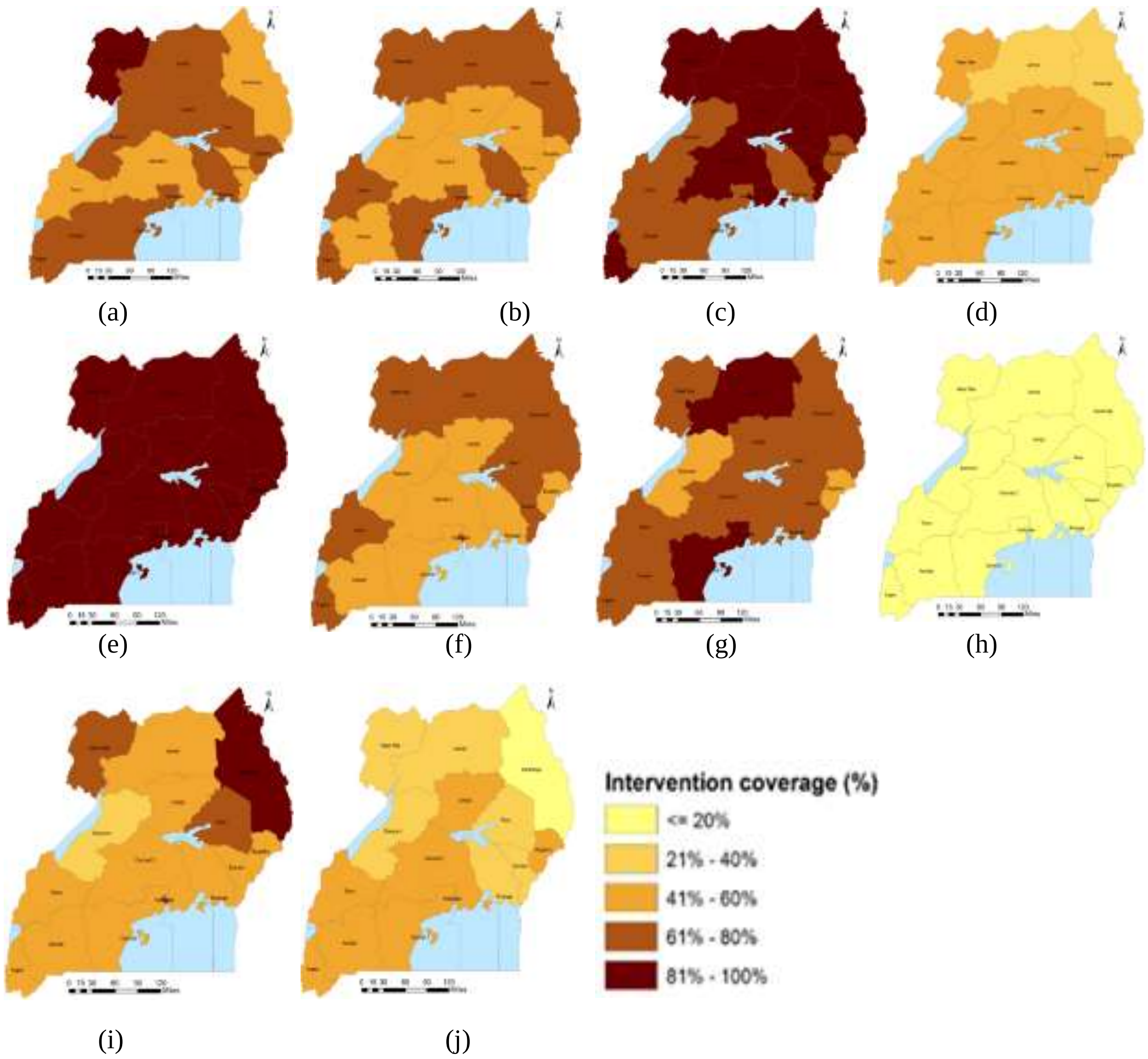
Bayesian negative binomial model

Bayesian negative binomial models (Banerjee et al., 2015) were fitted to assess the effect of interventions on maternal mortality adjusted for the geographical variation of socio-economic factors, healthy facility assessment readiness indicators and characteristics.

Let Y_i be the number of all-cause maternal deaths reported in region i. Y_i is assumed to follow a negative binomial distribution, that is, $Y_i \sim dnegbin(p_i, r)$, $p_i = \frac{r}{r+\mu_i}$, where p_i is the probability of observing a maternal death in region i, μ_i is the mean number of maternal deaths in region i, and r being the parameter quantifying the amount of extra Poisson variation. Then Y_i is related to its predictors using a log-linear regression model as:-

$log(\mu_i) = \log(F_i) + \beta_0 + \boldsymbol{\beta}^T \boldsymbol{X}_i + W_i$ where, F_i is the offset, the number of live births in region i, β_0 is the intercept, $\boldsymbol{X}_i$ is a vector of predictors in region i, $\boldsymbol{\beta}^T = (\beta_1, \ldots, \beta_p)$ is the vector of regression coefficients with $\exp(\beta_l)$, $l = 1, \ldots p$, corresponding to the mortality rate ratios (MRRs). Random effects at regional levels W_i were used to capture spatial dependence in mortality across regions i.e. regions in closer proximity are expected to have similar mortality rates due to common exposures. Spatial dependence among the regions is introduced via a conditional autoregressive (CAR) prior for $W_i, i = 1,2, \ldots, 15$ (Besag et al., 1991). The CAR assumes that the mean of each region, w_i, conditional on the neighbouring regions, w_j, follows a normal distribution with mean equal to the average of the neighbouring regions, w_j, and variance inversely proportional to the number of neighbours, n_i, that is $w_i/w_j \sim N(\gamma \sum_{l \in \delta_i} w_j , \frac{\sigma_w^2}{n_i})$ where γ quantifies the amount of spatial correlation present in the data and σ_w^2 measures the spatial variance. w_i and w_j are adjacent regions in the set of all adjacent regions δ_i of region i, and n_i are the number of adjacent regions.

To complete Bayesian model formulation, we assumed vague priors; non-informative normal priors for regression coefficients, β, that is, $\beta_l \sim N(0, 10^2)$ for $l = 1, \ldots p$, a similar prior was adopted for the intercept, an inverse gamma prior for spatial variance and the dispersion parameter, r, with known parameters, i.e. $\sigma_w^{-2}, r^{-1} \sim IG(2.01, 1.01)$. Model parameters were estimated using Markov Chain Monte Carlo simulation (Gibbs sampling) (Smith and Roberts, 1993). Starting with some initial values, a two chain algorithm for 2 000 000 iterations with an initial burn-in of 15,000 iterations was run. Convergence was assessed by visual inspection of trace and density plots and analytically by the Gelman and Rubin diagnostic (Rubin and Gelman, 1992).



Supplementary Figure 6. 1: Geographical distribution of maternal health intervention coverages by region, Uganda DHS 2016; (a) Percentage of pregnant women who slept under an ITN the night before the survey, (b) Percentage of pregnant women making four or more ANC visits during their entire pregnancy, (c) Percentage of mothers whose most recent live birth was protected against neonatal tetanus, (d) Percentage of women who received intermittent preventive treatment for malaria during pregnancy, (e) Percentage of women who during the pregnancy of their most recent live birth took iron tablets or syrup, (f) Percentage of women who took deworming medication during pregnancy of last birth, (g) Percentage of births that took place with the assistance of a skilled provider, (h) Percentage of live births in the 5 years preceding the survey delivered by caesarean section, (i) Percentage of women with a postnatal check during the first 2 days after birth, (j) Percentage of married women using any family planning method.

Chapter 7: General discussion, limitations and further research, conclusions and recommendations

We developed Bayesian geostatistical proportional hazards models to assess the ffects of interventions and childhood diseases on under-five mortality at the national and sub-national scales, and to estimate high mortality clusters in the country. Also, Bayesian geostatistical logistic regression models were developed; to quantify the contribution of childhood diseases to the geographical distribution of fever risk among children less than five years, and to estimate the effect of the presence of soap and water at handwashing places in households on the risk of diarrhoea and ARI among the under-five. Furthermore, Bayesian negative binomial conditional autoregressive (CAR) models were employed to quantify the effects of maternal health interventions on all-cause maternal mortality. The analysis adjusted for confounding effects of demographic, socio-economic, health care seeking behaviour, environmental/climatic factors, health facility readiness indicators as well as health facility characteristics. We analysed data obtained from different sources including the National Population and Housing Census (NPHC), nationally representative household surveys, such as Demographic and Health Surveys (DHS), the Malaria Indicator Surveys (MIS), and health facility assessment surveys, specifically, the Uganda Service Delivery Indicator (SDI) Survey. Remote sensing sources also provided data on climatic/environmental factors.

7.1 Significance of the PhD Thesis

The thesis is structured into five chapters (2-6), each comprising a detailed explanation and discussion of the findings as well as their implications. In this section, we discuss the contribution of the major findings to epidemiological methods; the data; under-five mortality, childhood diseases and interventions; the presence of soap and water at handwashing places in households and the risk of diarrhoea and ARI among the under-five; maternal mortality, interventions and health facility readiness indicators; and the socio-economic status.

7.1.1 Epidemiological methods

In Chapters 2, 3 and 4, we developed models with spatially varying coefficients to estimate the effects of interventions and childhood diseases on U5MR and the prevalence of fever at the national and sub-national scale. The effects of interventions and childhood diseases on U5MR varied by region. Similarly, the effects of childhood diseases on the prevalence of fever differed amongst regions. These models provide information that can be used by control programs in the development of locally adapted and evidence-based interventions, unlike national level estimates that ignore discrepancies in childhood diseases and interventions at a local scale.

In Chapter 5, we developed geostatistical models to quantify the effect of the presence of soap and water at handwashing places in households on the risk of diarrhoea and ARI among the under-five. The odds of diarrhoea and ARI in children who lived in households having soap and water at handwashing places were less than those of children living in households without the intervention. Our analysis takes into account spatial correlation in disease outcomes in contrast to the standard methods that assume independence of outcomes in adjacent locations. Indeed, spatial correlation in disease outcomes was strong especially in the ARI risk, suggesting the need to take into account spatial dependence when analyzing these disease outcomes.

In Chapter 6, we applied Bayesian negative binomial CAR models on the NPHC maternal mortality data collected during 2014. In this work, we took into account neighbourhood dependence in mortality across regions by introducing regional-specific random effects via a CAR prior distribution. This approach is more practical for maternal mortality data since regions in closer proximity are expected to have similar mortality rates due to common exposures such as indirect causes e.g. malaria. This improves model estimates for mortality compared to studies which assumed independence of maternal outcomes.

7.1.2 The data

Civil death registration is considered the gold standard source of disease-specific mortality, however, due to the dysfunctional civil registration system in Uganda; we used DHS data in this thesis to quantify the effects of childhood diseases on the U5MR. The presented methodology can be applied to other countries with dysfunctional civil registration systems, and be used as a tool for providing information for decision making in programming of interventions at sub-national scales to address under-five mortality.

This thesis used national-level data (DHS, NHPHC and USDI) to investigate the effects of maternal interventions on maternal mortality different form previous studies that used health facility data (Mbonye, 2001; Mbonye et al., 2007b, 2007a). Moreover, the current study assessed several maternal interventions (antenatal care, skilled birth assistance, postnatal care) contrary to a few national studies that evaluated a single category of interventions (number of antenatal visits) (Atuhaire and Kaberuka, 2016). Therefore, this thesis provides more reliable and informed estimates of interventions effects for policy formulation and implementation aimed at improving maternal health in Uganda.

7.1.3 Under-five mortality, childhood diseases and interventions

The country-wide mortality map identifies hotspots of under-five mortality and can be used as a practical tool by control programmes for decision making support, resource mobilization and improving coverage of important interventions, especially at high mortality clusters in Uganda.

Results showed that childhood diseases, that is, malaria, anaemia, diarrhoea and malnutrition increase the risk of under-five mortality in Uganda. These diseases have been described in various settings as some of the major global, regional and national causes of child mortality (Liu et al., 2016, 2015, 2012). Other studies also found important relationships between under-five mortality and malaria (Gemperli et al., 2004; Kazembe et al., 2007), diarrhoea (Walker et al., 2013), malnutrition (Vella et al., 1992b, 1992a) and anaemia (Brabin et al., 2001; Scott et al., 2014).

The study further demonstrated that malaria, diarrhoea and ARI were associated with a higher risk of fever among children less than five years in Uganda. Our findings are in line with those of other studies, for example, in Uganda (Ssenyonga et al., 2009) and pooled analysis of MIS data obtained from six countries (Djibouti, Kenya, Namibia, Angola, Liberia and Senegal) (Okiro and Snow, 2010). However, majority of fevers among the under-five are attributed to diarrhoea, followed by ARI.

Findings also indicated that child health interventions played an important role in reducing the risk of U5M in Uganda. National level estimates pointed out that ACT, initiation of breast feeding within one hour of birth, IPT, ITN access and improved source of drinking water were the most important health interventions associated with a reduction in U5M. Other interventions that were associated with a significant reduction in mortality include ITN use, improved sanitation facilities, skilled delivery, postnatal care, complete DPT and measles vaccination, vitamin A supplementation, deworming medication and ORS or RHF. Similarly, these variables are among the essential health interventions that have been found to be associated with a decrease in child mortality (Lassi et al., 2014).

Results further showed that despite their important effects on U5MR, coverage of many interventions was low in the country and varied by region; for example, ORS/RHF, WASH practices and antibiotics. This emphasizes inequalities in health services delivery which may be a result of a dysfunctional health system in the country.

Our results demonstrated varying effects of childhood diseases and interventions on U5MR across regions. Also, the contribution of childhood diseases to the prevalence of fever differed by region. These results can partly be tagged to disparities in childhood disease prevalences and intervention coverage across regions. This calls for regional-specific intervention programing and implementation in Uganda rather than a universal approach. While malaria could have had the largest impact on U5MR in some regions, and reinforcing malaria-related interventions would alleviate malaria-related mortality in those areas, in other regions U5MR might be improved by anaemia, diarrhoea, malnutrition or ARI interventions.

7.1.4 The presence of soap and water at handwashing places in households and the risk of diarrhoea and ARI among the under-five

The presence of soap and water at handwashing places in households was associated with a lower risk of diarrhoea and ARI among the under-five. However, coverage of the intervention is low with more than half of the households in Uganda lacking water and soap at hand washing places (Uganda Bureau of Statistics (UBOS) and ICF, 2018). Thus, coverage of the intervention should be scaled up. The protective association between handwashing with soap and water, and the risk of diarrhoea and ARI among the under-five have been found in previous studies (Kamm et al., 2014). However, there is paucity of literature on studies assessing handwashing with soap and water, the risk of diarrhoea and ARI in the same age group in Uganda. Therefore, results of this study will be essential for policy formulation and advocacy to programmes that aim to reduce the burden of diarrhoea and ARI among the under-five in Uganda. Moreover, the study adds to the body of literature that the presence of soap and water at handwashing places in households can reduce the risk of diarrhoea and ARI among the under-five.

7.1.5 Maternal mortality, interventions and health facility readiness indicators

Study results indicated that intermittent preventive treatment, iron supplements, skilled birth attendance, family planning, availability of standard precautions and diagnostic laboratory tests were associated with a reduction in the rate of maternal mortality. These findings have been observed in other studies (Alvarez et al., 2009; Buor and Bream, 2004; Mbonye et al., 2007b, 2007a; Piane, 2008; Robinson and Wharrad, 2001). However, coverage of intermittent preventive treatment and family planning is low in the country. Additionally, health facility readiness to provide all standard precaution items for infection prevention and all diagnostic laboratory tests is poor, indicating a weak health system.

7.1.6 Effect of socio-economic status

The study indicated a negative relationship between higher socio-economic status and, U5MR and fever. Higher mortality rates persist in regions with the low socio-economic status in Uganda that is, the North-East, West-Nile, East-Central, Lango and Acholi. The poor socio-economic status in the country is partly responsible for the prevailing high mortality and disease burden which weakens the effect of health interventions. Actually, our study has shown that higher socio-economic status is protective against mortality and fever. Consistent relationships have been reported in Uganda (Bbaale, 2015), Nigeria (Ezeh et al., 2015; Yusuf et al., 2010) and Tanzania (Njau et al., 2006). This is because wealthier households are in a better position to provide preventive and curative measures to household members including children less than five years (Victora et al., 2003).

7.3 Limitations and further research

The main limitation of our study was sparsity of data. For instance, disease and intervention data for the dead children were not available and therefore we were not able to estimate the disease or intervention-related mortality using disease or intervention information at individual level. Instead, we treated the disease prevalence at the DHS primary sampling unit (the cluster) as an exposure, aggregated intervention coverage at the cluster level and quantified the associations with U5MR, adjusting for birth-related factors at the individual level, maternal and household characteristics. Our results are therefore prone to ecological fallacy; however, they inform about geographical distribution of the effects of childhood diseases and interventions on U5MR in Uganda. These estimates provide information for decision making in programing of interventions at sub-national scales to address U5MR.

Also maternal mortality data at a sub-national scale was scanty. This hindered the estimation of intervention effects on maternal mortality at a local-scale. Such analysis would provide insights into factors explaining persistent disparities in maternal mortality at a local scale. These findings would provide information that can be used by control programs in the development of locally adapted and evidence-based interventions to address maternal mortality. This would reduce within country maternal mortality discrepancies and consequently speed up the achievement of SDG target 3.1 in Uganda.

This study did not estimate the effects of diseases and interventions on mortality and the prevalence of fever over time. This analysis would inform on the impact of changes in interventions coverage and disease burden on mortality and fever over time and guide control activities in a timely manner.

7.4 Conclusions and recommendations

The work in this thesis is essential for monitoring progress in all-cause under-five and maternal mortality as well as their key determinants (diseases and interventions). The methods developed in this thesis can be applied to estimate effects of childhood diseases and health interventions at the national and sub-national scale. The results can inform evidence-based implementation of disease prevention and treatment interventions, particularly at a local scale.

The under-five mortality country-wide map is essential for identifying hotspots of mortality. This will inform targeted interventions at priority settings to maxmise benefits and optimizing resources for achieving SDG mortality targets in Uganda. Along the same line, the Uganda government launched the Reproductive Maternal, Newborn and Child Health Sharpened Plan (RMNCHSP) in 2013, as part of the global “Committing to Child Survival: A

Promise Renewed" movement, to end maternal and child deaths across the country (Ministry of Health, 2013a). The plan is also anchored within the country's 2040 Vision (Ministry of Health, 2013a). This Plan envisions strategic shifts including; focusing geographically on areas with the highest number of child and maternal deaths; increasing access of health services to deprived and vulnerable populations and emphasizing high impact interventions that target the direct causes of death (Ministry of Health, 2015a).

To achieve the RMNCHSP, there is a need to identify high mortality areas, diseases that influence mortality in those areas and most high impact interventions targeting those diseases. The under-five country-wide mortality map and results on the effects of interventions and diseases on under-five mortality obtained in this PhD thesis, can aid the implementation of the vision of Uganda. However, the Uganda Ministry of Health, in particular, the Maternal and Child Health division needs to build capacity in novel methods such as Bayesian spatial models that have been developed in this thesis, which can be used to identify high mortality areas as well as diseases which influence mortality and high impact interventions at a local scale.

Furthermore, data availability to monitor progress especially in maternal mortality should be improved. For example, by incorporating data collection modules on maternal indicators in national surveys which clearly state the location of the mother at the time of death so as to obtain representative estimates at sub-national scales.

In conclusion, the government should invest more finances into the health sector from a mere 6% as per the 2018/2019 national budget to reinforce the poor health system that hinders universal delivery of health services. In line with this, the government should improve the socio-economic status of its nationals by prioritizing programs such as the President's Initiative to eradicate poverty and Modernisation of Agriculture, designed to fight and eliminate poverty that deteriorates the impact of disease control and treatment interventions.

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Yeka, A., Gasasira, A., Mpimbaza, A., Achan, J., Nankabirwa, J., Nsobya, S., Staedke, S.G., Donnelly, M.J., Wabwire-Mangen, F., Talisuna, A., Dorsey, G., Kamya, M.R., Rosenthal, P.J., 2012. Malaria in Uganda: Challenges to control on the long road to elimination. Acta Tropica 121, 184–195. https://doi.org/10.1016/j.actatropica.2011.03.004

Yusuf, B., Adeoye, B., Oladepo, O.O., Peters, D.H., Bishai, D., 2010. Poverty and fever vulnerability in Nigeria: A multilevel analysis. Malar J 9:235. https://doi.org/10.1186/1475-2875-9-235

Zhang, C., Mosa, A.J., Hayward, A.S., Matthews, S.A., 2013. Promoting clean hands among children in Uganda: a school-based intervention using 'tippy-taps.' Public Health 127, 586–589. https://doi.org/10.1016/j.puhe.2012.10.020

Zhang, G., Hu, Y., Wang, H., Zhang, L., Bao, Y., Zhou, X., 2012. High Incidence of Multiple Viral Infections Identified in Upper Respiratory Tract Infected Children under Three Years of Age in Shanghai, China. PLOS ONE 7, e44568. https://doi.org/10.1371/journal.pone.0044568

Curriculum vitae

1. Personal Details

Name:	Betty Bukenya Nambuusi
Date of birth:	11th December, 1979
Nationality:	Ugandan
Official address:	C/O Makerere University School of Public Health Department of Epidemiology and Biostatistics P.O. Box 7072 Kampala, Uganda
E-mail:	bettynambuusi@gmail.com
Languages:	English (Excellent at written and spoken)

2. Personal profile

A Biostatistician trained in the theory and application of Bayesian and frequentist methods in epidemiology and public health.

Competent in the following statistical modeling and inference areas: Bayesian modeling, areal modeling, geostatistical modeling, hierarchical/multi-level models, longitudinal data analysis, survival data analysis, meta-analysis, multivariate data and stochastic variable selection.

Proficient in statistical programming, data management and analytical software packages including STATA, R, WINBUGS/OpenBUGS, ArcGIS, SPSS, Epi-Info

3. Personal interests

Main epidemiological research areas of interest include development of Bayesian hierarchical models with special interest in mortality and neglected tropical diseases to assess disease (e.g. malaria, diarrhoea, respiratory infections and malnutrition) and interventions effects on spatial changes in health outcomes; Disease mapping for determination of the geographical distribution of health outcomes aimed at targeted public health interventions; Development and application of methods to assess spatial patterns of health outcomes and detect high risk areas for targeted interventions.

4. Education Background

Institution	Degree	Period
Swiss Tropical and Public Health Institute, University of Basel, Switzerland	PhD in Epidemiology with a specialisation in Bayesian modeling and disease mapping	Feb 2015 - May 2019
University Hasselt, Belgium	MSc. Biostatistics	Sept 2006-Sept 2007
University Hasselt, Belgium	MSc. Applied Statistics	Sept 2005-Jul 2006
Makerere University, Kampala-Uganda	BSc. Statistics	Sept 1999-Mar 2003

5. Work Experience

Feb 2015 – Dec 2018	**Research fellow** on the geographical distribution of the determinants of Under-five and Maternal Mortality in Uganda, Swiss Tropical and Public Health Institute, University of Basel, Switzerland **Assistant lecturer**, Makerere University, College of Health Sciences, School of Public Health, Department of Epidemiology and Biostatistics
Jan 2014 - Dec 2014	**Biostatistician**, Rakai Health Sciences Program, Uganda Virus Research Institute
2011-2013	**Biostatistician/assistant lecturer**, Makerere University, College of Health Sciences, Clinical Trials Unit (MakCTU)/ School of Public Health
2007-2010	**Member of the academic staff**, University Hasselt, Belgium
2004-2005	**Statistical Research Associate/Data Manager**, Medical Research Council Unit on HIV/AIDS, Uganda
2003	**IT and Banking officer**, Dfcu Bank, Uganda

6. Publications

Peer-reviewed publications

- Ssempiira, J., Nambuusi, B.B., Makumbi F., Kasasa S., Vounatsou P. Measuring health facility readiness and its effects on severe malaria outcomes in Uganda (in press scientific reports)
- Ssempiira, J., Kissa, J., Nambuusi, B.B., Mukooyo, E., Opigo, J., Makumbi, F., Kasasa, S., Vounatsou, P., (2018). Interactions between climatic changes and intervention effects on malaria spatio-temporal dynamics in Uganda. Parasite Epidemiology and Control. 3(3) e00070. doi:10.1016/j.parepi.2018.e00070.
- Ssempiira, J., Kissa, J., Nambuusi, B.B., Kyozira, C., Rutazaana, D.; Mukooyo, E., Opigo, J.; Makumbi, F., Kasasa, F., Vounatsou, P., (2018). The effect of case management and vector-control interventions on space-time patterns of malaria incidence in Uganda. Malar Journal. 17(1):162. doi: 10.1186/s12936-018-2312-7.
- Ssempiira, J., Nambuusi, B.B., Kissa, J., Agaba, B., Makumbi, F., Kasasa, S., Vounatsou, P., (2017). The contribution of malaria control interventions on spatio-temporal changes of parasitaemia risk in Uganda during 2009–2014. Parasites & Vectors. 10(1):450. doi: 10.1186/s13071-017-2393-0.
- Ssempiira, J., Nambuusi, B.B., Kissa, J., Agaba, B., Makumbi, F., Kasasa, S., Vounatsou, P., (2017). Geostatistical modelling of malaria indicator survey data to assess the effects of interventions on the geographical distribution of malaria prevalence in children less than 5 years in Uganda. PloS ONE 12(4): e0174948. https://doi.org/10.1371/journal.pone.0174948

Monographs

- Nambuusi, B.B., (2010). Placental Uptake of Environmental Chemicals and Children Allergy: Relationships Between Environmental Chemicals Transferred Through the Placenta and Allergy Outcomes in Childhood Years. LAP Lambert Academic Publishing AG & Co. KG, Theodor-Heuss- Ring 26, 50668 Köln, Germany, ISBN 978-3-8383-5746-1.

Conferences

- Nambuusi, B.B., Hermans, E., Brijs, T. and Wets, G., (2010). Sensitivity of road safety outcomes to uncertainties in the computational model for assessing the impact of policy measures at the regional level. 2010 6th International conference on sensitivity analysis of model output (SAMO), Milan, Italy. Social and Behavioral Sciences, Elsevier Proceedings

Reports

- Nambuusi, B.B., Hermans, E., Brijs, T. and Wets, G., (2010). Combination of policy measures: Linearity, synergy and substitution effects on road safety. Ministry of the Flemish government. www.steunpuntmowvver keersveiligheid.be.
- Nambuusi, B.B., Hermans, E., Brijs, T. and Wets, G., (2010). The impact of uncertainties in input factors on road safety savings at the regional level: Applying sensitivity analysis to a computational model for assessing the impact of policy measures at the regional level. Ministry of the Flemish government. www.steunpuntmowvver keersveiligheid.be.
- Nambuusi, B.B., Hermans, E., Brijs, T. and Wets, G., (2010). A computational model to assess the impact of a set of policy measures on road safety at the regional level. 2010 15th International conference on road safety on four continents (RS4C), Abu Dhabi, United Arab Emirates.
- Nambuusi, B.B., Hermans, E., Brijs, T. and Wets, G. (2009). A computational model to assess the impact of policy measures on traffic safety in Flanders: Theoretical concepts and application. Ministry of the Flemish government. RA-MOW-2009-006.
- Nambuusi, B.B., Hermans, E., Brijs, T. and Wets, G., (2008). A review of Accident Prediction
    - Models. Ministry of the Flemish government. RA-MOW-2008-004.

Submissions

- Nambuusi, B.B., Ssempiira, J., Makumbi F., Kasasa S., Vounatsou P. Geographical distribution of the effects of childhood diseases on under-five mortality in Uganda (Submitted to Parasite Epidemiology and Control journal).
- Nambuusi, B.B., Ssempiira, J., Makumbi F., Kasasa S., Vounatsou P. The contribution of childhood diseases on the geographical distribution of fever risk among children less than five years in Uganda (Submitted to Plos One)
- Nambuusi, B.B., Julius Ssempiira, Fredrick E Makumbi, Simon Kasasa, Penelope Vounatsou. Geographical variations of the effects of health interventions on all-cause under-five mortality in Uganda (Submitted to the International Journal of Health Geographics).

- Kiwanuka, N., Mpendo, J., Asiimwe, S., Ssempiira, J., Nalutaaya, A., Nambuusi, B.B., et al. A randomized trial to assess retention rates using mobile phone reminders versus physical contact tracing in a potential HIV vaccine efficacy population of fishing communities around Lake Victoria, Uganda (Submitted to the journal of BMC Infectious Diseases)

7. Personal development

2018

- Data Analysis in Epidemiology
- Statistical Methods in trial Designs
- Academic Writing in Health Sciences
- Composing attractive Abstracts
- An introduction to systematic reviewing: From literature search to meta-analysis
- Systematic Reviews and Meta-analysis: A practical approach
- Advanced Methods in Observational Epidemiology
- Missing data in epidemiology: implications and analysis techniques
- Observational epidemiological workshop: Advanced methods for data and exposure-response analysis

2017

- Walking in the Editor's shoes Peer reviewing and journal editing for young researchers in health sciences
- Essentials in Health research methodology
- Writing a Journal article and getting it published
- How to prepare a job application in and outside academia

2016

- GIS for Public Health

2015

- Malaria epidemiology and Control
- Bayesian Statistics
- Concepts in Epidemiology
- Epidemiological Methods
- Programming in STATA
- Mathematical Modelling of Infectious Diseases
- Key issues in Public and International Health

- Biostatistics Journal Club

2012

- Survival analysis for epidemiologists course

2004

- Logical framework approach to project planning, monitoring and evaluation
- Performance management and development seminar

Referees

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