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THE SURVIVAL AND NUTRITIONAL STATUS OF CHILDREN IN RELATION TO ASPECTS OF MATERNAL HEALTH: FOLLOW-UP STUDIES IN RURAL UGANDA

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THE SURVIVAL AND NUTRITIONAL STATUS OF CHILDREN IN RELATION TO ASPECTS OF MATERNAL HEALTH: FOLLOW-UP STUDIES IN RURAL UGANDA

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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This book is dedicated to David Amiye, for his kindness and love, and for his endless support to me from childhood; his selflessness will always be remembered.

ABSTRACT

Background: Low income countries continue to experience high under-five mortality and a high prevalence of protein energy malnutrition (PEM) among surviving children. There is lack of empirical data for accurate tracking of child survival and for determining the consequences of early childhood PEM on future health and education.

Main aim: To assess under –five mortality trends and associated factors to inform the design of child survival interventions, and also examine the impact of childhood PEM on future adolescent health and schooling among survivors in a rural population in Uganda.

Methods: Four studies were nested in the Kyamulibwa Health and Demographic Surveillance Site in southwestern Uganda. In study 1, prospective data collected between 2002 and 2012 were extracted for 10,118 children under the age of five years and used to estimate age-specific mortality rates using the synthetic cohort life-table method. Calendar year-specific hazard rates and risk factors were explored by Cox regression. In study II, women of reproductive age were enrolled and stillbirth rates were compared using i) 12 months recall of pregnancy outcome (n= 1800) (method 1) and ii) lifetime recall (method 2) and associated risk factors were explored. In study III, 1054 children followed to adolescence were categorised as stunted/wasted, recovered, deteriorated and normal after three nutritional assessments between 1999 and 2011. Mean blood pressures and schooling years achieved measured in 2011 were compared in the 4 groups. In study IV, a pragmatic trial, involving registration of pregnancies and delivering stage-of-pregnancy-specific text message (SMS) via community health workers to pregnant women in 13 intervention villages (n=262) compared with pregnant women in control villages (n=263) with no intervention. Place of birth (home or health facility) was the main outcome.

Results: Under-five mortality was 92 per 1000 live births. Overall mortality declined by 33% between 2002 and 2012 with the highest decline observed in the post-neonatal period. Early neonatal mortality did not change. Stillbirth rates differed by method of estimation; 26.2/1000 births versus 13.8/1000 births respectively by methods 1 and 2. No decline in stillbirth rates was observed. Under-five mortality increased with decreasing child age, HIV infection of the child, a birth interval <1 year, having an unmarried mother, a maternal parity >4 and a home delivery. Stillbirth risk increased with maternal age and reduced with increasing parity. In study III, wasting was negatively associated with systolic blood pressure (-7.90 95%CI [-14.52,-1.28], p= 0.02) and diastolic blood pressure (-3.92, 95%CI [-7.42, -0.38], p= 0.03) among surviving children. Recovery from wasting was positively associated with diastolic blood pressure (1.93, 95%CI (0.11, 3.74] p=0.04). Both stunting and wasting regardless of recovery were negatively associated with school achievement. In study IV, the SMS intervention was associated with lower odds of homebirths [AOR=0.38, 95%CI (0.15-0.97)]. Home births were associated with muslim religion [AOR= 4.0, 95%CI (1.72-9.34)], primary or no maternal education [AOR= 2.51, 95%CI (1.00-6.35)] and health facility distance ≥ 2 km [AOR= 2.26, 95%CI (0.95-5.40)].

Conclusions: Survival of children in rural Uganda is improving, and could improve further with increased uptake of family planning and facility births. Promoting community health workers' role in improving child survival through use of mobile phones for delivering tailored messages to mothers is a potential strategy that could be scaled up in rural communities.

Key words: child mortality, protein energy malnutrition, cardiovascular disease, schooling, mobile phone SMS, facility delivery, community health workers, Uganda

LIST OF SCIENTIFIC PAPERS

I. Gershim Asiki, Robert Newton, Lena Marions, Janet Seeley, Anatoli Kamali, and Lars Smedman, 'The Impact of Maternal Factors on Mortality Rates among Children under the Age of Five Years in a Rural Ugandan Population between 2002 and 2012', *Acta Paediatrica* (2015).

II. Gershim Asiki, Kathy Baisley, Robert Newton, Lena Marions, Janet Seeley, Anatoli Kamali, and Lars Smedman, 'Adverse Pregnancy Outcomes in Rural Uganda (1996–2013): Trends and Associated Factors from Serial Cross Sectional Surveys', *BMC pregnancy and childbirth*, 15 (2015), 1.

III. Gershim Asiki, Robert Newton, Lena Marions, Anatoli Kamali, Lars Smedman, 'The effect of childhood protein energy malnutrition on adolescent health and school achievement in rural south-western Uganda: a prospective cohort study', *Submitted.*

IV. Gershim Asiki1, Robert Newton, Leonard Kibirige, Anatoli Kamali, Lena Marions, Lars Smedman, 'Feasibility of using smartphones by village health workers for pregnancy registration and effectiveness of mobile phone text messages on reduction of homebirths: a pragmatic trial in rural Uganda', *Submitted.*

CONTENTS

LIST OF ABBREVIATIONS

ALPHA	Analysing Longitudinal Population based HIV/AIDS data on Africa
App	A small self-contained program or software designed for a purpose
BCG	Bacillus Calmette-Guerin
CCM	Community Case Management
CDD	Community Drug Distributors
CHW	Community Health Worker
CI	Confidence intervals
“Cloud”	Use of advanced remote computers to which phones connect or other computers connect to upload and store data
CMD	Community Medicine Distributors
ENAP	Every New-born Action Plan
GEE	Generalized Estimating Equations
GOBI	Growth monitoring Oral rehydration Breast feeding Immunization
GPC	General Population Cohort
HDL-C	High Density Lipo Protein Cholesterol
HDSS	Health and Demographic Surveillance System
HR	Hazard ratio
ICCM	Integrated Community Case Management
IMCI	Integrated Management of Childhood Illnesses
ITU	International Telecommunication Union
LDL-C	Low Density Lipoprotein Cholesterol
LMIC	Low–and Middle-Income Countries
MAMA	Mobile Alliance for Maternal Action
MCH	Maternal and Child Heath
MDGs	Millennium Development Goals
mHealth	Mobile health
MNCH	Maternal, New-born and Child Health
MOH	Ministry of Health
MOTECH	Mobile Technology for Community Health
MRC	Medical Research Council
NHP	National Health Policy
OPV	Oral Polio Vaccine
OR	Odds ratio
PEM	Protein Energy Malnutrition
PMTCT	Prevention of Mother to Child Transmission of HIV
PVT	Pentavalent vaccine against Diptheria, Pertussis, Tetanus, Hepatitis B and Haemophilus Influenza
SDGs	Sustainable Development Goals
Smartphone	A cellular phone that performs many functions of a computer
SMS	Short Messaging Service
SSA	Sub-Sahara African

TC	Total Cholesterol
TG	Triglycerides
UBOS	Uganda Bureau of Statistics
UDHS	Uganda Demographic and Health Survey
UN	United Nations
UN IGME	United Nations Inter-agency Group for Child Mortality Estimation
UNCST	Uganda National Council of Science and Technology
UNFPA	United Nations Fund for Population Activities
UNICEF	United Nations Children’s Fund
UVRI	Uganda Virus Research Institute
VHTs	Village Health Teams
WHO	World Health Organization

1 INTRODUCTION

1.1 GLOBAL TRENDS IN CHILD MORTALITY

Child survival has been a focus of global attention for decades, not only as an index of child health and nutritional status but also as an important indicator of overall population health and socio-economic development. Monitoring child mortality overtime enables tracking of progress in child survival and improvements in the welfare of the entire population. The United Nations Children's Fund (UNICEF), the World Bank and the United Nations (UN) pioneered the reporting of global child mortality trends dating back as far as the 1950s (Ahmad et al., 2000). Child mortality declined at the end of the 19th century in high income countries while in low income countries declines only started after the First World War. Between 1950 and 2000, a global decline in under-five mortality of 150 to 40 per 1000 live births was observed with a wide gap between high and low income countries. For example, in 1955–59 under-five mortality in Sweden was 21 per 1000 live births compared to 381 per 1000 in Sierra Leone. In 1995–99 in Sweden, Finland, Luxembourg and Norway child mortality was estimated to be 5 per 1000 live births compared to 334 per 1000 in Niger. In general, African countries showed the least decline in mortality from 264 deaths per 1000 live births in 1955–1959 to 152 per 1000 in 1995–1999 and more than half of the countries achieved a decline of less than 20% in the entire period 1950-2000. Other regions showed a decline of 60% to 72% over the same period (Ahmad et al., 2000).

Child survival continues to be a major concern and a center of focus by the international community. In 2000, world leaders adopted the eight millennium development goals (MDGs), with a fourth goal (MDG-4) of reducing under-five mortality by two thirds between 1990 and 2015 (Ellis and Allen, 2006). In order to accurately monitor progress towards this goal the UN Inter-agency Group for Child Mortality Estimation (UN IGME) was established in 2004 by leading academic scholars and independent experts in demography and biostatistics to report under-five mortality rates annually. The UN IGME includes UNICEF, the World Health Organization (WHO), the World Bank and the United Nations Population Division of the Department of Economic and Social Affairs as full members. The UNI GME pools nationally representative data such as vital registration, population censuses, and household surveys, assesses their quality and fits statistical models to estimate child mortality for each country.

1.2 CHILD MORTALITY BETWEEN 1990 AND 2015

According to the 2015 UN IGME report (UNICEF et al., 2015) , a global decline in under-five mortality of 53% (from 91 to 43 deaths) per 1000 live births was achieved during the period 1990-2015, falling below the MDG target of two-thirds reduction. The progress is uneven across regions, countries and within countries with wide variations observed between urban and rural communities, and poor and wealthy households. As shown in figure 1 only four regions including Northern Africa, Latin America and the Caribbean, Eastern Asia and Western Asia achieved the MDG-4 target. At the country level, 62 countries including 12 low-income countries (Cambodia, Ethiopia, Eritrea, Liberia, Madagascar, Malawi, Mozambique, Nepal, Niger, Rwanda, Uganda and United Republic of Tanzania) met the MDG-4 target. Besides regional variations curtailing the global effort in achieving the fourth MDG goal, a slower decline in neonatal mortality was a major setback; 47% reduction in the neonatal period compared to 58% in the post-neonatal period was reported. Broad interventions not taking into consideration regional and age specific variations in mortality observed will not improve the pace of mortality reduction. There is a need to critically define the specific factors responsible for under-five mortality especially in the regions with the highest burden.

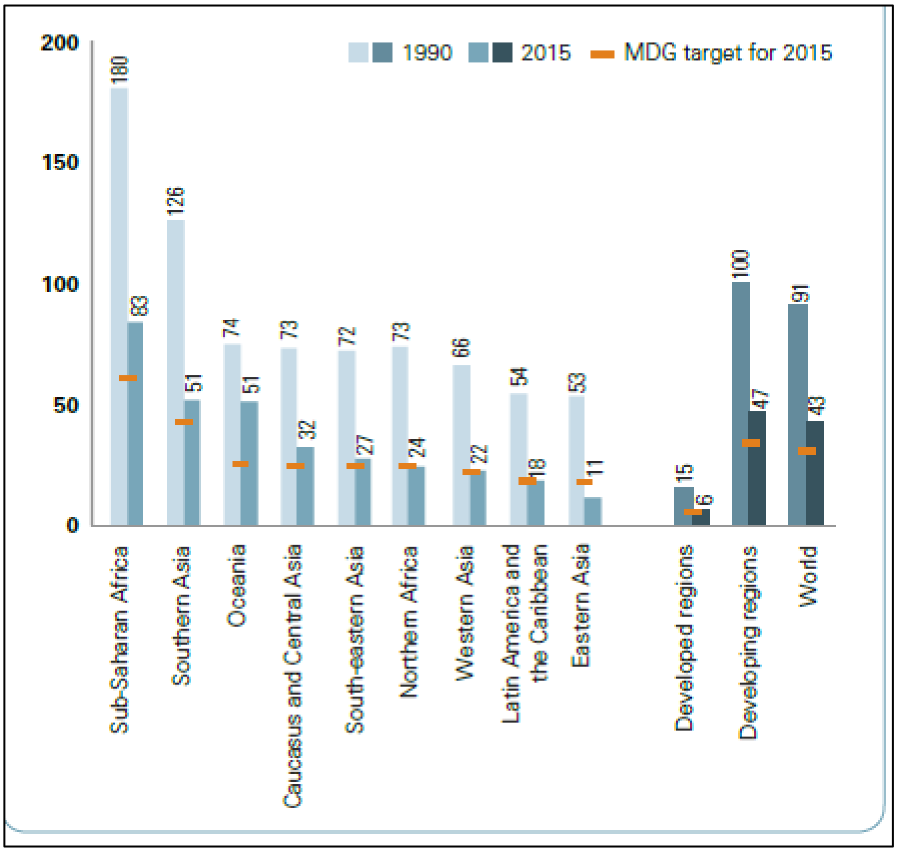


Figure 1: Under-five mortality rate by Millennium Development Goal region, 1990-2015 (deaths per 1000 live births)

Source: UN IGME report 2015 (UNICEF et al., 2015)

1.3 CHILD MORTALITY BURDEN IN LOW INCOME COUNTRIES

Although several strides have been taken in improving child survival globally, reaching the desired levels of child survival especially in low income countries has been a formidable challenge. Of all children dying globally every year before their fifth birth day, over 90% are from 42 poorest nations in Africa and south East Asia (Ellis and Allen, 2006, Bhutta, 2004, Black et al., 2003). Mortality in the Sub-Sahara African (SSA) region is 12 times more than the average for high income countries and SSA is home to seven countries with under-five mortality more than 100 per 1000 live births (Alkema et al., 2016). With SSA having the fastest population growth, it is estimated that 40% of live births will occur in this region by 2050 and 37% of all children under-five will live in the region (UNICEF et al., 2013b). This means majority of child deaths will occur in Africa if no sufficient declines in mortality are achieved.

1.4 THE NEW TARGETS OF CHILD SURVIVAL IN THE SUSTAINABLE DEVELOPMENT GOALS

The international community further demonstrated a renewed global commitment to improving child survival through an agreement on a new framework – the Sustainable Development Goals (SDGs). The third goal of the SDG is a health goal: "Ensure healthy lives and promote well-being for all at all ages (UNDP, 2016)". In the child health sub-goal, under SDG-3, all countries are targeting to reduce neonatal mortality to at least 12 deaths per 1,000 live births and under-five mortality to at least 25 deaths per 1,000 live births by 2030. Going by these targets, 79 countries currently with under-five mortality rate above 25 will need to accelerate their efforts to achieve the desired target. If the current pace of mortality reduction continues, it is projected that 47 countries (34 from SSA) will not meet the SDG target by 2030 (UNICEF et al., 2015). If all countries achieved the SDG targets, it is estimated that 38 million lives of children under the age of 5 years would be saved between 2016 and 2030 (Alkema et al., 2016).

1.5 CHALLENGES OF ESTIMATING CHILD MORTALITY IN LOW INCOME COUNTRIES

In order to accurately measure under-five mortality at population level, reliable sources of data are needed. Child mortality can be estimated using direct or indirect methods depending on availability of data. For a direct estimate, complete and accurate vital registration of births and deaths is required and is the most reliable way to estimate mortality. Unfortunately, low income countries where child mortality is highest, lack comprehensive vital registration systems to accurately estimate under-five mortality. Globally, two thirds of deaths and half of the children are not registered (WHO, 2013). Mortality in these settings is estimated using indirect methods based on suboptimal data from censuses, surveys and a heavy reliance on statistical modeling.

Indirect methods of estimating child mortality

In the absence of complete and accurate vital registration systems, most countries typically in Africa, Asia and Latin America rely heavily on indirect estimates of child mortality levels and trends based on information collected on children ever-born and the proportion surviving by age of mother obtained from population censuses and household surveys (Brass, 1964). Brass devised methods of using data from censuses and surveys to compute the proportion of children dead classified into their mother's 5 year age-groups and used life tables to convert proportions of deaths into probabilities of dying between child birth and different ages of children (Brass, 1975). Census and survey data are limited by variations in quality over time or between countries hindering accurate trend estimates and comparability across countries. The commonest errors include omissions of births and deaths, misreporting of ages at death, and misreporting of maternal ages leading to underestimation of mortality and distortion of time trends. Mathematical models have been developed by international agencies and academic institutions to fill gaps in non-comparable statistics derived from several data sources. However models are dependent on several assumptions that could bias findings. These data give many countries the false impression that empirical data are available thus reducing pressures on governments to improve their own data. Another challenge with modeled estimates is that countries may not fully own the data. Additional challenges include the high cost of surveys and non-representative data at national level.

Mortality estimates based on indirect methods lag behind by 5-10 years because they rely on retrospective data therefore do not provide current trends to inform policy and program implementation. Prospective data gathered through vital registration and regular population censuses are more reliable. A synthetic life-table approach to the analysis of such data has the advantage of capturing the real and current experience of populations to inform policy. A synthetic cohort is a hypothetical cohort of people who would be subject at each age to the age-specific rates of one specific period. Unlike real cohorts that examine mortality experience of individuals born at the same time through their lifetime, the synthetic cohort method describes age specific mortality at a specific time and permits assessment of most current data.

Vital registration systems

Registration of births and deaths generates information crucial for health intelligence and other social benefits such as provision of entitlements and access to services and also offers legal identity to individuals and families. Sweden and England were the first countries to implement vital registration on routine basis since the 18th Century. This reportedly contributed greatly to improvement of their health and socioeconomic development (Szreter, 2007). A recent systematic review published in the Lancet, showed that a well-functioning vital registration system is directly associated with a reduction in maternal and under- five mortality, and an improvement in life expectancy (Phillips et al., 2015). Despite this evidence and inclusion of birth registration as one of the universal rights, population coverage with functional vital registration systems is still very slow (Setel et al., 2007, Mahapatra et al., 2007b).

Table1 shows the distribution of the global population according to completeness of registration between 1965 and 2004. Globally both birth and death registration coverage stagnated at approximately 30% with no substantial improvements and in some cases a drop in the coverage in a period of 40 years. Europe has had the highest coverage of vital registration followed by Americas. Africa and South East Asia had the least coverage, hardly reaching 7%. In Africa death registration coverage only improved marginally from 2% to 7% while birth registration coverage reduced from 7% to 5%.

Table 1: Percentage of population living in countries with complete (at least 90% of events registered) civil registration systems, by WHO region

	Deaths				Births			
	1965-74	**1975–84**	**1985–94**	**1995–2004**	**1965–74**	**1975–84**	**1985–94**	**1995–2004**
Total	27%	25%	28%	26%	33%	31%	28%	30%
Africa	2%	4%	2%	7%	7%	7%	9%	5%
Americas	69%	66%	64%	61%	58%	55%	53%	53%
Eastern Mediterranean	17%	21%	15%	1%	21%	25%	17%	42%
Europe	62%	61%	92%	86%	95%	94%	93%	92%
South-East Asia	1%	1%	1%	1%	1%	1%	1%	1%
Western Pacific	12%	11%	10%	13%	12%	14%	13%	18%

Figures for 1965—94 adapted from the Demographic Yearbook (historical supplement 1948–1997), UN Statistics Division, New York, 2000. Figures for 1995–2004 are based on the Demographic Yearbook 2004

In 2007, a *Lancet* Series echoed that weak vital statistics miss the poorest and most vulnerable people in society (Hill et al., 2007, Mahapatra et al., 2007b, Mahapatra et al., 2007a, Lopez et al., 2007). This poses a significant challenge in planning services for vulnerable populations. Subsequent assessments have shown a marginal increase in the coverage of vital registration (Mikkelsen et al., 2015). Most improvements in vital registration were driven by external resources and therefore collapsed soon as the resources ended. Over the last five decades, both the WHO and the UN invested in developing national capacities for health statistics, firstly with the UN Fund for Population Activities (UNFPA) particularly supporting vital registration in about 20 developing countries in the 1970s-80s (Padmanatoha and York, 1993). In 1991, the UN adopted the International Program for Accelerating the Improvement of Vital Statistics and Civil Registration Systems to support countries in the achievement of complete vital registration but not much was achieved with this effort. UNICEF has been actively promoting birth registration as a human right as well and has supported several national initiatives (UNICEF., 2009).

There is a mismatch between investments for disease control programs and investments for strengthening vital registration as source of data for measuring development progress by both national governments and development partners. However, through advocacy, a number of countries are starting to recognize the value of vital registration and have set an ambitious goal of achieving universal vital registration by 2024. The latest addition to the improvement of vital registration in low income countries is the introduction of mobile phone technology through use of short messaging service (SMS) for notification of vital events from communities to health or civil registration authorities (Toivanen et al., 2011, AbouZahr et al., 2015). This is a new initiative and remains to be evaluated.

Under-reporting of stillbirths and early neonatal deaths

Historically, stillbirths and early neonatal deaths were classified as perinatal deaths but perinatal epidemiologists are now discouraging this combination for two major reasons. First, the evolving definition of fetal deaths according to age of gestation resulting from advances in neonatal care in industrialized countries led to several definitions of stillbirth making comparison between countries difficult (Lawn et al., 2001). Secondly, under-reporting of stillbirths is more problematic than for neonatal deaths, so combining them would mask data weaknesses for stillbirths. For international comparison, WHO defines a stillbirth as death occurring at gestation age of at least 28 weeks or at least 1000 g birth weight (WHO, 1996, WHO, 1992).

The first global estimate of stillbirth rate was reported in 2005 and gave a total of 3.3 million stillbirths (WHO, 2005). Stillbirths continue to be under reported especially in middle and low income countries because almost half of births occur outside the formal healthcare system. Globally, only 2% of stillbirths are reported during vital registration but this is not a problem in countries that have high rate of institutional deliveries. Less than 5% of births globally happen in settings where there is complete vital registration or representative health facility data (Lawn et al., 2010). Up to 98% of stillbirths occur in settings where there is no or incomplete data registration and no reliable health facility data. Reporting of stillbirths in such settings is reliant on retrospective household surveys. Household surveys rely on pregnancy histories that only estimate about 50-85% of recognized pregnancy losses in prospective studies (Casterline, 1989).

Globally, out of an estimated 210 million pregnancies, 75 million end in abortions or stillbirths (UNICEF, 2009). Prior to 2005, no organization had published global, regional or country-specific stillbirth rates. In the last decade, there has been a notable increase in attention to stillbirths because of the emerging evidence of a high correlation between maternal mortality, neonatal mortality and stillbirths (McClure et al., 2007). Lawn and colleagues noted that 28 countries reporting the highest stillbirth rates contributed the highest maternal mortality rate worldwide (Menon-Johansson et al., 2006). In 2009, of 2.6 million stillbirths reported globally, more than three quarters were reported from Africa and South East Asia (Kim and Kim, 2008).

The problem of low uptake of facility births and poor vital registration in middle and low income countries also affects reporting of early neonatal deaths because babies born at home who soon die after birth are also less likely to be registered than babies who die several days later (Chen et al., 1998). A study in Vietnam found that only one quarter of neonatal deaths were reported in the official statistics (Målqvist et al., 2008). New-born deaths could be under-reported because they are misclassified as stillbirths due to lack of knowledge, lack of careful assessment for signs of life, or lack of audit review of birth attendants.

Under-reporting of neonatal deaths and stillbirths gives a false picture of the magnitude of the problem, thus an obstacle to prioritizing neonatal health. In the effort to improve child survival, there is need to continually explore ways of improving community level registration of stillbirths and neonatal deaths in low income countries where about 50% of births occur outside the formal healthcare system. Registration and tracking of pregnancies to an outcome (abortion, stillbirth or live birth) is one such avenue that has the potential to provide more accurate population denominators in improving neonatal deaths and stillbirth registration. The existence of CHWs and emerging mobile phone technologies offer immense opportunities to improve completeness and accuracy of registration.

1.6 POPULATION LEVEL DETERMINANTS OF CHILD SURVIVAL

Child survival in low income countries is determined by interplay of social and biological factors (Mosley and Chen, 1984). Henry Mosley and Lincoln Chen summarized these factors in a conceptual framework with two major levels; distal and proximate factors depending on their proximity to the outcome of mortality or growth faltering. Figure 2 shows a hierarchical relationship between the distal and proximate factors for child survival derived from the Mosley-Chen model.

Distal determinants

The distal factors are further off the causal chain and affect child health outcome indirectly through the proximate variables. Examples of distal factors include social, economic, cultural, and health system variables jointly referred to as socio-economic factors.

Socioeconomic factors: Socioeconomic factors are grouped into three broad categories; i) individual factors under which parental education and occupation, cultural factors including tradition, beliefs, norms and practices that affect health seeking behavior are classified, ii) household level variables mainly referring to income and wealth of households and iii) community level factors including ecological setting such as geography and climate, political economy and health system factors (Arah et al., 2005, Mutangadura, 2004). Low socioeconomic status is associated with child mortality (Bradley and Corwyn, 2002) but it is difficult to measure income in low income countries where people do not earn a regular income. Proxy indicators such as ownership of household items, type of house owned, living conditions, parental occupation and education status are often used for estimating socioeconomic status. Poverty impacts on child health through lack of access to material and non-material resources which affect living conditions and access to health and food (Bradley and Corwyn, 2002). Ethnicity was found to be associated with child mortality in SAA (Brockerhoff and Hewett, 1998, Brockerhoff and Hewett, 2000). This may be a proxy to cultural practices or economic advantage.

Proximate determinants

Proximate variables are influenced by distal factors and these include; i) maternal factors such as mother’s age, parity and birth spacing ii) environmental contamination including crowding, pollution, food, water, sanitation, insect vectors iii) nutrient deficiency particularly focusing on maternal and child malnutrition, iv) injury-accidental and intentional and v) personal illness control encompassing preventive and curative measures.

Environmental factors: Environmental factors such as overcrowding, air pollution, lack of access to clean water and sanitation directly increase the risk of respiratory and diarrheal diseases which are known to be major causes of child mortality (Smith and Mehta, 2003, Curtis et al., 2000). Exposure to environmental risk factors is determined by socio-economic status.

Nutrient deficiency: Access to adequate food and food choices are determined by socio-economic status of the child’s parents and cultural practices regarding child nutrition. Child malnutrition therefore tends to be among parents with poorer socio-economic status

(Wagstaff, 2002). Malnutrition contributes approximately one third to half of under-five mortality and exclusive breastfeeding for at least 6 months is protective against child hood infections and malnutrition (Black et al., 2003, Fishman et al., 2004, Kramer et al., 2001). The survival of children may also be affected by the mother's nutritional status right before and during pregnancy (Duggan and Fawzi, 2001, Ashworth and Antipatis, 2001).

Injuries: Injuries such as accidental falls and burns/scalds tend to be more common among children from low socioeconomic background. For example there is a higher risk of burns in developing countries among children from low socio-economic background and whose mothers are less educated (Delgado et al., 2002). Injuries directly result in higher mortality especially among infants.

Personal illness control: Use of health services such as vaccinations, seeking professional health at delivery and prompt treatment of diseases affect child mortality risk (Mosley and Chen, 1984, Abdulla et al., 2001). Socioeconomic gradient affects each of these preventive approaches with profound effects on children (Koenig et al., 2012, UNICEF, 2001). A study in Brazil showed that poor health seeking habits contribute up to 70% child deaths (de Souza et al., 2000). The healthcare seeking decisions are also determined by socio-economic status (Gwatkin et al., 2007).

Maternal factors: Maternal factors such as age of mother at childbirth, birth interval and parity and maternal diseases such as HIV have been found to be associated with child survival in rural African communities in Congo (Van Den Broeck et al., 1996). These factors are in turn determined by socioeconomic status. Child survival especially in the neonatal period is inextricably linked to maternal health. Poor maternal health and maternal deaths significantly impact the ability of newly born babies to survive and thrive to childhood. Neonatal deaths are concentrated in the same countries where maternal mortality is highest, facility utilization lowest, and the quality of available care poorest. For example, countries in SSA contribute 56% of all maternal mortality in the world `and also have the highest neonatal mortality rate of 32 per 1000 live births (You et al., 2010). Maternal and child health interventions are therefore closely linked. Increasing attention to maternal health during pregnancy, labor, delivery and in the immediate postpartum period has been shown to improve fetal, new-born and child health outcomes (Lawn et al., 2005).

1.7 CONSEQUENCES OF CHILD SURVIVAL WITH PROTEIN ENERGY MALNUTRITION (PEM)

Global prevalence of protein energy malnutrition among children who survive to the age of 5 years

An estimated total of 159 million children were stunted globally in 2014, a decline to 23.8% from 39.6% in 1990. However the decline in malnutrition has been unequal in the various regions with Africa only achieving a stunting reduction from 42.3% to 32%. Whereas the number of stunted children reduced in other regions, the number of stunted children rose from 47 million in 1990 to 58 million in 1990 with Eastern Africa, Middle Africa and Western Africa having rising numbers of stunted children (De Onis et al., 2012). In the entire Africa region, Eastern Africa has the highest stunting with approximately 40% of children less than five years stunted. The number of stunted children in this region is projected to rise to 25 million by 2025 (Onis et al., 2013). In 2012, the World Health Organization adopted a resolution to reduce by 40% the number of stunted under-five children by 2025. Many low income countries may not achieve this goal. Because of the rising numbers of stunted children in Africa, no substantial reduction is anticipated to happen. Although less common than stunting, wasting was experienced by 50 million children globally in 2014 and no sub-region in Africa falls within the acceptable level of wasting (less than 5%). Wasting results from an acute shortage of food and can lead to immediate death of a child. However, there is scanty information on the long term consequences of wasting among survivors.

Long term consequences of surviving with PEM

As shown in the modified Mosley-Chen model (figure 2) children may survive with growth faltering or protein energy malnutrition (PEM). Severe and acute forms of PEM contribute up to one third of under-five mortality. However, in its moderate to mild forms PEM may not directly lead to mortality but may predispose to long term health consequences later in life. Available evidence from industrialized countries shows that even in its mild or moderate forms PEM could lead to an increased risk of cardiovascular disease (Cohen, 2004, Martin et al., 2003, Osmond and Barker, 2000, Schroeder et al., 1996, Sesso et al., 2004, Victora et al., 2008a, Portrait et al., 2011) and poor educational achievement in later life (Victora et al., 2008b). Most of these observations regarding the long term effects of malnutrition on adult health were made in industrialized countries where growth faltering was followed soon by a catch-up growth and could also be confounded by socio-economic differences. In low and middle income countries where children are likely to continue in a malnourished state for their entire life, it is not known if the pattern of cardiovascular disease risk development would be similar to that in western countries. Emerging evidence through a systematic review of studies focusing on middle income countries mainly from Asia and South America has shown that growth failure in early childhood is associated with increased prevalence of risk factors for cardiovascular disease including high blood pressure, impaired glucose control and body composition manifesting in late adolescence (Stein et al., 2005). In 2008, a Lancet series on malnutrition, through a meta-analysis of studies from low and middle income countries including South Africa also showed a positive correlation between PEM and blood glucose, blood pressure and lipids levels and an inverse relationship with achieved schooling (Victora et al., 2008b) but the evidence was more appealing in the middle income countries in which epidemiological transition could account for the rise in cardiovascular disease risk factors. Studies on adolescent consequences of PEM in low-income countries are scarce and are of particular interest because about half of adolescents experience malnutrition during childhood. Low income countries will particularly provide evidence on a group of children that remain malnourished up to adolescence to compare with those who recover from malnutrition. In 2010, Schulz stressed that abrupt and large change in nutritional conditions after exposure to a prolonged period of nutritional stress is more important in cardiovascular disease risk development than just nutritional deprivation at any particular age (Schulz, 2010). The Leningrad Siege study found no difference in glucose tolerance, blood pressure and lipid concentration in adulthood between the subjects exposed and unexposed to starvation in utero or during infancy which is a sharp contrast to the Dutch Hunger study which, with a similar design (Stanner and Yudkin, 2001) found a strong link between early exposure to starvation and adult cardiovascular risk (Schulz, 2010). The major difference in the findings of the two studies were attributed to a return to a complete diet which occurred quite quickly after the time of severe starvation in the Dutch hunger study, but not in the Leningrad Siege study where starvation was prolonged. These findings are not conclusive because there are major variations in the secular trends in the two study areas. For more reliable conclusions there is need to undertake studies that compare populations in the same environment. Owing to the rising prevalence of cardiovascular disease risk factors in low income countries and increased school enrolment, it is important to assess the effects of early childhood exposure to PEM on both cardiovascular health and school achievement.

1.8 STRATEGIES FOR IMPROVING CHILD SURVIVAL

Several milestones have been achieved in implementing strategies to improve child survival globally. The strategies include primary health care (1978), the child survival and development revolution (1980), integrated management of childhood illnesses (1996), and integrated community case management of childhood illnesses (2004).

Primary health care

In 1978, the Alma-Ata Declaration led to the adoption of primary health care, the ultimate aim of which was health for all. Increase in child immunization coverage and increase in access to safe water and sanitation were some of the aspects of primary health care that contributed to reduction of under-five mortality. However, financial barriers, health worker shortages and the HIV pandemic limited the full realization of equitable access to health care (WHO, 2008).

Child survival and development revolution

Infant and child mortality were identified as indices for measuring development of countries in the 1980s. Interventions such as **g**rowth monitoring to track child nutritional status, **o**ral rehydration for diarrheal diseases, **b**reast feeding as the perfect nutrition start in life and **i**mmunization jointly referred to as GOBI were promoted. Approximately 12 million deaths of children under five years were averted as a result of these interventions using simple technologies in the 1990s (UNICEF, 1996). The major weakness in this strategy was the implementation of the elements as vertical programs with immunization taking the largest proportion of the budget.

Integrated management of childhood illnesses

In 1996, integrated management of childhood illnesses (IMCI) was introduced to prevent diseases and health problems during childhood, to detect and treat illnesses and promote healthy habits within the family and community. It involved training of health workers on prevention and management of childhood illnesses, strengthening the health system, and improving family and community practices. IMCI was meant to achieve a reduction in infant mortality and serious childhood illnesses, improve child growth and development (Benguigui, 2001). Although IMCI led to improvement of health worker performance and a better quality of care and rational drug use at an affordable cost, it did not achieve the expected outcome of child mortality reduction largely due to poor health seeking behavior of the caretakers (Nguyen et al., 2013, Gouws et al., 2004, Mason et al., 2009, Chopra et al., 2012).

Integrated community case management of common childhood illnesses

Following on the poor treatment seeking behavior observed in IMCI, a community case management (CCM) was introduced to bridge the gap between communities and health facilities. This did not only target treatment of children in the communities but promotion of timely health seeking as well. CCM targeted leading causes of child deaths including malaria, diarrhea, pneumonia, malnutrition and neonatal conditions (de Sousa et al 2011). The key drivers of this strategy are the community health workers with a role of linking communities and health facilities. Since children suffer from multiple diseases simultaneously, integrated community case management of childhood illnesses (ICCM) was recommended to replace CCM (WHO and UNICEF, 2004). In ICCM community health workers are trained to assess children for malaria, pneumonia and diarrhea and treat appropriately. The major limitations of this approach have been the ability of community health workers to manage several diseases and frequent drug stock-outs (Achan et al., 2011, Kangwana et al., 2009, Blanas et al., 2013).

1.9 INTEGRATION OF MATERNAL AND CHILD HEALTH INTERVENTIONS

A number of evidence based integrated maternal and child health interventions exist but the main challenge is the low coverage in most middle and low income countries (Bhutta et al., 2013). The greatest need is to devise mechanisms to make sure these interventions are accessible to mothers and babies in rural communities. Some studies have shown the benefit of community based delivery platforms such as reducing maternal morbidity, stillbirths and neonatal mortality through changes in household behavior and practices leading to improved uptake of antenatal care, facility-based births, early initiation of breastfeeding and improved immunization (Lassi et al., 2014, Lewin et al., 2010). A longitudinal study conducted in rural south-western Uganda between 1993 and 2007 among children under 13 years showed that child survival improved with facility-based births, completion of vaccinations and exclusive breastfeeding for 6 months (Zhang et al., 2013). Despite this evidence services are inaccessible and unevenly distributed. For example, 40 million mothers worldwide give birth at home every year and more than half of the mothers in low income countries deliver alone without professional help, often resulting in complications including maternal death, stillbirths and early neonatal deaths. Child immunization coverage ranges between 12% and 78% (median 48%) in African countries (Webster et al., 2005). In a review of coverage of services in 42 countries that contributed 90% of child deaths in 2000, breastfeeding of infants aged 6–11 months was the only intervention that reached nearly all children. Measles vaccination reached two-thirds of children under five years and the coverage of all other interventions could hardly reach 60%, yet the full implementation of these interventions could avert 63% of under-five deaths (Bryce et al., 2003). Coverage is lowest in the poorest countries and among the poorest populations (Gwatkin, 2001). In order to achieve the desired reduction in child mortality, innovative community-based initiatives for delivery of these interventions are needed to extend the services to rural communities in most need. Systematically collecting age-specific survival data for the children, preferably based on the registration of pregnancies, is an important evaluative effort in this context, with at least two purposes. One is the guidance in terms of health policy and interventions that can be obtained from such data, when they are interpreted against the background of local clinical pediatric experience. Another purpose is the creation of awareness among parents and child health experts not only as a family concern but also a community problem amenable to concerted action. To serve these double purposes, however, the observed survival data need to be collected and processed so as to reflect the present situation rather than historical experiences. Therefore, prospective data collection and processing methods are preferred to indirect techniques based on “complete obstetric histories”.

1.10 COMMUNITY HEALTH WORKERS IN MATERNAL AND CHILD HEALTH INTERVENTIONS

There is a renewed interest globally in the role of community health workers (CHWs) in delivering maternal and child health services (Haines et al., 2007, Janowitz et al., 2012, Singh and Sachs, 2013). The term community health worker (CHW) is loosely used to refer to several groups of people promoting health services at community level. They are sometimes called lay workers, community drug distributors (CDD), village malaria workers, community medicine distributors (CMD) and village health teams (VHTs). By definition, CHWs are lay people from the communities in which they live and work, selected by, and answerable to those communities, supported by the health system, and with shorter training than professional health workers (Love et al., 1997). Because of their close contact with the people, they bridge between the communities and the formal health structure. The concept of CHWs has been active for close to 60 years but the quest to meet the MDG targets prompted new discussions on how best they could be effectively engaged to deliver services to rural communities. Many countries including Ethiopia, Brazil, India and Pakistan have registered success in scaling up CHWs activities and integrating them as part of the formal healthcare system (Liu et al., 2011). Evidence is mounting on the role of community health workers in child health promotion in rural communities as a way to improve child survival (Perry and Zulliger, 2012, Haines et al., 2007). More work is needed in understanding their role and the motivations to promote maternal and child health.

1.11 ENHANCING COMMUNITY HEALTH WORKER ROLE WITH MOBILE PHONES

Mobile phones hold great promise in aiding community health interventions. By the end of 2013, there were approximately 6.8 billion mobile subscriptions worldwide with 89% of them in developing countries (ITU, 2013). The rapid proliferation of mobile phone use even in remote, rural places where public health systems are struggling to gain ground could offer opportunities for using mobile phones to support health and health care commonly referred to as “mHealth”. However, using phones to relay health text messages to rural communities is limited by inability to read text messages because of low literacy levels, lack of phone ownership or limited access to phones by a vast majority of rural communities. Relaying phone text messages through village health workers offers a platform to strengthen the delivery of services to the rural poor who do not own phones or illiterate individuals who may not read text messages. Text message alerts to community health workers in Rwanda (Ngabo et al., 2012), postnatal visit reminders in Ethiopia (Tesfaye et al., 2014), mobile technology for community health in Ghana (MOTECH, 2011) and Rapid SMS-MCH in Uganda (UNICEF, 2014) are some of the projects that have successfully engaged community healthworkers through text messages. However all these are exploratory pilot projects not adequately designed to evaluate effectiveness. A randomized trial in Zanzibar recruited pregnant mothers from antenatal clinics of 24 health centers (clusters), and showed an increase of facility births from 47% to 60% (Lund et al., 2012b) but in their study, SMS was sent directly to mothers who owned phones and were attending antenatal clinics leaving out rural women who could have had worse pregnancy outcomes. A recent systematic review and meta-analysis on the effectiveness of mHealth interventions for maternal, newborn and child health (MNCH) in low– and middle–income countries (LMICs) revealed that most studies on mHealth for MNCH in LMIC are of poor methodological quality (Lee et al., 2016). More evidence is needed in this field before such interventions can be scaled up.

1.12 UGANDA COUNTRY PROFILE

Uganda is located in East Africa bordered by Kenya in the East, Democratic Republic of Congo in west, and South-Sudan in the north and Tanzania in the south. According to the 2014 census (UBOS, 2015), Uganda has a population of 34.6 million people in an area of 241,038 square kilometers with population density of 173 persons per square kilometer and a population growth of 3.03%. Life expectancy at birth is 63.3 (male= 62.2, female= 64.2). A vast majority of the population is rural with only 18% living in urban areas and agriculture is the main economic activity. As of 2015, the gross national income per capita for Uganda was estimated to be 670 US dollars by Atlas method and 1780 international dollars by purchasing power parity method, with a global ranking of 199 and 194 globally respectively (World Bank, 2016). It is estimated that 19.7 % of Ugandans are poor, and rural populations contribute 89.3% of national poverty. Literacy among females is lower (68%) compared to males (77%) and is higher in urban than in rural areas. Children under five years constitute about 17% of the population (UBOS, 2015).

Nutritional status of children under five years of age in Uganda

Protein energy malnutrition contributes directly and indirectly to 60% of child mortality in Uganda (MOH, 2009a). Uganda’s stunting prevalence for children under -five years of age was estimated to be 38% and wasting 6% (FANTA2, 2010). According WHO classification, Uganda falls within the bracket of countries categorized with a high prevalence of stunting and medium prevalence of wasting (WHO, 2016). The nutritional status of children is worse in the rural areas where more than 40% of children are stunted.

Child mortality in Uganda

Although Uganda is one of the few African countries that met the MDG-4 goal with a under-five mortality reduction from 187 to 55 deaths per 1000 live births between 1990 and 2015 (Alkema et al., 2016), rural communities may still be experiencing a higher mortality. According to the 2011 Uganda Demographic and Health Survey (UDHS) report (UBOS, 2012), there was a wide gap between under-five mortality in urban and rural communities (77 versus 111 per 1000 live births). The same report showed under-five mortality of 72 versus 123 per 1000 live births among wealthy and poorest households respectively. Mortality data from rural communities is scarce and may be masked by the generalized national estimates. It is therefore critical to accurately estimate under-five mortality in rural areas and understand contextual factors driving mortality in order to identify the most appropriate strategies for improving child survival.

The health system and service delivery

Uganda runs a decentralized healthcare system that is coordinated centrally by the ministry of health but service provision is decentralized to districts and health sub-districts. The ministry of health is responsible for policy formulation, setting standards and quality assurance. The healthcare services are provided by both public and private health facilities in equal proportions. As shown in table 2, the healthcare system is graded into seven levels in order of functional hierarchy (MOH, 2010b). The health center I comprise 5-7 lay community health workers per village commonly referred to as village health teams (VHTs). Their role is to mobilize communities for immunization, sanitation, control of diseases, making home visits to assess newborn babies, distributing drugs for chemoprophylaxis and treatment of childhood illnesses and promotion of health seeking behavior. They may also have a role of birth and death registration at community level. Health center II is managed by a nurse, or midwife or nurse assistants and they provide outpatient services such as treatment of common illnesses, immunizations, community outreach programs and referrals. Meanwhile health center III provide maternity services in addition to outpatient, laboratory services and minimal inpatient services managed by clinical officers (physician assistants), nurses and midwives. Health center IVs are mini-hospitals headed by medical officers serving as referral center for health sub-districts. They manage emergencies such as caesarean sections and offer both outpatient and inpatient services, and provides support supervision to health centers in the health sub-district. Hospitals offer a range of services and serve as referral sites that become more specialized from regional to national level. The functionality of most of these health facilities is limited by low financing to the health sector. The per capita expenditure on health was estimated to be US$ 52 in 2014 which one of the lowest in the sub Saharan region (World Bank, 2014). This coupled with low coverage of staffing estimated at 60% of the targeted number and frequent drug stock outs, makes delivery of the minimum health care package a challenge (Zikusooka et al., 2009).

Table 2: The structure of the Ugandan health system

Health facility level	Function	Location	Estimated population served
Health Centre 1 (VHT)	No physical structure but village health teams facilitate health promotion, community participation and utilization of services	Village	500
Health Centre II	Outpatient services, community health outreaches offered and linkage with village health teams	Parish	5,000
Health Centre III	Outpatient services, maternity and general ward for inpatient services. Laboratory services included	Sub-county	25,000
Health Centre IV	Outpatient, maternity, general ward, laboratory services, theatre and blood transfusion services	County	100,000
District Hospital	All services and radiology services	District	100,000-1,000,000
Regional Hospital	Specialized care, research and teaching	Region	5,000,000
National Referral Hospital	Comprehensive specialized care, research and teaching	National	35,000,000

Source: Health Sector Strategic and Investment Plan 2010/11-2014/2015 (MOH, 2010a).

National health policies supporting maternal and child health

Uganda's national health policy II (NHP II) covers the period 2010-2020 and was developed with a focus on health promotion, disease prevention and early diagnosis and treatment of diseases. NHP II is delivered through the Uganda National Minimum Health Care package consisting of the most cost-effective priority health care interventions targeting high burden diseases. Maternal and child health is considered high priority because it contributes 20.4% of total burden of ill health and avoidable death in Uganda. The government of Uganda has the national child survival strategy that was formulated in 2007 as one of the avenues to achieve MDG-4 target (MOH, 2009b). In this strategy, use of trained VHTs was emphasized to support referrals of sick children to health facilities. Uganda also developed a reproductive maternal, neonatal and child health plan to accelerate child survival in line with the global initiative of "A Promise Renewed". In this context, five strategic shifts were proposed to end preventable maternal and child deaths including; i) increasing geographical focus on districts with highest number of under-five deaths, ii) refocusing districts to prioritize services access to highly burdened populations, iii) focusing on high impact solutions, iv) increasing focus on environmental sanitation, education of girls and empowerment of women economically and in decision making, and v) mutual accountability of results at all levels of the health system. This plan recognizes the period surrounding labor and childbirth as critical for achieving the highest impact of interventions and estimates that child and maternal mortality can be reduced by 40% and 26% respectively in four years (2014-2017) if these interventions are implemented (MOH, 2014).

Community health worker role in maternal and child health programs in Uganda

Due to the scarcity of trained professional health workers in Uganda, the Ministry of Health through the district health departments adopted a nationwide strategy of VHTs delivering a government-endorsed package of community-based health services. The CHWs facilitate health promotion, drug distributions for home management of fevers and deworming programs and encourage in utilization of services. However, gaps remain in the community health worker literature, particularly on the evidence of their effectiveness in delivering maternal and child health programs (Perry and Zulliger, 2012). Studies including randomized trials assessing maternal and new-born care packages or child health programs delivered by CHWs are concentrated in south Asia. These studies have shown improved benefits on new-born and child survival through community health worker programming (Baqui et al., 2008, Manandhar et al., 2004, Bhutta et al., 2011, Walt et al., 1989). There are few studies from Africa that have evaluated the role of CHWs in integrated delivery of maternal and child health services. A study conducted in south-western Uganda found that health promotion by CHWs improved child health practices and reduced child morbidity and mortality within a short intervention period of 3 years (Brenner et al., 2011). However, the CHWs in this study chose their own focus for health promotion activities which may have lessened impact on selected reporting indicator. Due to the limited knowledge and short trainings that community health workers receive, they are unable to reach communities with accurate health messages. There is need to empower CHWs with specific messages tailored to improve the impact of their health promotion efforts. New mobile health technologies, are offering opportunities to deliver specific health messages from health workers through CHWs to effectively reach mothers and children. The new technologies will also enable improved data collection from communities and supervision methods which will make the effectiveness of evidence-based community-based protocols delivered by CHWs easier to measure.

1.13 CONCEPTUAL FRAMEWORK FOR THE THESIS

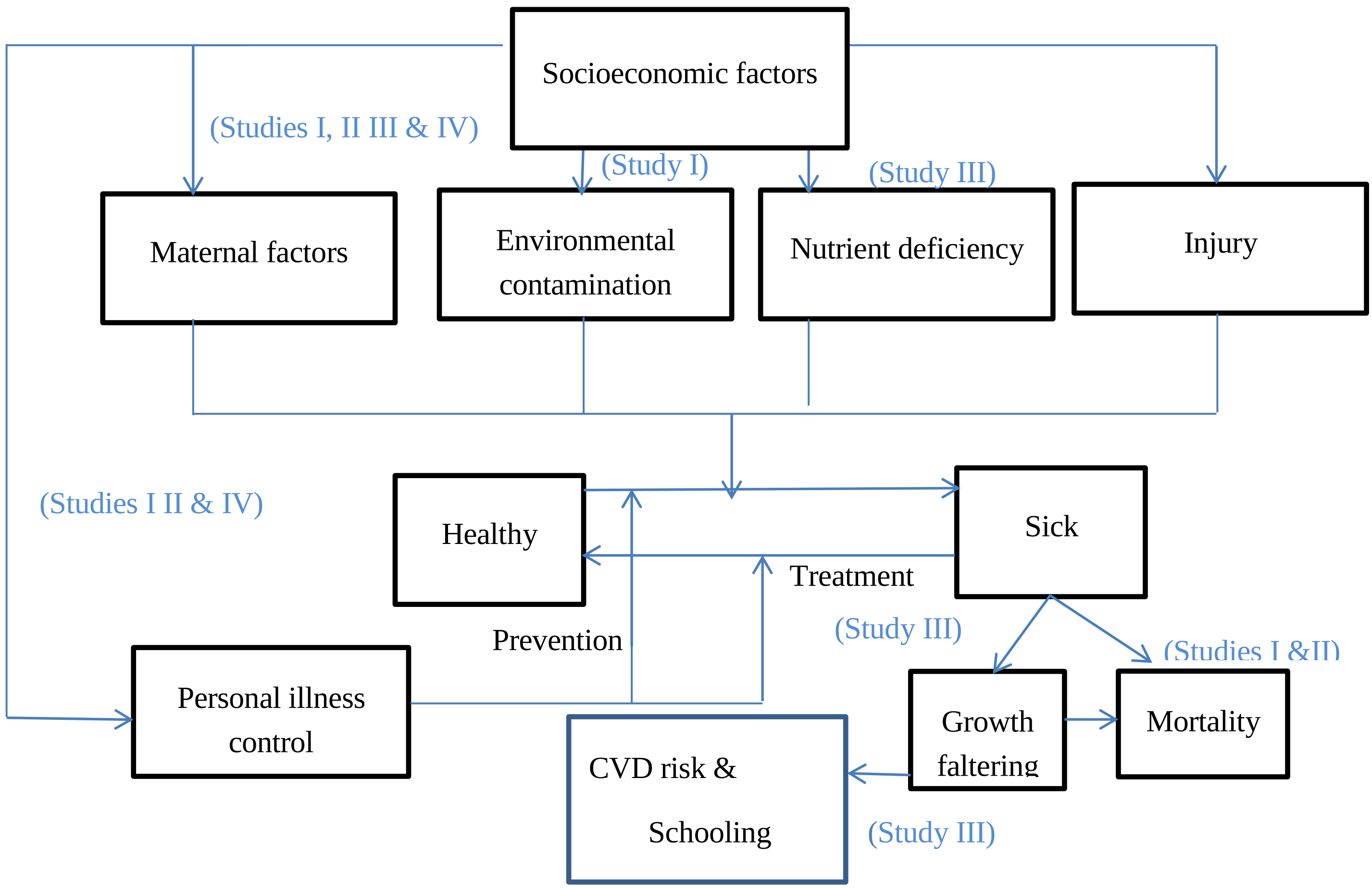


Figure 2: Conceptual framework showing the determinants mortality and effects of PEM on later cardiovascular and school grades.

Source: Adapted from Mosley Chen model (Mosley and Chen, 1984)

This conceptual framework adapted from the Mosley-Chen model considers two levels of factors determining child mortality or growth faltering as the main outcomes of the study. These factors are interrelated. The distal factors exert their influence through the proximate factors. In this thesis, socio-economic status as a distal factor was measured during census. Household heads were interviewed on their household socio-economic conditions by examining the level of education of each member of household, occupation of the parents, the type of construction materials for the wall and roof of their house, both monetary and non-monetary income was estimated through costing of their household expenses and assets. We also collected data on ethnicity and religion as a proxy for beliefs and traditions that could influence child survival. These data were extracted from 11 rounds of census conducted between 2002 and 2012.

In this thesis four proximate variables; maternal, environmental contamination, nutrient deficiency and personal illness control were examined. In studies I, II and III maternal factors were extracted from medical surveys conducted from 1996-2015. This included mother's age, marital status, parity, birth spacing and HIV status measured through a self-report and HIV testing. Crowding was the only environmental factor consistently measured through all census rounds. Crowding index (number of people per room) was computed based on information on the number of rooms available in their dwellings and the number of people living in the household (study I). In very few study rounds data on sanitation was available but not sufficient to be included in the risk factor analysis for mortality. Nutrition deficiency was measured in only four medical survey rounds and could not be applied in the model as a determinant of child mortality but was instead used a determinant of adolescent cardiovascular disease risk and school achievement among children who survive beyond 13 years of age (study III). Personal illness control for both the child and mother were measured by looking at the preventive and treatment measures taken by pregnant women for their own health or for their children's health. Uptake of childhood vaccinations, HIV testing behavior, antenatal and facility births were the main variables examined (studies I, II and IV). In study IV we specifically intervened to improve personal illness control by encouraging pregnant women via SMS to take up facility births. Child injuries were not measured and therefore not included on the model.

1.14 RATIONALE FOR THE STUDIES

Under-five mortality in low-income countries has remained high because of high mortality in rural settings. Unfortunately, where mortality is highest population level data are inadequate or lacking yet such data are needed to focus interventions in order to attain the highest impact of interventions. Most low income countries lack comprehensive vital registration systems making a direct estimation of under-five mortality a challenge. The situation is worse in rural communities where health facility data are unreliable for estimating mortality because of differential use of services. Establishing data collection mechanisms or improving existing weak processes of data collection by community health workers may provide a good base for accurate estimation of under-five mortality and understanding population specific determinants of child mortality. Uganda's reproductive, maternal, neonatal and child health plan to accelerate child survival emphasizes increasing geographical focus to districts with the highest number of deaths and prioritizing services to highly burdened populations. These priorities can only be identified if data are available at every level where interventions are needed.

We have used several data sources collected at household level in a rural community including vital registration by lay community health workers to estimate trends in under-five mortality and associated determinants. A critical appraisal of the data led to devising additional ways of improving data collection including data collected by community health workers using mobile phones.

Studies in high and middle income countries have shown that when children survive through their childhood with protein energy malnutrition, they are prone to developing cardiovascular diseases and having impaired cognitive development leading to low school grades (Stein et al., 2005, Sesso et al., 2004, Victora et al., 2008a, Martin et al., 2003). However there seems to be a sharp contrast in the findings from low income countries regarding cardiovascular disease risk resulting from early childhood PEM. Few studies from low income countries have investigated the association between early childhood nutritional deprivation and cardiovascular disease. It is uncertain if the cardiovascular disease profile observed in high and middle income countries are not as a result of epidemiological transition. It is also unknown if later diet in life or the period of recovery from PEM contributes to cardiovascular disease risk. Historical cohort data in a rural community in Uganda provided us an opportunity to trace children to adolescence and examine cardiovascular disease risk and school achievement in relation to PEM experienced in childhood. The results generated from this study will be crucial for planning future health services for children who survive with PEM.

As part of global initiative of “A Promise Renewed” the reproductive, maternal, neonatal and child health plan to accelerate child survival recognizes the interventions around child birth as key in achieving a substantial reduction in under-five mortality (MOH, 2014). But often, community level data are not available or if available, not used to inform context specific interventions. Using community level data on determinants of child mortality to address the issue is the most practical way to intervene. Data from studies I and II were used to inform the design of an intervention to improve survival of children at birth. Engaging community health workers through focused household visits is shown to improve child survival but this assumes that community health workers who work entirely as volunteers will conduct the home visits. Another assumption with use of community health workers to reach mothers with health messages is that community health workers have the appropriate knowledge to deliver accurate health information. Some studies have shown that community health workers are less confident to deliver health services because of lack of knowledge.

Mobile phones offer a platform to transmit messages from professional health workers through village health workers without losing content. The delivery of such messages to mothers relies heavily on the community health workers trust and compliance with household visits. Although there is increasing interest in engaging community health workers with mobile phones, evidence on the potential benefits of mobile phone use for delivery of maternal and child health services is limited and this makes it difficult to scale up such strategies into broader maternal and child health programs. In a review of 34 articles and reports for maternal health mobile phone interventions, only four had a quantitative design (Tamrat and Kachnowski, 2012). Tomlinson et al. showed lack of high quality and peer reviewed randomized trials for such interventions. Some studies have shown a high acceptability of text message for communicating health messages in resource constrained settings (Curioso and Kurth, 2007, Shet et al., 2010). In Uganda, a high acceptability of text messages for communicating HIV results to rural HIV positive patients was reported, but there were concerns about the difficulty in interpreting messages, technical difficulties and confidentiality (Siedner et al., 2012). Jo and colleagues through mathematical modelling showed that skilled birth attendance and increased facility delivery are the best targets for mobile phones to provide the biggest mortality impact relative to other intervention scenarios (Jo et al., 2014). More robust evidence is needed on the effectiveness of mobile phone health messages delivered to pregnant women by community health workers and improving uptake of facility delivery. It is also essential to evaluate the use of mobile phones for collecting data by community health workers.

2 AIM AND OBJECTIVES

2.1 GENERAL AIM

To assess survival trends and associated factors among children below the age of five years and assess the statistical impact of childhood protein energy malnutrition on adolescent cardiovascular disease risk and school achievement among children who survived in a rural population in south-western, Uganda.

2.2 SPECIFIC OBJECTIVES

1. To estimate under-five mortality trends from 2002-2012 and associated social determinants in a rural population in south-western Uganda

2. To estimate trends of stillbirths and associated factors among women in rural south-western Uganda between 1996 and 2013.

3. To assess the statistical effect of childhood protein energy malnutrition on adolescent cardiovascular disease risk and schooling among children followed from the age of 2-5 years to adolescence (13-19 years) in a rural population with a high prevalence of malnutrition

4. To assess the feasibility of community health workers using mobile phones to register pregnant women in their homes and to deliver gestation age specific health information, and the effect on home births.

3 MATERIALS AND METHODS

3.1 STUDY SETTING

The General Population Cohort (GPC) in rural Uganda

The studies were conducted within a general population cohort (GPC), which is a Health and Demographic Surveillance System (HDSS) in Kyamulibwa sub-county in Kalungu district. Kalungu is located in southwestern Uganda approximately 120 km west of the capital, Kampala. The GPC study was established in 1989 by the UK Medical Research Council (MRC) in collaboration with the Uganda Virus Research Institute (UVRI) initially in 15 neighboring villages (numbered 11-25) and expanded by 10 more villages (numbered 1-10) in 1999/2000 (figure 3). One village outside the study area but within Kyamulibwa sub-county was reserved as a pilot village where all study tools are pre-tested. The population estimated to be 22,000 people is predominantly the native Baganda, forming 75% of the study population. The Baganda are the largest ethnic group in Uganda constituting 17% of the Ugandan population (UBOS, 2015). The other ethnic groups constituting 10% and 15 % of the study population respectively are from the other parts of Uganda and neighboring countries (Rwanda, Burundi, Congo, and Tanzania). Agriculture is the main economic activity characterized by rain-fed small farms for growing mainly bananas, coffee, beans, groundnuts, vegetables and a few root crops such as cassava and potatoes for subsistence; cattle, goats and pigs are also reared. A few of them are engaged in small scale trade mainly selling coffee, food crops and fish. Education levels are generally low with only one third of the population attaining secondary education. Five health facilities serve the population with basic medical care, three of which offer family planning, antenatal care and deliveries. MRC established a clinic in the study area to offer free outpatient services to the population. One health center level IV within the study area and a hospital 20 km away both privately owned by the catholic church offer emergency obstetric services including caesarean sections. Despite the presence of these health facilities, 50% of births occur at home. The details of the cohort are in the data resource profile (Asiki et al., 2013).

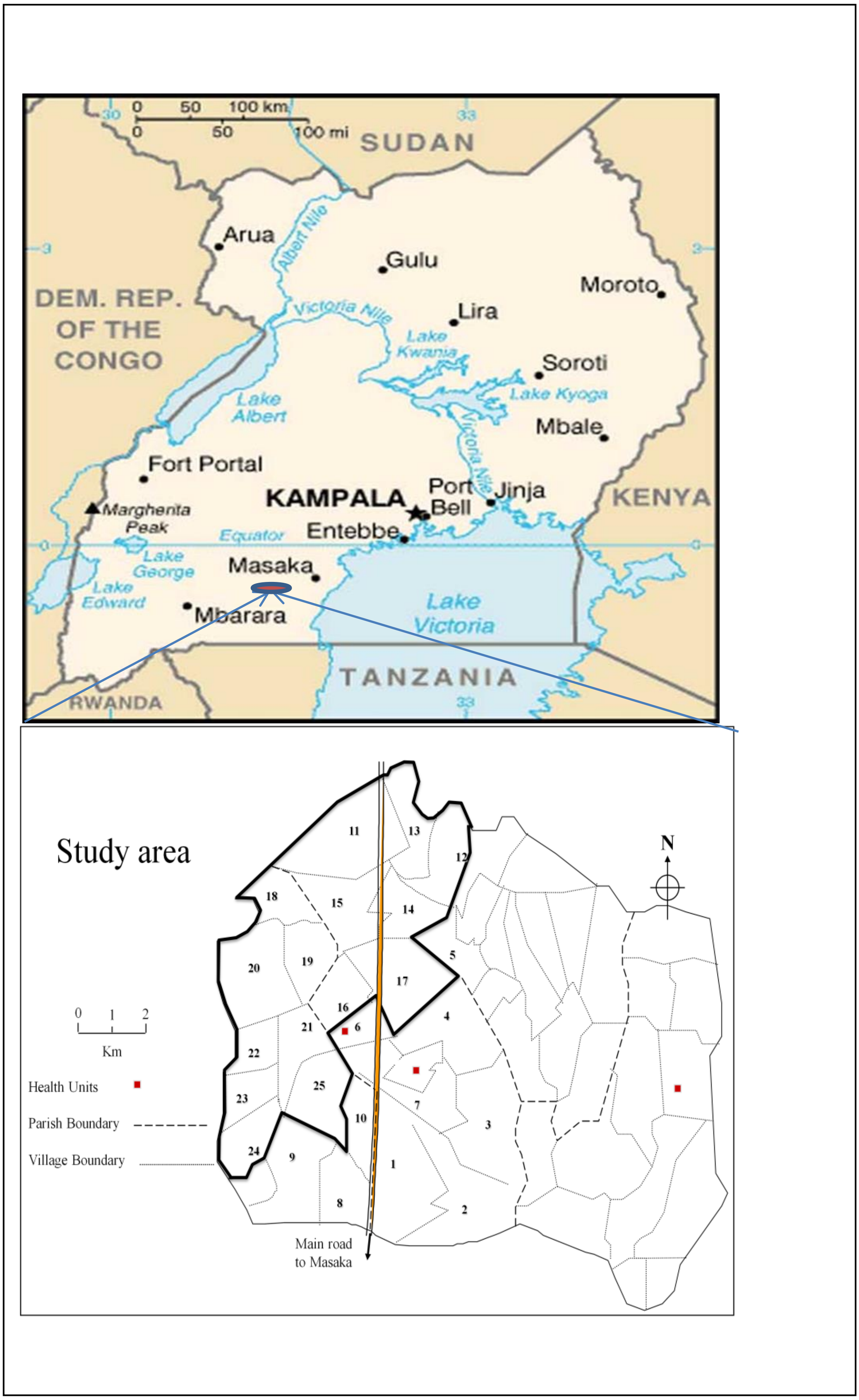


Figure 3 Map showing Kyamulibwa, the study site

The initial aims and methods of data collection in the GPC

The GPC was started at the peak of the HIV epidemic in Uganda. At the time, health services and research were concentrated in urban centers and there were virtually no population based data on HIV in rural populations. The primary aim of the cohort was therefore to document the trends of HIV prevalence and incidence and understand the drivers of the epidemic in rural populations. To achieve this aim, data were collected through an annual mapping and census rounds, and annual health surveys. Before each round of data collection, communities were sensitized to the study before being requested to consent by trained MRC field workers. After consent, mapping, census and a health survey were piloted in one village reserved for this purpose followed by actual data collection in the 25 study villages in succession taking a period of approximately 11 months per study round. During mapping, details of household locations, with the names of household heads and prominent topographical features were obtained. The maps were used to locate households during the census. In 2014, the GPC joined the International Network for the Demographic Evaluation of Populations and their Health (INDEPTH) (Sankoh and Byass, 2012) and also contributes data to the Network for Analysing Longitudinal Population based HIV/AIDS data on Africa (ALPHA) (Reniers et al., 2016).

The GPC as data resource for longitudinal maternal and child health studies

The information obtained on every member of the household including children was linked by a unique personal identification number that was assigned to each member of the household at birth or when a member joins the household. This number was maintained in all studies. Additionally, a mother's unique identification number was linked to that of child at birth. Relationship codes assigned at census also enabled linkage of a child to both the mother and father. Although maternal and child health data were not collected in every study round it was possible to link various data sources collected serially using the unique identification numbers.

3.2 STUDY DESIGN, POPULATIONS STUDIED AND METHODS

Data collection methods

The general population cohort was an open cohort where members of a defined study area joined or left the study. Serial cross sectional surveys were conducted every year in the same villages but linked using identification numbers in order to create a longitudinal dataset.

Pregnancy registration

Pregnancy registration was introduced in the study area in 2002 as part of a project for prevention of mother to child transmission of HIV (PMTCT). The aim was to improve linkage of mothers to health facilities to enhance uptake of anti-retroviral therapy for prevention of HIV transmission. Less than half of the pregnant mothers delivered in a health center and yet a number of interventions preventing HIV transmission were offered at birth in health facilities. In 2002, local residents were trained as village informants to register pregnancies based on their observation as to whether a woman was pregnant or not. No laboratory diagnosis was made. The village informant recorded the pregnancies on a simple registration form that included the household location, name of head of household, name of the mother and submitted the forms on monthly basis to the survey office. A study clerk received the reports and linked the mothers name to their unique identifier using the census data base. In 2014, we introduced more variables including age of gestation at first registration and a pregnancy follow up form to update the status of every pregnancy on monthly basis as “still pregnant”, “delivered”, "pregnancy lost” and “pregnant woman left the study area”. Registration of pregnancies using mobile phones was also piloted from April 2014 to November 2015.

Birth and death registration

Although birth registration in Uganda was made compulsory in 1903, only 4% of all births could be registered in 2001, increasing to only 30% in 2011 with a lower proportion in rural communities. In the study area, birth registration was introduced right from inception of the cohort in 1989. A village informant was trained to register births and deaths and submit monthly reports to the study office located within the study area. The village informant was trained to actively follow births and deaths in their village since there was no notification system in place for parents to inform them of these events. They were specifically trained to differentiate between births and deaths to non-resident mothers. This would later help the study clerk to search the mother’s identification number in the database and decide whether to allocate an identification number to the baby or not. Babies born to non-resident mothers in the study were not assigned identification numbers. Village informants also noted if a child was born dead or alive and died soon after to differentiate between stillbirths and early neonatal deaths. The same village informants were the village health workers who were later trained to register pregnancies and follow women with text messages (study IV).

Census data

As in most rural communities in Uganda, no updated community registers were available in Kyamulibwa. Population denominators were based on projections from national census which is only conducted once every 10 years. In order to establish an accurate population denominator and sampling frame, a census was therefore a necessity in the study area. The villages in the study were all mapped and a baseline census was conducted at inception of the cohort and repeated every year to update migrations, new births, deaths and socio-economic status of the population. Field workers were trained by MRC to collected data on socio-demographic characteristics such as age, sex, religion, tribe, vital status, migrations, relationships of every member of the household, overall housing condition (roof material, floor material) and socio-economic indicators (ownership of land, employment of domestic workers and other household possessions) using a standard questionnaire administered to the head of household or any adult representative. The resident status during every census round was updated for every member previously enumerated, akin to a *de jure* census approach

Health surveys

Although health surveys were established in the study area to mainly study HIV dynamics in the population, a number of other health problems were investigated. Study themes were determined by the principal investigators on annual basis and the population for the study was selected using the most recent census preferably conducted within the same year.

Maternal health surveys

Annual adult health surveys included residents aged at least 13 years who were interviewed individually on their demographic information and, in the case of women, their reproductive history. Maternal topics were covered in several rounds starting from 1996. In selected health surveys conducted in1996, 2004, 2006, 2009, 2010, 2011 and 2013, all women aged 15–49 years were asked if they had been pregnant in the previous year and those who had been pregnant were asked specifically about the outcome of each pregnancy. In 2013, we introduced a question probing their life time experience of all pregnancies and the outcome of each pregnancy (abortions, stillbirths and live births) to compare reported outcomes with the existing method in which women were only asked the most recent experience in the past year. Women were also asked about the total number of children ever born alive and how many were still alive.

Child health surveys and anthropometric measurements

Child specific surveys gathered detailed information on every child below 13 years. The mother or caretaker of the child provided informed consent and children aged 8-13 years additionally provided assent before any study procedures. The child's age was estimated from recalled date of birth by the mother or using immunization cards and baptism records. Mothers or caregivers were also interviewed to ascertain whether the child was delivered at home or health facility, how they were fed during infancy and the vaccination status of the child (also verified by checking the information on a child health card when available, or the presence of a scar for Bacillus Calmette-Guerin (BCG)). Anthropometric assessments were conducted in 1999-2000, 2001-2002 and 2004-2005 during which weights and heights of children were measured. The weight for children aged 0–2 months was recorded using a digital scale (Seca productions). A Salter spring was used for those aged 2–12 months with a pouch suspended from a firm bar and for children more than one year old who could stand, a spring balance weighing scale was used. All weight measurements were estimated to the nearest 0.1 kg. For height measurement, length for young children unable stand was measured using 100 cm rod while lying horizontally. For children able to stand, a standing rod was used with one end of the rod placed on a flat surface, on which the child stood with bare feet, with the heels, back and buttocks touching the rod, and arms hanging at the sides. A flat board was placed at 90 degrees to the rod lightly compressing the child's hair and his/her height was read to the nearest 0.1 cm.

Cardiovascular disease risk assessment at adolescence

In 2011, all residents aged 13 years and above were assessed for some selected cardiovascular disease risk factors using WHO STEPwise Approach to Surveillance questionnaire,(WHO) , adapted for the study. Socio-demographic data including levels of education, ethnicity, and religion and dwelling conditions (wall type) were collected followed by data on consumption of starch, fruit and vegetables, alcohol, tobacco smoking and physical activity through a self-report. Height was measured using the Leicester stadiometer to the nearest 0.1 cm and weight measured using (Seca 761) mechanical scales to the nearest 1kg with participants wearing only light clothing and no shoes. Blood pressure was measured on the right arm using an appropriate cuff (with a digital Omron M4) in the sitting position, taken three times, five minutes apart. The mean of the second and third reading was recorded. Biochemical analyses were performed using the Cobas Integra 400 plus chemistry analyser to determine HbA1c from whole blood samples and high density lipoprotein cholesterol (HDL-C), Total cholesterol (TC) and triglycerides (TG) from serum samples. Low density lipoprotein (LDL-C) was estimated by modified Friedwald formula: LDL-C= TC-(HDL-C +TGX0.16) mmol/L.

The intervention study- pragmatic trial

Informed by findings from studies I and II, the period ranging from the last trimester of pregnancy to the day of birth and the first week (perinatal period) were critical for child survival. We designed and implemented a community based intervention that aimed to improve child survival through targeting uptake of maternal health services in the most critical period.

This was a pragmatic trial with a village as a cluster unit. Unlike experimental trials, that measure efficacy of interventions in ideal settings, pragmatic trials measure benefit of interventions in real settings and put less emphasis on homogeneity of study populations (Roland and Torgerson, 1998). Whereas experimental trials tend to maximize internal validity by assuring rigorous control of all variables other than the intervention, pragmatic trial focus more on maximizing external validity to ensure generalizability of results.

In our pragmatic design, the GPC study area was divided into intervention (13 adjacent villages allocated to monthly mobile phone health text message sent through CHW to pregnant woman) and control (13 villages where pregnant women did not receive any text messages). One CHW per village was trained for this purpose.

The intervention arm

The main aim of the intervention was to link pregnant women to their nearest primary health care facility during pregnancy and birth. The intervention had two components; (i) registering pregnant women by village health workers using smartphones (ii) tracking the pregnant women with mobile phone short messages (SMS) sent from a centralized database. One village health worker, already trained to conduct vital registration previously, received additional training for one day to enable them to register and follow pregnant women in their own community using an electronic form customized for this purpose. The doForm web based application (DoFORM) was used to construct electronic pregnancy registration forms and the forms were then dispatched via the cloud to smartphones provided to the village health workers. The village health worker filled the forms and sent back the encrypted data via the cloud to our database every month. From the database, we generated health messages specific to gestational age adapted from the Mobile Alliance for Maternal Action (MAMA) website (MAMA), and sent to the village health workers who in turn delivered the messages to the pregnant women. The MAMA messages are based on WHO and UNICEF guidelines and have been developed in close collaboration with a group of global health experts to cover a period of gestation from five weeks to 42 weeks. They provide information on importance of antenatal care, safe delivery, nutrition and motivate mothers to get the right care at the right time. Each month, a health text message translated to the local language was sent to mothers grouped according to gestation age. When the village health worker received a message from a central web database on their personal mobile phones, they visited the pregnant woman in their homes and read the messages verbatim. During the same visit, the village health worker updated the pregnancy status of the mother as; “baby delivered” or “still pregnant” or “pregnancy lost” or “mother not available at home”. The pregnancy forms also captured basic demographic information on the mother and household.

Control arm

In the control arm, the village health workers registered and followed pregnancies monthly using paper registers only and did not receive a health text message to be delivered to the mothers.

Village health workers from all study villages attended quarterly meetings during which refresher trainings were conducted. A trained field worker provided technical support to the village health workers in the field on demand especially when they had technical problems with the smart phones.

A summary of the four studies, their design and data sources are provided in table 3.

Table 3: Summary of the methods for the studies constituting the thesis

Studies	**Design**	**Data sources**	**Years**	**Articles**
Under-five mortality and determinants	Cohort	vital register, census, health surveys	2002-2012	1
Stillbirth rates and associated factors	Serial cross sectional studies	health survey-interview of mothers	1996-2013	II
Protein Energy malnutrition and consequences on CVD risk and schooling	Cohort	child health surveys, adult health survey	1999-2011	III
Mobile phone SMS intervention to improve uptake of facility births	Intervention	GIS data, census, pregnancy register, vital register, doForm website	2014-2015	IV

3.3 STATISTICAL ANALYSES

All data collected were entered in MS Access (2013) and cleaned before exporting into SAS for analysis. All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Evaluation of the quality of data collected by community health workers

Pregnancy, birth and death data for several years were collected prospectively by lay community workers. We evaluated these datasets for completeness and accuracy before using the data for longitudinal analysis.

Completeness of birth registration was examined using birth concentration index and sex ratio at birth.

Birth concentration index estimates the proportion of births correctly registered in a particular year. This was computed for each year of birth registration based on the formula;

Birth Concentration Index = $\frac{200B_t}{B_{t-1}+B_{t+1}}$

Where B_{t-1}, B_t and B_{t+1} are the number of births in the t-1, t, and t+1 calendar years. This index should be close to 100. A value less than 100 means fewer births were registered than expected and a value more than 100 means more births were documented from another calendar year which could result from wrong dates of birth.

Sex ratio at birth: The natural "sex ratio at birth" is often considered to be around 105 meaning that at birth on average, 105 males are born for every 100 females. A sex ratio above the normal denotes an under-registration of female births and if below the normal it could be due to under registration of males. We computed this ratio for all the years when births were registered.

Death registration was checked by comparing deaths reported in the census conducted by trained MRC field workers with deaths reported by village health workers in the corresponding periods. We also examined the proportions of neonatal deaths occurring on the first day and first week of life to test the two-thirds rule. According to this rule, at least two thirds of neonatal deaths occur in the first week of life and that two thirds of the early neonatal deaths happen within the first 24 hours of life. We also checked for evidence of age heaping at the age of 7 days.

Pregnancy registration: We also assessed how well lay community health workers used smart phones to register pregnancies at home by comparing corresponding data fields in the data collected by phones with those in paper based registration. Using the command "PROC COMPARE" in SAS, we determined whether matching observations in the two dataset were comparable by comparing every field in corresponding variable responses for each village health worker.

Child mortality estimate and trends using the synthetic cohort life table method

For this analysis we used a combination of data sources in a complementary manner including; repeated censuses, vital registration, pregnancy registration and health survey rounds conducted between 2002 and 2012. We merged these datasets using the participant unique identification numbers. The follow-up period for each child included in the analysis was based on dates of the study entry and exit. The entry dates were taken from the birth register or census data bases and defined as follows: (i) the date of birth of the child if a record of pregnancy existed before the child was born or when the child was registered on the day of birth, (ii) the date of reporting birth if birth registrations happened after date of birth (iii) date of first registration in the census was considered as the entry date for children less than five years if the child was missing from in the birth register either because they were born outside the study area and joined the study area later or they were missed during birth registration. The exit dates were derived from census or death register as follows (i) the date when the child was last reported alive in the census, or ii) the date when they moved out of the study area, or (iii) the date of death or (iv) the date when the child reached five years of age. If the exact date of moving out of the area was unknown, the date mid-way between the last two dates of the census interviews were used for as the exit date.

The probabilities of survival were calculated for each age interval and by sex (Table 8) by the synthetic cohort life-table method (Rutstein and Rojas, 2006). This was carried out by dividing the number of deaths by the number of child days of follow-up in that interval, taking into account the length of each interval based on a set formula (Table 8, columns 6, 11, 16). Survival (S) by age interval was computed (Table 8, columns 7, 12, 17) as a conditional probability (P_i survival through interval i'| 'survival through interval i-1') and multiplied by 1000. Survival in each one of these synthetic cohorts was also translated into an age interval-specific hazard rate (Table 8, columns 8, 13, 18). To determine trends in child mortality, corresponding hazard rates for each calendar year were computed using five-year moving average (Fig. 4).

Determinants of child mortality

Cox regression with a random effects model was used to explore risk factors for mortality and 95% confidence intervals were obtained. First, bivariate associations were computed, adjusted for age. A multivariate model was then built using a conceptual framework (Victora et al., 1997). Potential risk factors for under-five mortality were considered in four groups: socio-economic factors, maternal reproductive factors, child health factors and individual child factors. An initial model only included socio-economic factors. Only the type of material for wall construction defined as mud and brick, mud and poles or concrete and brick was used as a measure of wealth and was included a priori in all models, to assess the contribution of socio-economic status as a distal determinant of child mortality. All other socioeconomic factors for which the association reached p=0.1 were included in a multivariate model. Factors that remained independently and significantly associated with the outcome ($p< 0.1$) were retained. Next, the association between each determinant in the maternal reproductive factors group, child healthcare factors group and the child individual characteristics group were assessed by adding the single determinant into the multivariate model, including the subset of independently significant socio-economic factors. A multivariate model was built that included the subset of socio-economic factors in the first multivariate model plus any maternal reproductive, environmental or child factors for which the p-value was 0.1 after adjusting for the socio-economic factors. For variables with substantial numbers of missing values, a dummy variable category with missing values was included

Estimating stillbirths and associated risk factors

In Uganda the gestation age cut-off for abortion and stillbirth is 28 weeks. We defined a stillbirth as a baby born with no signs of life after 28 completed weeks of gestation. Stillbirth rate is the number of stillbirths per 1000 births. Analysis of pregnancy outcomes reported in the past12 months (live birth, stillbirth, abortion) and rates were examined by study round. We explored factors associated with stillbirth in all study rounds, and estimated odds ratios (OR) and 95 % confidence intervals (CI) for the associations using random effects logistic regression to account for clustering within women who reported more than one pregnancy. Age was included in all models as an a priori confounder. Because the numbers of stillbirths were small, we did not attempt to build a full multivariable model for this outcome. We conducted a separate analysis based on lifetime experience of pregnancies; computed for those who reported at least one pregnancy, the number and proportion of pregnancies ending as livebirth, abortion and stillbirth and summarized the results by age, marital status, religion education occupation, residence, phone ownership and parity. The proportion of women in the reproductive age reporting live births, stillbirths and abortions was also determined. We examined risk factors for stillbirths using negative binomial regression because the number of stillbirths reported was considered a count outcome and were over-dispersed (variance greater than the mean); robust clustered standard errors were used to account for correlation of repeated pregnancies among women. The logarithm of the total number of pregnancies for each woman was included in the model as an offset. Age was considered an a priori confounder and included in all models. Factors whose age-adjusted association with the outcome was significant at $p<0.10$ were included in a multivariable model and retained if they remained associated at $p < 0.10$. Lastly, we compared the results of two survey approaches; annual surveys between 1996 and 2013, when women were interviewed on their pregnancy experience in the preceding 12 months, versus the single survey in 2012–2013 when women were interviewed on their complete obstetric histories. This was done to evaluate the methodological biases associated with each approach.

Long term effect of childhood PEM on cardiovascular disease risk and education among children surviving to adolescence

For this analysis we derived baseline data for children below five years of age by combining data collected in two child health surveys (1999/2000 and 2001/2002). We then merged this with data for 2004/2005 and 2011 surveys used as follow-up. We included only children who were available at baseline and follow-up. Children missing the outcome variables (blood pressure, lipids, HbA1c, or years of schooling) in 2011 were excluded from analysis.

Nutritional status assessment

We first derived z-scores for height-for-age and weight-for-height using the WHO-igrow SAS macro based on WHO growth standards 2006 for children under five years (WHO, 2006) and WHO growth reference 2007 for those aged 5-19 years (WHO, 2007). PEM was defined as stunting if height-for -age < -2.0 z score, and as wasting if weight- for- height < -2.0 z score. Individuals with extreme values of z scores which were considered biologically implausible (height- for- age z- score < -6.0 or > 6.0 and weight-for-height z- score < -5.0 or > 5.0) were excluded from analysis. We grouped children into four categories respectively for height-for-age and weight-for-height z scores measured during childhood/baseline, and adolescence/ follow-up; the first group referred to as “normal” were children whose z scores were normal (-2.0 to 2.0) in the entire follow up period. The second group named “stunted” or “wasted” were those with z scores below normal (< -2.0 z scores) throughout the follow-up period. The third group labeled as “recovered” were those with z scores below normal at baseline but recovered to normal during follow-up and the fourth group labeled as “deteriorated” were normal at baseline but fell below normal during follow up. Proportions of children in each of these categories were computed.

All the outcomes (blood pressure, blood lipid levels, HbA1c and years of schooling) were treated as continuous variables and examined for deviations from symmetrical Gaussian distribution using tests of skewedness, and by observing their histograms. Since there was no evidence of skewedness, a generalized linear model was used to compare mean values of the outcomes for the four independent groups (normal, stunted/wasted, recovered, and deteriorated) respectively for height-for-age and weight-for-height. HbA1c and lipid levels showed no association with PEM. Multiple generalized linear regression analyses were used to examine the relationship between blood pressure and schooling achieved each with the nutritional categories of children defined above and other covariates shown to have association at $p<0.10$ in the bivariate analysis. Age, sex and socio-economic factors were added as *a priori* factors into the models. Clustering of children within households was adjusted for using Generalized Estimating Equations (GEE).

Effect of village health worker-led SMS to pregnant women on uptake of deliveries

To compute the effect of the intervention, we considered place of delivery as our primary outcome. We first computed relative frequencies by place and month of delivery stratified by study arm to show how the incidence of home births changed in comparison to facility births. We then used the intention to treat analysis principle to evaluate the effect of the intervention. Logistic regression along with generalized estimating equations was used to account for cluster correlation within households. Explanatory variables were entered in a stepwise manner and those with likelihood ratio test $p<0.10$ were retained. In the final model age, education, tribe, religion, distance to nearest health center, visit by village health worker, and intervention arm were retained. Results were expressed as odds ratios (ORs) for home delivery, with 95% confidence intervals (95% CIs). We also conducted a sub-analysis to compare mortality among infants who were delivered in the intervention and control villages.

3.4 ETHICAL CONSIDERATIONS

All the studies were approved by the Uganda Virus Research Institute (UVRI) Research Ethics Committee and by the Uganda National Council of Science and Technology (UNCST). Participants were given detailed information on the studies before being requested to provide a written consent. Participants who were illiterate were asked to nominate an impartial witness who assisted them in confirming information written in the consent form. They used a thumb print to confirm their consent. For children aged 0-7 years, parental or guardian consent was obtained while those aged 8-17 years provided assent after the parental/guardian consent. Participation was voluntary and all information about the study was kept confidential. Those who were mentally incapacitated were excluded from the studies. As an appreciation for their time in the study, each participating household was given a bar of soap. No money was given to the participants. Healthcare was provided to families participating in the study and appropriate referrals given to those requiring further management. Transport was provided for emergency referrals to higher health facilities.

4 RESULTS

4.1 CHARACTERISTICS OF STUDIED POPULATIONS

Table 4: Summary of selected participants' characteristics for the four studies

Characteristics	**Study 1**	**Study II**	**Study III**	**Study IV**
Sample size	10118	n1=1800, n2=2158	1054	525
Age	0-5 years	15-49 years	13-19 years	15-49 years
Gender	51% female	All female	49% female	All female
Baganda tribe	78%	73%	73%	77%
Christian versus Muslim	65% vs. 30%	71% vs. 24%	74% vs. 26%	64% vs 29%
Education >7 years	15-30% of their mothers from (2002-2012)	10-37% from (1996-2013)	21% in 2011	38% in 2015
Lived in house with concrete and brick wall	15-17%		36%	
HIV prevalence	Child; 1-3% Mother; 8-10%	8-11%	10%	
Utilization of health services	Vaccinations BCG: 52-59% Polio: 25-36% PVT: 52-46% Measles: 44-40% 54-63% delivered in a health facility from 2002-2012	Antenatal Attendance fluctuated between 82% and 87%		Facility delivery 84.2% (after intervention)

n1= number of women interviewed on pregnancy outcomes in past 12 months; n2=number of women interviewed on lifetime pregnancy outcome

Table 4 shows a summary of characteristics for the studied populations. The study participants were drawn from the same study area. The study participants were predominantly from the same ethnic group *(Baganda)* and one third were muslims. The women enrolled in studies I, II and IV were all of reproductive age and from the same study area and thus the similarity in their characteristics. The women were followed through several study rounds (studies I and II), before an intervention was established in study IV with an ultimate goal of improving child survival from the perinatal period to the age of 5 years. The proportion of women going beyond seven years of education (secondary education) increased from 10% in 1996 (study II) to 38 % in 2015 (study IV). HIV prevalence also increased from 8% to about 10% (studies I and II). We also observed that the uptake of maternal health services improved over time, the most notable one being delivery at a health facility from 54% in 2002 to 63% in 2012 (study II), hitting 84% in 2015. Antenatal attendance was already higher than 80% in early 2000 and fluctuated between 82% and 87% with no obvious increase over time.

In study I, a cohort of children under five years was enrolled. The children entered the cohort from birth or immigration to the study area and exited at age five, or emigration or death. Equal proportions of boys and girls were enrolled. In the entire follow up period (2002-2012), no substantial change was observed in the housing conditions for children under five years to the extent that only 15-17% of children lived in concrete walled houses. A vast majority lived in houses constructed with mud and poles. Vaccination uptake was generally low with marginal increases observed in uptake of BCG and OPV (oral polio vaccine) and a decrease in the uptake of the pentavalent vaccine (PVT) and measles vaccine in the latter period. The HIV prevalence of 1-3% was a result of maternal transmission either in utero, during birth or breastfeeding.

In study III, only a cohort of adolescents followed from childhood (below the age of 5 years) was enrolled. Between the ages of 13-19 years they were assessed to ascertain how a change in their nutritional status influenced cardiovascular disease risk and schooling outcomes. Only one fifth of these children had attained education beyond seven years. A higher proportion of adolescents lived in better housing environment compared to living conditions for children below five years.

4.2 DATA QUALITY CHECK

Lay community health workers conducted community based registration of births, deaths and pregnancies in the study area.

Birth concentration index

Based on the formula; Birth Concentration Index= $\frac{200B_t}{B_{t-1}+B_{t+1}}$

Where B_{t-1}, B_t and B_{t+1} are the number of births in the t-1, t, and t+1 calendar years, table 5 shows birth concentration index in selected years in the entire survey period.

Table 5: Completeness in reporting of births by community health workers estimated using the birth concentration index (2003-2015).

Year	Births reported	$(B_{t-1})+(B_{t+1})$	$200B_t$	Birth concentration index
2003	244	-	-	-
2004	457	753	91400	121
2005	509	941	101800	108
2006	484	876	96800	111
2007	367	833	73400	88
2008	349	768	69800	91
2009	401	624	80200	129
2010	275	678	55000	81
2011	277	653	55400	85
2012	378	601	75600	126
2013	324	759	64800	85
2014	381	682	76200	112
2015	358	-	-	-

A value of less than 100 implies fewer births than expected for year t were recorded by the lay community workers. As shown in the table the birth concentration index was close to 100%. In 2004, 2009 and 2012, 20-30% more births were reported than expected. In 2007, 2010, 2011 and 2013, fewer births than expected were registered. Although there were fluctuations in the number of births registered, the peak was in 2004-2006 and the number of births reduced steadily over the years.

Sex ratio at birth

As shown in table 6, we computed sex ratio at birth for each calendar year.

Table 6: Sex ratio by year of birth

Year	Boys	Girls	M:F ratio
2003	127	117	0.92
2004	237	220	0.93
2005	244	265	1.09
2006	212	272	1.28
2007	179	188	1.05
2008	184	165	0.90
2009	188	213	1.13
2010	136	139	1.02
2011	133	144	1.08
2012	178	200	1.12
2013	179	145	0.81
2014	185	196	1.06
2015	170	188	1.11
Total	2352	2452	1.04

Overall, male to female ratio at birth was within the expected limits. For four calendar years (2005, 2007, 2010, 2011 and 2014) sex ratio was found to be in the expected value range. In 2003, 2004, 2008, and 2013, less male babies were registered than female babies. In 2006, 2009, 2012 and 2015 slightly more than expected male babies were registered than female babies.

Registration of deaths

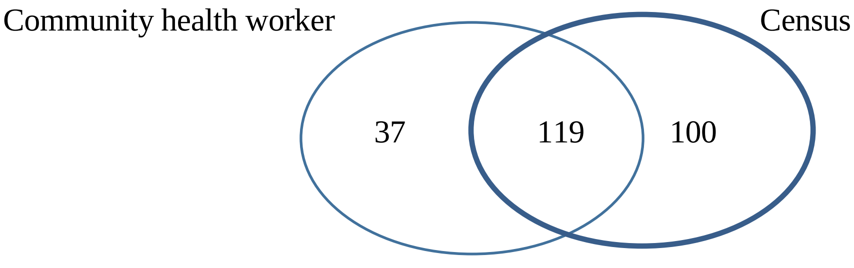


Figure 4: Comparison deaths registered census and vital registration for children below 5 years of age (2002-2012)

For a total of 256 deaths of children under- five years registered between 2002 and 2012, 37 were missed in the census but identified by lay recorders while 100 were missed by the lay recorders but recorded in the census. Both data methods together registered 119 deaths in common. In summary CHWs registered 156 (60.9%) of all deaths recorded while trained

MRC field workers registered 219 deaths (85.5%) of the total child deaths. In our analysis we therefore used all deaths combined from all sources.

Two thirds rule for neonatal deaths

According to the rule of two thirds, at least two thirds of neonatal deaths occur in the first week of life and that two thirds of the early neonatal deaths happen within the first 24 hours of life. In our study, among neonatal deaths, 6 were registered by the village recorders with date of death before birth (negative age), 36/39 neonatal deaths (92.3%) happened in the first week of life and 17 (47.2%) of 36 deaths in the first week occurred within the first 24 hours of life. There was no evidence of age heaping at day 7 (only one death reported) perhaps because lay recorders reported date of birth but not age.

Comparison of paper and mobile phone registration of pregnancies

We also assessed how lay community health workers used smart phones to register pregnant women at home by comparing with paper based registration of pregnancies by the same community health workers in their own villages. There was a high level of similarity (86%-95%) when corresponding numeric data fields were compared between paper and phone registration. Community health workers had challenges in entering text responses on their phone to the extent that only 38%-48% of the corresponding fields compared on paper and phone were similar (table 7).

Table 7: Comparison of selected data fields for paper and mobile phone registration of pregnancies by community health workers in rural Uganda (2014-2015)

Variable	Variable type	[1]Same value (%)	[2] Difference (%)
ALL fields		577/795 (72.6%)	
Household number	numeric	151/159 (95.0%)	- 2.50%
Date of registration	numeric	137/159 (86.2%)	0.02%
Gestation age (months)	numeric	151/159 (95.0%)	-0.61%
Facility birth (Yes/No)	Character	61/159 (38.4%)	N/A
Name of Health facility	Character	77/159 (48.4%)	N/A

[1]Proportion of variable values that are the same in both paper based and phone registration
[2]Percent difference in mean values on paper and phone

4.3 CHILD MORTALITY TRENDS

Under-five mortality trends

From 2002 to 2012, 10,118 children (male=4963, female=5155) under five years of age contributed 18,268 (667810/365) child years of follow-up and 256 children died within this period. Table 8 shows that a member of an imaginary cohort of 1000 newborns, exposed in each age interval to the mortality that we observed, would have a 0.908 (${}_5p_0$=908/1000) probability of survival to his or her fifth birthday, corresponding to a probability of death (${}_5q_0$) of 0.092 (92/1000). As expected, girls survived better than boys, with the bulk of the difference emanating from the late neonatal period (age 7 days up to completing 28 days of age - ${}_{21}p_7$). Post-neonatal infant mortality (${}_{11}q_1$) was similar (19/1000) for both boys and girls (calculated as 1-932/950 and 1-958/977, respectively). The life-table also allows us to read, for example, the “1-4 years child mortality rate” as ${}_4q_1$= 1-908/945 = 39/1000 (35/1000 for boys and 43/1000 for girls).

Comparing the synthetic cohorts calculated for each calendar year (2002-2012), under-five mortality declined by 33% (from 96 to 64 per 1000).

Figure 5 shows how the mortality hazard rate trends (as calculated in footnote to table 8) for specific age groups varied over time between 2002 and 2012. In the first seven days of life no change in mortality was observed. In the neonatal period 7-27 days some decline was observed between 2002 and 2006 but later plateaued. The most notable decline was observed in the post-neonatal period (28 days to 11 months). For the children aged 1-4years, mortality only declined between 2002 and 2005 and stagnated thereafter with a slight increase observed after 2005.

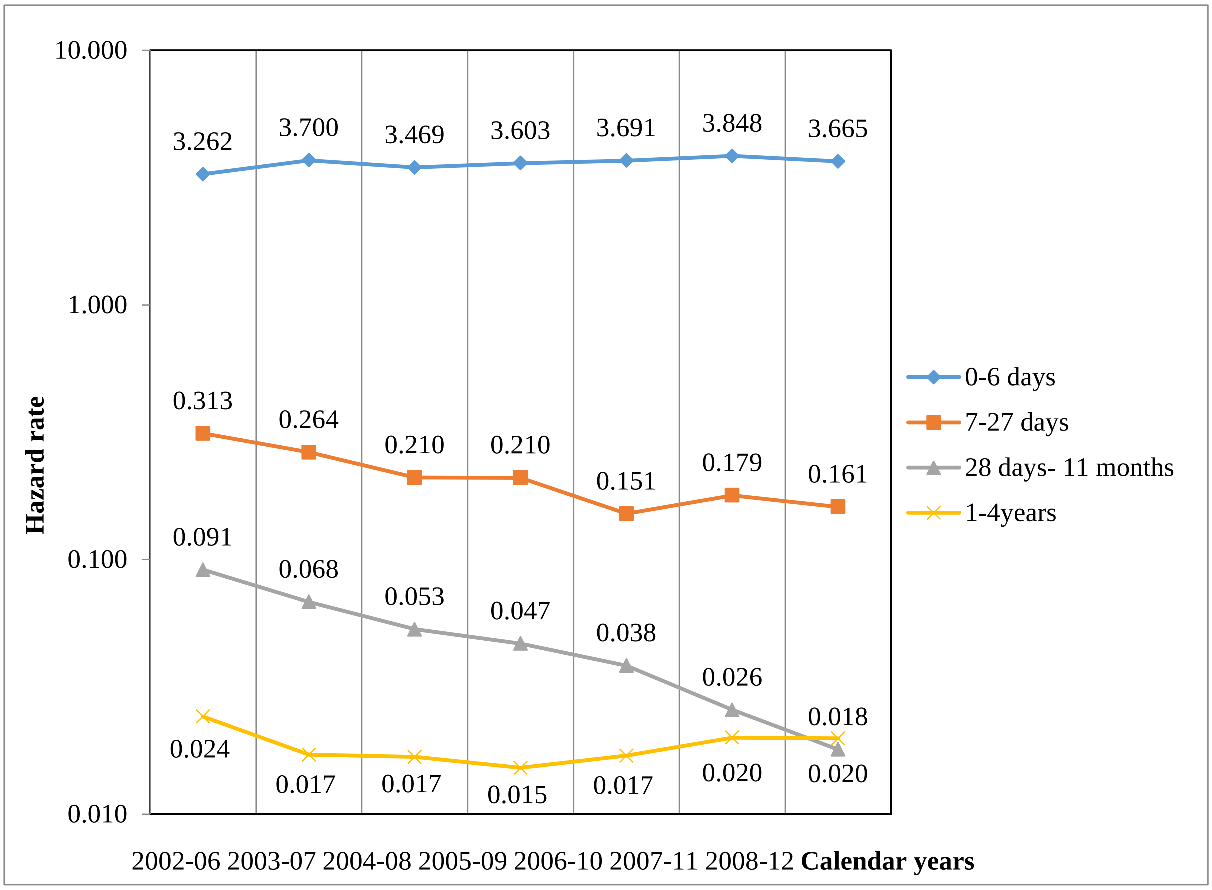


Figure 5: Age interval specific mortality hazard rates (5 year-moving average) for children under-five in rural south-western Uganda (2002-2012)

Maternal factors associated with under-five mortality

In the unadjusted analysis, relative risk of death was significantly higher among children born to mothers with higher parity, children delivered at home, those not exclusively breastfed for six months, children who missed vaccinations, children younger than 12 months and those with HIV infection. Mortality risk among children surveyed before 2004 was six times higher than for children in the later period (2009-2012). Children living in houses built with mud and brick or mud and pole compared to concrete and brick walls had 45% higher risk of death but this was not statistically significant. Similarly, children from other tribes compared to Baganda, Christian religion compared to Muslims, those whose mothers had attained primary or less education, those with HIV-positive mothers, children from crowded households (crowding index >5 children per room) had non-statistically significant higher risk of death (not shown).

After a hierarchical modeling of risk factors, maternal factors remained the major driver of under-five mortality. Mortality was higher among children delivered at home (HR=1.70, 95%CI [1.04-2.79]), children born to mothers who were never married (HR=2.17, 95%CI [0.88-5.32]) and among children born to mothers with parity of more than four (HR=2.08, 95% CI [0.84-5.13]). Mortality risk was lower among children with a preceding birth interval of 1-

2 years (HR=0.45, 95%CI (0.21-0.97). HIV positive status of the child (HR=3.02 95%CI [1.10-8.27]) or unknown HIV status of child (HR=3.02 95%CI [1.10-8.27]) were also associated with under-five mortality (table 9).

Other factors associated with under-five mortality included; age of the child with those under one year having higher hazard of death compared to children older than one year (HR=10.67 95%CI [3.03-37.58]) and missing pentavalent vaccine at some stage (HR=1.76, 95%CI [0.82-3.76]). Children living in houses built with brick/mud or pole/brick had a higher hazard of death compared to those in houses with concrete and brick but this effect was attenuated with sequential introduction of maternal factors, child-care practices and child individual factors (from HR= 1.36 to HR=1.10).

Children born to Christians compared to Muslims, education of mothers only up to primary were also associated with higher under-five mortality but without statistical significance

Table 8: Synthetic cohort life table showing survival of children under-five in rural south-western Uganda

Interval		ALL						Boys					Girls				
(i)	Age group	N_i	P_i	d_i	† p_i	‡S*1000	H*1000	P_i	d_i	† p_i	‡S*1000	H*1000	P_i	d_i	† p_i	‡S*1000	H*1000
1	0-6 days	7	6027	27	0.969	969	4.341	2899	17	0.96	960	5.63	3128	10	0.978	978	3.127
2	7-27 days	21	41132	11	0.994	964	0.266	19711	10	0.989	950	0.502	21421	1	0.999	977	0.047
3	1-2 months	64	186606	9	0.997	961	0.048	89021	6	0.996	946	0.067	97585	3	0.998	975	0.031
4	3-5 months	91	297880	19	0.994	955	0.063	144041	11	0.993	939	0.076	153839	8	0.995	971	0.052
5	6-8 months	92	322980	18	0.995	950	0.055	158340	7	0.996	935	0.044	164640	11	0.994	965	0.066
6	9-11 months	91	333853	19	0.995	945	0.057	165267	7	0.996	932	0.042	168586	12	0.994	958	0.071
7	12-18 months	183	712838	43	0.989	935	0.06	357452	18	0.991	923	0.05	355386	25	0.987	946	0.069
8	19-23 months	183	774927	35	0.992	927	0.045	390609	18	0.992	915	0.046	384318	17	0.992	938	0.044
9	24-35 months	366	1653719	38	0.992	919	0.023	834363	21	0.991	907	0.025	819356	17	0.992	931	0.021
10	36-47 months	366	1601669	23	0.995	915	0.014	814027	9	0.996	903	0.011	787642	14	0.994	925	0.018
11	48-59 months	366	736179	14	0.993	908	0.019	374889	5	0.995	899	0.013	361290	9	0.991	917	0.025

N_i= length (days) of i: th age-interval, P_i=person days followed in interval i, d_i=no. of deaths in age-interval i

† p_i =survival probability through age-interval i, and the probability of death $=q_i=1-p_i$

‡ S= survival probability to the last age day of the interval (given survival to its first day) =

$$= 1{,}000 \prod_{i=1}^{x} p_i$$

p_i where x is the number of intervals included and $p_i = e^{-M_i N_i}$, where M_i is d_i/P_i

H= hazard rate computed from the formula; $H = \frac{f(t)}{S(t)}$ where f(t) is the probability density function for death and S(t) is the corresponding survival function and the conditional incidence density (of death) through the age interval (Δt) is calculated from

H(t)= $\frac{S(t1)-S(t2)}{(t2-t1)S(t1)} = \frac{S(t)-S(t+\Delta t)}{\Delta t S(t)}$. Where H= hazard rate, S=survival to the start of the age interval and Δt is the length in days of the age-interval under consideration. With Δt approaching zero, we obtain the instantaneous conditional probability of failure for each point on the survival curve, which can now be thought of as continuous

h(t)= $lim_{\Delta t \to 0} S(t) - S(t + \Delta t)/\Delta t S(t)$

Assuming an exponential distribution of failure, we get Cox' regression model

$h\ (t|x) = exp(\beta 0 + \beta 1x)$

which is parameterized into $h(t)=h0(t)r(x,\beta x)$;

where h0(t) stands for the hazard rate's dependence on time alone and $r(x,\beta x)$ describes its dependence on the other x covariates in the form of a regression equation (applied in table 3 for risk factor analysis).

Table 9: Risk factors for under-five mortality in rural Uganda (Multivariate analysis)

Determinants	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)	Model 4 (Final) HR (95%CI)
Socio-economic factors				
Wall material				
Concrete and brick walls	1	1	1	1
Mud and pole, mud and brick	1.36 (0.70-2.67)	1.31 (0.67-2.54)	1.21 (0.52-2.80)	1.10 (0.45-2.65)
Mothers education				
Secondary or more	1	1	1	1
None	0.43 (0.17-1.07)	0.41 (0.17-1.03)	0.46 (0.15-1.45)	0.35 (0.10-1.19)
Primary	1.27 (0.71-2.26)	1.23 (0.68-2.21)	0.81 (0.35-1.87)	0.62 (0.25-1.48)
Mothers marital status				
Ever married	1	1	1	1
Never married	1.34 (0.80-2.23)	1.42 (0.83-2.43)	2.34 (1.04-5.27)	2.17 (0.88-5.32)
Mothers reproductive life				
Birth interval				
< 1 year		1	1	1
1-2 years		0.63 (0.41-0.98)	0.47 (0.23 -0.98)	0.45 (0.21-0.97)
>2 years		2.47 (1.35-4.52)	3.67 (1.63-8.26)	1.26 (0.40-3.97)
Parity of mother				
1-4 children		1	1	1
5-9 children		1.17 (0.52-2.61)	2.32 (0.97-5.52)	2.08 (0.84-5.13)
10 or more		1.35 (0.69-2.65)	2.21 (0.91-5.39)	2.01 (0.77-5.23)
Childcare practices				
Oral Polio vaccination				
Received all vaccinations			1	1
Missed some vaccinations			0.80 (0.41-1.54)	0.79 (0.40-1.56)
Missed all vaccinations			2.35 (0.84-6.62)	1.88 (0.57-6.20)
Pentavalent vaccine for age				
Received all vaccinations			1	1
Missed some vaccinations			1.68 (0.88-3.20)	1.76 (0.82-3.76)
Missed all vaccinations			0.46 (0.17-1.24)	0.58 (0.18-1.92)
Measles vaccine				
Received			1	1
Missed			1.74 (0.84-3.63)	1.61 (0.69-3.76)
Place of birth				
Health facility			1	1
Home			1.52 (0.99-2.34)	1.70 (1.04-2.79)
Child's individual factors				
Age of child				
1- 4 years				1
Under 1 year				10.67 (3.03-37.58)
HIV status of the child				
Negative				1
Positive				3.02 (1.10-8.27)
Unknown				2.59 (1.08-6.17)

Model1: Socioeconomic factors (wall type, tribe, religion, mother's education, mother's marital status); Model2: Model1 +maternal reproductive characteristics (birth interval, parity). Model3: Model2 +access to health services (childhood vaccinations, place of birth) ; Model4: Model3+ child's individual factors (age, breastfeeding, HIV status) . The national childhood vaccination guidelines: BCG and oral polio vaccine (OPV) at birth, OPV and diphtheria-pertussis-tetanus (DPT) at age 6, 10 and 14 weeks, and measles vaccination at age 9 months. Haemophilus influenza vaccine and Hepatitis B vaccine were combined with DPT (pentavalent vaccine) since 2002.

Trends of stillbirth rates in Kyamulibwa, rural Uganda (1996-2013)

We estimated stillbirth rate by using two methods: (i) a shorter period of recall where women were asked to report the outcome of their pregnancy in the past 12 months and, (ii) longer recall period in which women were interviewed on their lifetime experience of pregnancies.

Stillbirths by 12 months obstetric history

In the shorter recall method, a total of 1800 women aged 15–49 years were interviewed on the outcome of their pregnancy in the past 12 months. These interviews were conducted in eight selected surveys between 1996 and 2013. Of the pregnancy outcomes reported in each survey, 81–93 % was a live birth, 1–5 % was stillbirth and 5–15.5 % was abortion. Except for the peak value of stillbirth rate in 2007, there was a slight reduction in stillbirth rates over time (figure 6). Over all a stillbirth rate of 26.2 per 1000 live births was estimated by this method.

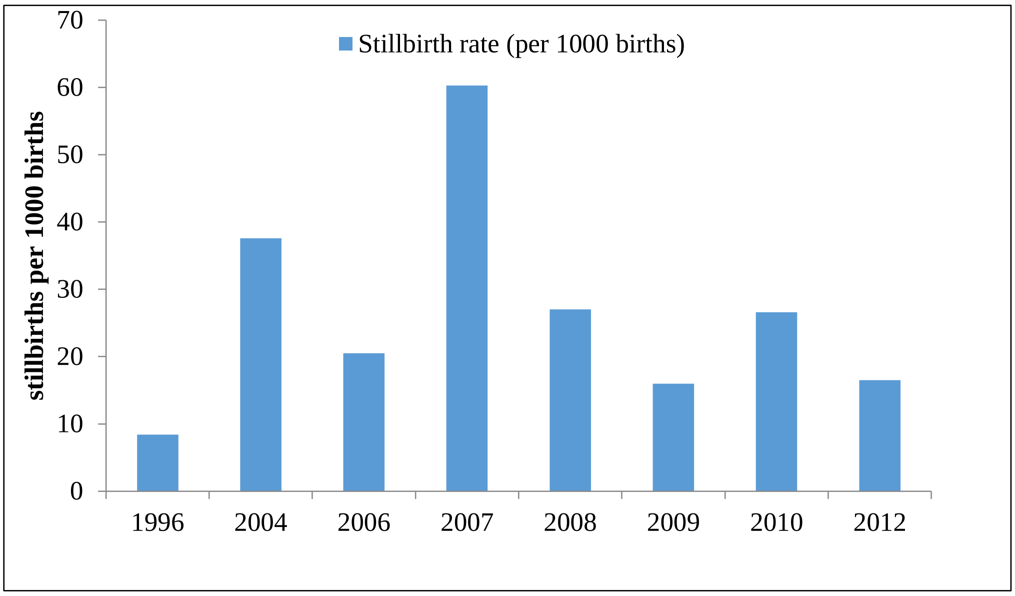


Figure 6: Trends of stillbirth rates among women interviewed in rural Uganda (1996-2013)

Stillbirths estimated by lifetime recall of obstetric history

In 2013, we interviewed women on the outcomes of pregnancies in their lifetime. In total 2657 women aged 15–49 years responded to the questionnaire, 2158 of these reported being pregnant in their lifetime with 569 (26.4 %) ending as abortion and 120 (5.6 %) ending as stillbirths. In total 11,532 pregnancies reported by the women over their lifetime had 11,477 outcomes; 10500 (91.5 %) as livebirth, 830 (7.2 %) as abortion and 147 (1.3 %) as stillbirth. Stillbirth rate estimated by this method was 13.8 per 1000 total births, which is only half of the stillbirth rate estimated by short recall period.

Maternal factors associated with stillbirths

Table 10 shows the factors associated with 12 months recall of stillbirth and lifetime risk among women in rural Uganda. Stillbirths were more common among older women, unmarried women, women with lower education and among those who lived closer to a main road. In the unadjusted analysis, stillbirths reduced with increasing parity and there was evidence of higher odds of stillbirths among unmarried women compared to married women.

Though not statistically significant, stillbirth rate increased with age, closeness to the main road and reduced with increasing education (not shown)

After adjusting for age, marital status, education, village location and parity, stillbirth remained associated with increasing age and reduced with increasing parity. Being unmarried, lower education and closeness to the road were associated with stillbirths, though these did not reach statistical significance.

Table 10: Maternal factors associated with stillbirths among women in rural south-western Uganda

Characteristics	12 months recall Adjusted OR (95% CI)	Lifetime recall Adjusted RR (95% CI)[1]
Age group	P=0.19	P<0.001
<30	1	1
30–39	0.84 (0.44 -1.58)	2.21 (1.21 -4.03)
40–49	2.12 (0.84 -5.35)	3.60 (1.84 -7.04)
Ever married	P=0.92	P=0.44
Yes	1	1
No	1.05 (0.38 -2.89)	1.35 (0.63 -2.89)
Education	P=0.68	P=0.29
None/ <primary	1	1
Incomplete primary	1.28 (0.34 -4.77)	1.05 (0.55 -1.99)
Completed primary	1.84 (0.48 -6.98)	0.91 (0.45 -1.83)
Secondary or above	1.57 (0.41 -6.00)	0.63 (0.29 -1.34)
Village location		P=0.33
Away from main road		1
Along the main road		1.23 (0.81 -1.86)
Parity		P<0.001
0-4		1
05-Sep		0.35 (0.22 -0.56)
≥10		0.21 (0.10 -0.43)
Attended antenatal clinic[2]	P=0.64	P=0.48
Yes	1	1
No	0.57 (0.20 -1.66)	0.65 (0.19 -2.15)

[1]Adjusted for age, ever married, education, village location and parity. [2]Attended antenatal care for a pregnancy in the past 12 months. Restricted to 537 women reporting a pregnancy in the past 12months

4.4 CONSEQUENCES OF SURVIVING WITH PROTEIN ENERGY MALNUTRITION

In this section we describe what happened to children who survived beyond the age of five years up to adolescence. The main aim of the analysis was to understand how exposure to protein energy malnutrition (PEM) during childhood influenced future health. We particularly examined cardiovascular risk parameters and schooling outcomes among children who survived to the age of 13-19 years.

Nutritional status of the children during follow-up

In total, 1,054 children were followed from 1999 (when they were under five years) to 2011 (when they were adolescents aged 13-19 years). In the baseline assessment in 1999-2002, 39.2% of the children were stunted, 15.5% had wasting and 5.4% had both. During the follow-up, 261 (28.3%) maintained a normal height-for -age while 93 (10.1%) remained stunted throughout. A total 295 children (31.5%) who were stunted had recovered from stunting and 275 (29.8%) who were initially normal had become stunted. Meanwhile 12 children (1.3%) remained wasted in the entire follow up period, 245 (15.6%) had recovered from wasting and 307 (33.1%) who were normal at baseline assessment had become wasted later during follow up and 464 (50%) did not experience any wasting throughout the follow up period. Boys dominated the category of children who remained with PEM throughout follow-up or deteriorated later in their nutritional status.

Dietary and lifestyle factors during adolescence

In the last year of follow up (2011) we interviewed the children who had reached adolescence on their diet and lifestyle factors that are potential cardiovascular disease risk factors.

The majority of adolescents (>50%) reported consumption of large quantities of starchy staples amounting to more than 5 servings per day. Conversely, low fruit consumption was commonly reported with only one third of children consuming the recommended 5 or more servings of vegetables and fruits. Approximately 30% of the adolescents reported being physically active with a frequency of physical activities four or less days in a week and 40% reported more than four days of physical activity in a week. Most of the physical activities adolescents undertook were related to walking, running and manual work. About 7-10% of the adolescents in the study reported taking alcohol. HIV prevalence was 10% and was higher among those who were stunted or wasted throughout the follow up period or those who became stunted later compared to those who did not experience PEM.

Malnutrition and adolescent cardiovascular disease risk factors and schooling

Table 11 shows mean values for blood pressure, lipid levels, HbA1c and years of schooling for categories of the children followed to adolescence. Children who experienced stunting or wasting throughout the follow up period had the lowest mean values for blood pressure and years of schooling. Those who were wasted throughout follow-up had the least mean values for TGs and HbA1c and higher mean of TC and HDL-C. Those who recovered from wasting had higher mean for diastolic pressure.

Years of schooling were affected by any exposure to PEM at any stage of their growth. Children who were stunted or wasted in the entire follow up period had the least number of schooling years achieved, followed by those who recovered from PEM, those who experienced PEM later. Children who never experienced any form of PEM had more years of schooling than those who had an episode of PEM.

Those who experienced both forms of PEM but recovered had higher mean blood pressure than the children who remained anthropometrically normal throughout.

Association between childhood stunting and adolescent blood pressure

Table 12 summarizes the result of a generalized linear regression analysis of the (independent) statistical influence of childhood PEM on adolescent blood pressure and achieved schooling. The analysis adjusts for the recorded socio-demographic, dietary, and lifestyle factors.

Childhood stunting and adolescent blood pressure

There was a tendency that being stunted during the entire follow-up period was negatively correlated with systolic blood pressure (-2.90, 95%CI [-6.41, 0.61] p= 0.10). This means children in this group had lower blood pressure than those who never experienced any stunting. Neither recovery from stunting nor getting stunted later in life was associated with blood pressure. We instead found other factors to be associated with higher blood pressure including; alcohol consumption (6.57 95%CI [2.30, 10.84] p<0.01 and 2.34 95%CI [-0.37, 5.05] p= 0.09) respectively for systolic and diastolic pressure. Girls had a higher mean diastolic pressure than boys (2.20, 95%CI [0.69, 3.72] p= 0.01).

Childhood wasting and adolescent blood pressure

As shown in table 13, compared to children who were normal in the entire follow-up, those who were wasted from childhood to adolescence had lower mean systolic blood pressure (-7.90 95%CI [-14.52-1.28], p= 0.02) and also lower mean diastolic pressure (-3.92 95%CI [-7.42, -0.38], p= 0.03). In contrast, those who were initially wasted but recovered from wasting had higher mean blood pressure compared to the normal children (1.93, 95%CI (0.11, 3.74] p=0.04). Becoming wasted later in life was associated with lower systolic pressure. Other factors independently associated with blood pressure among the adolescents were; tribe other than the indigenous (Muganda), associated with lower mean systolic blood pressure (-2.68 95%CI [-4.99, -0.45] p= 0.02).

Effects of stunting or wasting on schooling

Compared to normal children, those who remained stunted up to adolescence achieved less schooling years (-2.82, 95%CI [-5.48 -, -0.70] p=0.04). But among those who recovered from stunting or those who developed it later, no association was observed with schooling. Children who reported physical activity four or more times a week achieved less years of schooling (-2.28 [-4.42, -0.14] p= 0.04).

Children who were wasted from childhood to adolescence had fewer schooling years (-1.91 95%CI [-4.51, 0.68] p=0.04). Those who recovered from wasting or developed wasting later had also fewer school years; (-2.05 95%CI [-3.30, -0.79] p<0.01) and (-1.50, 95%CI [-3.17, 0.18]p= 0.08) respectively. Alcohol consumption also had a borderline negative correlation with school achievement (-1.64, 95%CI [-3.45, 0.15] p= 0.07).

4.5 CHILDHOOD WITH PEM AND ADOLESCENT BLOOD PRESSURE AND SCHOOLING

Table 11: **Distribution of adolescent cardiovascular disease risk factors and schooling outcomes by nutritional status**

Nutritional status		Mean Blood pressure (mmHg)		Mean Lipid level (mmol/L)				Glycaemia	Schooling
	Number	Systolic	Diastolic	TC	TGs	HDL-c	LDL-C	HBA1c	_Years
Height- for- age		Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)
Normal	261	119 (12.0)	70.4 (8.3)	3.6 (1.0)	1.2 (0.7)	1.0 (0.4)	2.0 (0.8)	3.8 (1.3)	9.0 (8.8)
Stunted	93	115 (11.5)	68.9 (8.8)	3.7 (0.9)	1.2 (0.5)	1.0 (0.3)	2.1 (0.7)	3.7 (0.6)	5.8 (3.0)
Recovered	295	118 (11.2)	70.1 (8.5)	3.7 (1.0)	1.2 (0.6)	1.0 (0.4)	2.1 (0.8)	3.7 (0.7)	8.4 (6.4)
Deteriorated	275	118 (11.9)	69.8 (8.5)	3.5 (0.9)	1.1 (0.5)	1.0 (0.4)	2.0 (0.7)	3.7 (0.6)	8.5 (11.5)
Weight- for - height									
Normal	464	118 (12.3)	70 (8.1)	3.6 (1.0)	1.2 (0.6)	1.0 (0.4)	2.1 (0.8)	3.7 (1.1)	9.2 (11.0)
Wasted	12	111 (9.2)	67 (4.2)	3.8 (1.1)	1.1 (0.5)	1.2 (0.4)	2.1 (0.9)	3.6 (0.5)	6.2 (2.5)
Recovered	145	119 (9.7)	72 (8.4)	3.7 (1.0)	1.2 (0.6)	1.0 (0.4)	2.1 (0.8)	3.7 (0.7)	7.8 (3.8)
Deteriorated	307	117 (11.2)	69 (8.2)	3.5 (0.9)	1.2 (0.5)	1.0 (0.4)	2.0 (0.7)	3.7 (0.6)	7.6 (6.3)
Experienced Both[1]									
Normal	269	117.7 (12.4)	69.8 (7.9)	3.6 (0.9)	1.2 (0.7)	1.0 (0.4)	2.0 (0.7)	3.7 (1.2)	9.8 (13.0)
Recovered	20	118.8 (9.7)	72.7 (8.8)	3.7 (1.0)	1.2 (0.5)	1.0 (0.4)	2.1 (0.7)	3.5 (0.5)	7.8 (4.2)
Never recovered	37	117.3 (10.3)	71,3 (8.3)	3.7 (1.0)	1.1 (0.5)	1.1 (0.4)	2.1 (0.8)	3.6 (0.6)	8.0 (3.3)

[1]Experienced both wasting and stunting

Table 12: **Association between childhood stunting and blood pressure, and school achievement during adolescence (multivariate analysis)**

Characteristic	Systolic blood pressure mmHg		Diastolic blood pressure (mmHg)		Education attained (years)	
	Coefficient (95%CI)	p-value	Coefficient (95%CI)	p-value	Coefficient (95%CI)	p-value
Height- for- age change						
Normal	1		1		1	
Stunted all through	-2.90 (-6.41 , 0.61)	0.10	-0.23 (-2.70, 2.22)	0.85	-2.82 (-5.48, -0.70)	0.04
Stunted but recovered	0.67 (-1.66 , 3.00)	0.57	0.19 (-1.55, 1.92)	0.83	-1.04 (-2.97, 0.90)	0.29
Normal but later stunted	0.99 (-1.84, 3.84)	0.49	0.15 (-1.56, 1.87)	0.86	-0.12 (-2.09, 0.86)	0.90
Age groups (years)						
13-14	1		1		1	
15-16	0.67 (-1.66, 3,00)	0.57	'-0.43 (-2.10, 1.23)	0.61	3.75 (1.91,5.56)	<0.01
17-18	0.99 (-0.92, -1.84)	0.49	0.60 (-1.35, 2.50)	0.54	4.91(2.79,6.87)	<0.01
Sex						
Male	1		1		1	
Female	-0.36 (-2.23, 1.50)	0.70	2.20 (0.69, 3.72)	0.01	0.87 (-0.69, 2.42)	0.28
Education						
Incomplete primary	1		1			
Completed primary	2.13 (-0.59, 4.85)	0.12	0.02 (-1.89, 1.94)	0.98		
Post primary	-0.06 (-2.51, 2.46)	0.98	-0.42 (-2.2, 1.37)	0.65		
Tribe						
Muganda	1		1		1	
Other	-2.14 (-4.40, 0.12)	0.06	-0.24 (-1.94, 1.46)	0.27	1.17 (-0.61, 2.95)	0.19
Wall type						
Concrete and brick	1		1		1	
Mud and brick	1.49 (-1.38, 4.37)	0.31	-1.18 (-2.91, 0.54)	0.17	0.08 (-1.98,-2.16)	0.87
Mud and pole	0.65 (-1.44, 2.85)	0.54	-0.28(-1.83, 1.27)	0.72	0.23 (-1.43, 1.90)	0.78
Reported alcohol consumption						
No	1		1		1	
Yes	6.57 (2.30, 10.84)	<0.01	2.34 (-0.37, 5.05)	0.09	-1.15 (-3.30, 1.01)	0.29
Physical activity per week						
None	1		1		1	
One to three times	1.17 (-1.51, 3.86)	0.39	0.33 (-1.50, 2.17)	0.72	-1.38 (-3.38, 0.62)	0.17
4 or more times	0.12 (-2.58, 2.83)	0.92	1.34 (-0.57, 3.26)	0.17	-2.28 (-4.42, -0.14)	0.04

Table 13: Association between childhood wasting and blood pressure, and school achievement during adolescence (multivariate analysis)

Characteristic	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Education attained (years)	
	Coefficient (95%CI)	p-value	Coefficient (95%CI)	p-value	Coefficient (95%CI)	p-value
Weight- for- height change						
Normal	1		1		1	
Wasted all through	-7.90 (-14.52 ,-1.28)	0.02	-3.92 (-7.42, -0.38)	0.03	-1.91 (-4.51, 0.68)	0.04
Wasted but recovered	-0.12 (-2.52 , -2.27)	0.91	1.93 (0.11, 3.74)	0.04	-2.05 (-3.30, -0.79)	<0.01
Normal but later wasted	-1.88 (-3.97, 0. 21)	0.08	'-0.77 (-2.11, 0.26)	0.28	-1.50 (-3.17, 0.18)	0.08
Age groups (years)						
13-14	1		1		1	
15-16	1.42 (-0.85, 3,70)	0.22	-0.16 (-1.70, 1.38)	0.84	3.71 (2.14,5.28)	<0.01
17-19	190 (-0.92, 4.71)	0.19	0.61 (-1.28, 2.50)	0.53	4.99 (3.11,6.87)	<0.01
Sex						
Male	1		1		1	
Female	-0.60 (-2.39, 1.18)	0.51	1.78 (0.36, 3.21)	0.01	0.91 (-0.37, 0.16)	0.16
Education						
Incomplete primary	1		1			
Completed primary	2.22 (-0.52, 4.96)	0.11	0.19 (-1.67, 2.05)	0.84		
Post primary	0.06 (-2.37, 2.49)	0.96	-0.26 (-2.02, 1.48)	0.76		
Tribe						
Muganda	1		1		1	
Other	-2.68 (-4.99, -0.45)	0.02	-0.85 (-2.36, 0.66)	0.27	1.13 (-0.81, 3.07)	0.25
Wall type						
Concrete and brick	1		1		1	
Mud and brick	2.30 (-0.52, 5.12)	0.11	-0.14 (-1.79, 1.50)	0.86	0.16 (-1.80,-2.11)	0.87
Mud and pole	0.74 (-1.34, 2.85)	0.49	-0.25 (-1.74, 1.24)	0.74	0.40 (-1.19, 2.00)	0.61
Reported alcohol consumption						
No	1		1		1	
Yes	4.51 (0.46, 8.57)	0.02	1.31 (-1.13, 3.99)	0.28	-1.64 (-3.45, 0.15)	0.07

4.6 MOBILE PHONE HEALTH TEXT MESSAGES AS AN INTERVENTION

Between April 2014 and November 2015, a total of 588 pregnant women were registered by CHWs in the 26 villages; 63 were excluded because they were non-resident, leaving 525 to be followed from registration to delivery. The mothers were enrolled at a mean gestation age of 6.3 (SD=1.4) months. In 13 intervention villages, 262 women were registered, while 263 were registered in the 13 control villages. The majority (80%) of the women were below the age of 35 years. There were some differences in the characteristics of women in intervention and control villages; women in the intervention village had better education (47.5% had attained post primary education compared to 28.6% in control villages), lived closer to health facilities (61.0% lived within a distance of two kilometers from a health facility compared to 27.8% in control villages). Although the text messages were sent only to the women in the intervention villages through their respective village health workers, it turned out that information "leaked" to more than 40% of the women in the control villages.

Effect of mobile phone text messages on choice of delivery place

When the 525 pregnant women were interviewed post-partum to ascertain the place of giving birth; 442 (84.2%) reported that they delivered in a health facility, while 18 (3.4%) reported delivering at home under the supervision of a traditional birth attendant, 54 (10.3%) delivered at home with the help of a relative or a friend and 11 (2.1%) delivered alone without any help.

Factors associated with home deliveries

Over all, there were fewer homebirths among women in the intervention villages compared to those in control villages (9.2% versus 22.4%). A higher proportion of homebirths was observed among older women (>35 years), women from non-indigenous ethnic groups, women with primary or no education, muslims and women living two or more kilometers away from a health facility.

In the bivariate analysis, homebirths were associated with age more than 35 years (OR=1.89, 95%CI [1.01-3.53]), belonging to a tribe other than Buganda tribe (OR=1.70, 95%CI [1.01-2.85]), muslim religion (OR=1.77, 95CI [1.03-3.03]), primary or no education (OR=3.01, 95CI [1.69-5.36]), living at least two kilometers away from a health center (OR=2.94, 95%CI [1.69-5.10]), and not receiving a health text message from a community health worker (OR=1.61, 95CI [0.99-2.62]) . After adjusting for correlations within households and village controlling for age, education level, tribe, distance from a health facility and the calendar period when birth occurred, being in the intervention arm was associated with lower odds of delivery at home (AOR=0.38 , 95%CI [0.15-0.97]). Muslim religion (AOR= 4.0, 95%CI [1.72-9.34]) and primary or no maternal education (AOR= 2.51, 95%CI [1.00-6.35]) were independently associated with homebirths. There was some evidence of association of homebirths with a distance of more than 2 km from a health facility (AOR=2.26, 95%CI [0.95-5.40]). Receiving a text message from a village health worker (AOR= 0.50, 95%CI [0.22-1.12]) and a woman’s age>35 years (AOR=0.46, 95%CI [0.19-1.09]) showed some association with lower odds of home delivery (table 14).

Comparison of child mortality in the intervention and control villages

In a sub-analysis, we looked at the effect of the health text message intervention on mortality of children in their first year of life.

In total, 379 births were registered by the village health workers between January 2015 and November 2015, and within this period 28 of these children died; 12 died out of 191 in the intervention villages (63 per 1000 live births) and 16 died out of 188 in the control villages (85 per 1000). Within 24 hours of birth 10 babies died with five deaths in the intervention village (26 per 1000) and also five deaths in the control villages (27 per 1000).

Table 14: Factors associated with home deliveries among pregnant women in rural south-western Uganda (2014-2015)

Characteristics	Home delivery N (%)	Unadjusted OR (95%CI)	Adjusted OR (95%CI)	p-value
Study villages				
Control arm	59 (22.4)	1	1	
Intervention arm	24 (9.2)	0.35 (0.21-0.58)	0.38 (0.15-0.97)	0.04
Age group (years)				
15-24	34 (15.5)	1	1	
25-34	29 (12.9)	0.81 (0.47-1.38)	0.87 (0.25- 2.99)	0.84
>35	20 (25.6)	1.89 (1.01-3.53)	0.46 (0.19-1.09)	0.08
Tribe				
Muganda	57 (14.5)	1	1	
Other	26 (22.4)	1.70 (1.01-2.85)	2.07 (0.78-5.48)	0.14
Religion				
Roman catholic	38 (13.1)	1		
Muslim	28 (21.1)	1.77 (1.03-3.03)	4.00 (1.72-9.34)	<0.01
Other	5 (17.2)	1.38 (0.50-3.84)	0.23 (0.03-1.99)	0.18
Education level				
Post primary	16 (8.3)	1	1	
None or primary	67 (21.3)	3.01 (1.69-5.36)	2.51 (1.00-6.35)	0.05
Distance from nearest health center				
< 2km	19 (8.7)	1	1	
≥ 2km	60 (21.8)	2.94 (1.69-5.10)	2.26 (0.95-5.40)	0.07
Received text message				
No	32 (12.9)	1	1	
Yes	49 (19.2)	0.62 (0.38 -1.01)	0.50 (0.22-1.12)	0.09
Calendar period of delivery				
Apr-Dec 2014	25 (12.5)	1	1	
Jan-Nov 2015	45 (17.6)	1.49 (0.88-2.53)	0.75 (0.33-1.77)	0.52

5 DISCUSSION

5.1 MAIN FINDINGS

This thesis analyzes age-specific child survival prospectively in a rural self-sustaining subsistence farming population in Uganda, relating child mortality to a registration of the pregnant mothers and their attributes and social environment. The children's anthropometric nutritional status assessments up to 5 years of age and later developmental progress into adolescence along with educational achievements and established risk factors for future cardiovascular disease were measured. The mortality risk factor analysis informed the design and implementation of a community based intervention to improve uptake of maternal and child health services.

The probability of survival to 5 years of age corresponded to a childhood mortality rate of 92 per 1000 live births, this mortality declining by approximately one third between 2002 and 2012. Most of the decline happened at the ages 1-12 months, whereas no corresponding tendency was observed for the neonatal period or for stillbirths. Child survival was negatively associated with birth at home, short birth intervals, high parity, and an unmarried mother. There was an association between PEM, defined by stunting and wasting during childhood and fewer year of schooling, as reported in adolescence. The relationship between PEM early in life on one hand and cardiovascular disease risk parameters at adolescence on the other hand tended to show no association with lipid profiles and glycemic control but being stunted or wasted in early life showed an association with lower blood pressure in adolescence. In contrast, recovery from wasting showed a rise in blood pressure denoting a higher cardiovascular disease risk among survivors who recovered from wasting.

A feasibility study informed by the mortality risk factor analysis, demonstrated that spreading pregnancy-stage-relevant messages to the pregnant women has a strong impact on the uptake of professional delivery care in a rural setting.

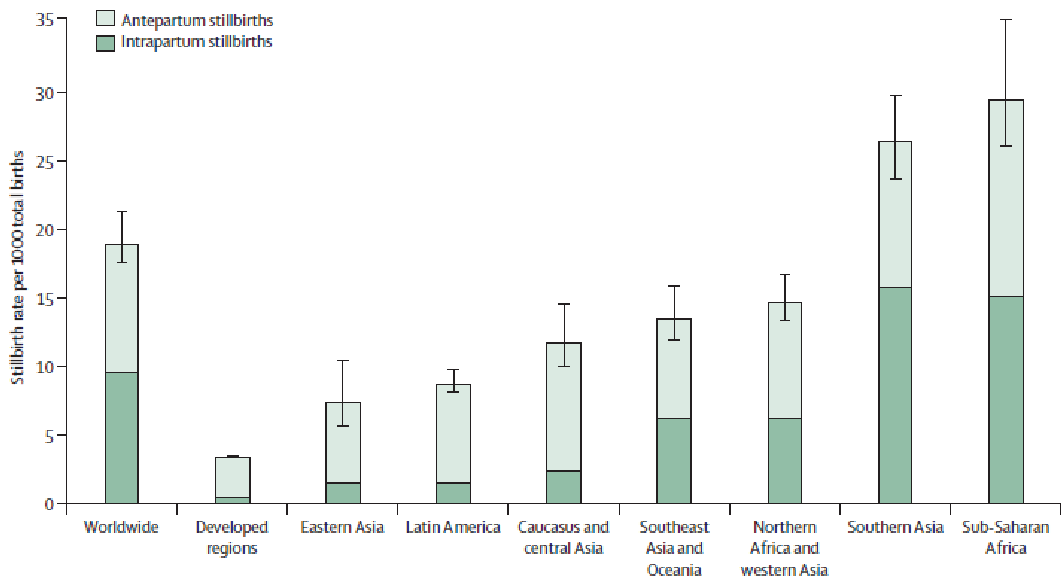
Child mortality trends

The mortality decline of 33% that we observed in the rural population in Uganda is lower than the national decline of 53% reported in the corresponding period (UNICEF et al., 2013a). Most of the decline in mortality was observed among infants in the post-neonatal period. Consistent with findings elsewhere (UBOS, 2012, Titaley et al., 2008, Gizaw et al., 2014), early neonatal mortality did not show any reduction in the entire study period (2002-2012). The neonatal mortality rate of 36/1000 is close to the 34/1000 reported in a rural community in Eastern Uganda but higher than the national average of 27/1000 reported in 2011 (Nankabirwa et al., 2011, UBOS, 2012). This suggests that mortality among neonates is higher in rural areas compared to the urban areas, contrary to the 2011 Uganda Demographic and Health Survey (UDHS) results that showed no difference in neonatal mortality between rural and urban areas (UBOS, 2012). According to the UN IGME report of 2015, Uganda is among the few African countries that met the MDG-4 target of reducing child mortality by two thirds between 1990 -2015. In order to meet this target a 4.9% annual rate of mortality reduction had to be achieved at the national level. In the rural population where we conducted the study, the annual rate of mortality reduction in the corresponding period was only 3.0%. It is therefore unlikely that rural populations reached the MDG-4 target. Depending on a national mortality estimate may generalize findings and mask important differences within countries especially between rural and urban communities or poor and wealthy communities. Understanding context specific mortality and associated determinants is crucial in tailoring appropriate interventions. The transition from MDG to SDG goals comes with ambitious SDG-3 sub-targets including reduction of under-five mortality to less than 25/1000 and neonatal mortality to less than 12/1000 by 2030 by all countries (UNDP, 2016). Meeting the new targets will require more focus on high mortality populations and in this regard rural communities and neonatal mortality are urgent priorities in low income countries.

Stillbirths in rural Uganda

During the MDG era, an estimated 2.6 million stillbirths were not included in the targets yet; 50% of stillbirths were reported to have occurred during delivery with similar causes to newborn deaths (Cousens et al., 2011). Maternal, newborn interventions cannot therefore be separated from stillbirth interventions. Thus, at the launch of the Every New-born Action Plan (ENAP) in mid-2014 (WHO and UNICEF, 2014), stillbirths were included among the 2030 targets for child survival. A target of 12 or fewer stillbirths per 1000 births was set to be achieved by all countries. However, despite increasing advocacy and research efforts in countries with high stillbirth burden, scanty data are available from such settings. We included stillbirth rate estimate in our study to close this information gap in a rural population in Uganda. Our population based data derived from serial surveys among women of reproductive age, conducted between 1996 and 2013, found a high stillbirth rate of 26.2 per 1000 births falling within the national stillbirth rate estimate with no substantial decline observed (Blencowe et al., 2016). These figures place Uganda among a group of high mortality countries. The slow decline in stillbirth rate over time is consistent with the global decline by 14% and 8% in Africa between 1995 and 2009 (Cousens et al., 2011). A recent Lancet series “Ending preventable stillbirths” (de Bernis et al., 2016) estimated that 98% of 2.6 million stillbirths reported in 2015, were from middle and low income countries. Sub-Saharan Africa bears the biggest burden of stillbirth amounting to 28.7/1000 births with 60% from rural communities and 50% as intra-partum stillbirths (figure7). Compared to under-five mortality, neonatal mortality and early neonatal mortality, stillbirths presented the least annual rate of reduction (Lawn et al., 2016).

In communities with the highest mortality burden (25 or more stillbirths per 1000 births), about half of births take place at home and quality of care is low at health facilities, supplies and healthcare staff are often lacking. The utmost priority in such populations is to link mothers to the healthcare system to receive professional care including skilled birth attendance and this has the greatest effect on maternal and neonatal deaths, and on stillbirths. The 2011 Uganda Demographic and Health Survey showed that only 48% of pregnant mothers completed the four recommended antenatal visits and only 40 % gave birth in health facilities in rural south western Uganda (UBOS, 2012). In our study population, facility births increased marginally from 53%-64% in a decade (2002-2012) and thus the high stillbirth rate. Stillbirth reduction in this setting will require increasing efforts in scaling up facility births and improving the quality of maternal health services.



	Worldwide	Developed regions	Eastern Asia	Latin America	Caucasus and central Asia	Southeast Asia and Oceania	Northern Africa and western Asia	Southern Asia	Sub-Saharan Africa
Estimated stillbirth rate per 1000 total births (uncertainty range)	18·4 (16·6–21·0)	3·4 (3·4–3·5)	7·2 (5·6–9·7)	8·2 (7·5–9·2)	11·9 (9·8–15·6)	12·2 (10·7–14·6)	14·5 (12·9–17·6)	25·5 (22·5–29·1)	28·7 (25·1–34·2)
Number of stillbirths	2620000	46700	129000	91000	23400	154900	148300	966600	1059700
Estimated intrapartum stillbirths	49·6%	10·0%	19·9%	16·8%	19·9%	45·7%	42·0%	59·3%	51·1%
Stillbirths in rural areas*	58·9%	23·0%	43·8%	24·9%	58·9%	54·5%	41·8%	65·5%	61·8%
Stillbirths born in health facilities*	61·2%	99·4%	99·5%	89·3%	97·1%	79·6%	81·5%	58·8%	49·0%

Fig 7: Regional variation in stillbirth rates and the proportion of intrapartum stillbirths in rural and urban communities 2015

Source: (Lawn et al., 2016)**.**

Factors associated with under-five mortality

We found a higher risk of mortality among children who were delivered at home which is consistent with earlier findings (Zhang et al., 2013, Nankabirwa et al., 2011, Van Den Broeck et al., 1996). In our own study area, facility births increased from only 54% to 63% (Asiki et al., 2015b) between 2002 and 2012. The direct impact of not seeking professional care during delivery is that risk factors and complications are not identified in time during the critical period of birth. Babies are thus exposed to birth trauma, asphyxia, and sepsis that can lead to death in the first days of life. Delivering a baby under the supervision of a professional health worker directly improves the level of care to the mother and baby during delivery, thus better survival. It has also been shown that mothers who deliver in health facilities are more likely to use other health services such as vaccinations, and adhere better to health advice (Zhang et al., 2013, Babirye et al., 2012) thus indirectly impacting on child survival.

Other factors that we found to be associated with under-five mortality included maternal factors such as short birth intervals, high parity, and marital status. Hobcraft et al in the 1980s conducted an analysis of DHS datasets from 17 countries and showed that child mortality decreased with increasing birth interval length up to 36 months and thereafter plateaued (Hobcraft et al., 1983). These findings were reproduced recently from an analysis of 47 DHS data sets which also confirmed that a shorter birth interval is associated with child mortality (Kozuki and Walker, 2013). In our study, children with a preceding birth interval of 1-2 years survived better than those with less than one year. It has been postulated that a biological mechanism might explain why a short birth interval is associated with child mortality. Maternal depletion syndrome has been advanced as the possible physiological mechanism leading to increased risk of child mortality based on studies conducted in Sweden, Hungary and USA (Miller, 1991, Winkvist et al., 1992). It is assumed that repeated pregnancies and close spacing negatively affect the nutritional status of women leading to poor future reproductive outcomes such as low birth weight and infant mortality. However, this hypothesis has been disputed by other studies including a study conducted in rural Uganda which showed that early pre-pregnancy nutritional status rather than cumulative nutritional depletion from frequent births was responsible for the negative reproductive outcomes (Winikoff and Castle, 1987). An alternative explanation from a social perspective views close spacing of children as a source of competition for finite resources leading to poor nutritional status and poor access to services , thus high mortality (Garg and Morduch, 1996). We controlled for socio-economic status in our analysis, however considering that we used proxy sources of data to estimate household income, we could not demonstrate such an association.

Our study also showed that mortality doubled among children born to women with a parity of more than four compared with those with lower parity. This is in agreement with a recent publication based on DHS data analysis from 10 countries that showed that utilization of maternal and child health services decreases as birth order increases (Sonneveldt et al., 2013). Institutional delivery and skilled birth attendance were the two most important maternal factors whose utilization reduced with increasing parity of mother. For all the ten countries in the analysis, women with low parity were more likely to seek health facility delivery and/or be attended to by skilled personnel than those with a parity of 10 or more. A high parity may limit attendance of professional services because of limited resources to handle several pregnancy demands or women feeling more confident with managing their own delivery as they feel more experienced with increasing parity.

Marital status of a mother also emerged as a risk factor for child mortality. Children born to mothers who were not married had a two-fold higher risk of mortality than those born to married mothers, a finding similar to that reported in Ghana showing that married women had 27% less risk of child death than those who were not married (Kanmiki et al., 2014). Married mothers are more likely to get support from their partners especially when seeking health care compared to single mothers. Additionally married mothers may pool resources with their partner to improve the provision of nutrition and healthcare services to their children, thus achieving better survival chances for their children.

Factors associated with stillbirths

Regarding stillbirths, we found an association with increasing maternal age and a reduction in stillbirths with increasing parity. Globally, advanced maternal age has been cited as stillbirth risk factor accounting for 6.7% of stillbirths (Lawn et al., 2016). In a study in rural India, stillbirth rate was twice among women 40 years or older compared to that among women aged 20 to 24 years (Sidhu, 1994). In Latin America, women older than 35 years had a stillbirth rate of 31/1000 compared to 16/1000 among younger women (Feresu et al., 2005). These findings are not exclusive to middle and low income countries. A study in the US showed that increasing maternal age is associated with an increased risk of unexplained stillbirth (Fretts et al., 1995). In our study, the stillbirth risk doubled with every addition of ten years to the mother's age after the age of 30 years.

Literature on the association of parity with stillbirth has not been conclusive. Some studies have shown increasing parity to be associated with stillbirth while other studies have cited primiparity as a risk factor (Fretts et al., 1995). Our study findings are in agreement with the latter, showing that increasing parity was associated with a decrease in stillbirths.

Child survival in an area with a high prevalence of protein energy malnutrition

Studies tracing children who survive beyond the age of five years are very rare in the African continent yet it is important to understand how children progress to adulthood especially in the context of exposure to PEM in the critical period of their growth. We had the unique opportunity of a longitudinal dataset to test this hypothesis in a low income country where the dynamics of recovery from malnutrition may be different from those observed in high income countries. We observed that 40% of children who survived beyond the age of five years had experienced stunting and 15% had experienced wasting when they were below five years of age. We tracked these children up to the age of adolescence. Only one third had recovered from protein energy malnutrition and an additional one third of children who were initially normal became malnourished later. We found differences in cardiovascular disease risk profiles among these different categories of children who experienced malnutrition.

Contrary to earlier findings elsewhere (Cohen, 2004, Clemente et al., 2012, Barker et al., 2009), our study found that PEM in childhood per se did not stand out as a risk factor for later cardiovascular disease risk during adolescence. Instead, adolescents who were wasted or stunted throughout their follow-up period had lower mean blood pressure compared to those who did not experience any form of PEM. However, a group of adolescents who had recovered from wasting had a higher mean diastolic pressure than those who had never been wasted or remained thin possibly associated with a higher cardiovascular disease risk in the former group. This observation is in agreement with the idea that recovery from PEM is more important for cardiovascular risk development than is PEM itself. Thus, a Finish birth cohort that was followed from 1944 to 2005 showed that coronary heart disease was predicted by the rate of childhood weight gain rather than by body size at any particular age (Barker et al., 2009). Schulz, in 2010 also observed that abrupt and large changes in nutritional conditions after exposure to a prolonged period of nutritional stress were more important in cardiovascular disease risk development than a one-off nutritional deprivation at any age (Schulz, 2010). We speculate that this is analogous to the contrasting findings of the Leningrad Siege Study in Russia and Dutch Hunger Winter study in Holland (Roseboom et al., 2001, Stanner and Yudkin, 2001). When the German Nazis in the winter and spring of 1944 restricted food rations to people including pregnant women and infants in Netherlands following a railway strike, they had a short period of starvation which was later followed by a prosperity and abundance of food after the world war. Meanwhile in Russia German armies besieged Leningrad, preventing food supplies from reaching the city, between September 1941 and January 1944 and had a more prolonged period of starvation. The Leningrad Siege Study found no difference in adult glucose tolerance, blood pressure and lipid concentration among subjects exposed and unexposed to starvation in utero or during infancy (Stanner and Yudkin, 2001). In contrast, the Dutch Hunger study, found a strong association between early exposure to starvation and adult cardiovascular risk (Roseboom et al., 2001). One major difference between these two populations was that the Russians continued to experience shortage of food in the Leningrad Siege Study while the Dutch were able to quickly return to a normal diet. Our observations seem to support a similar discrepancy between groups sharing one and the same environment. All other groups of children who experienced malnutrition in our study did not seem to have any cardiovascular disease risk but rather those who recovered from wasting. An underlying biological mechanism referred to as compensatory growth has been proposed to explain how recovery from malnutrition could lead to cardiovascular disease risk. One suggestion is that a higher rate of cell division at recovery, leads to rapid shortening of telomeres which hastens cell death and organ degradation (Hales, 2001, Barker et al., 2002).

Association between childhood protein energy malnutrition and schooling

We demonstrated that childhood malnutrition had a statistical impact on school achievements, consistent with findings from several studies that have shown a negative association between PEM and school grade attainment, cognitive development and social status in general (Casale et al., 2014, Chang et al., 2002, Christensen and Adair, 2003, Bork et al., 2015, Crookston et al., 2013, Fink and Rockers, 2014, Hall et al., 2001). A study in Uganda conducted in1970-1971, among adolescents aged 11-17 years who had suffered from severe PEM before the age of 27 months showed evidence of intellectual impairment (Hoorweg, 1976). The study found chronic malnutrition rather than acute malnutrition to be related to intellectual impairment. In contrast, we found that regardless of the form of PEM, children with any documented exposure to PEM had attained fewer years in school compared to normal children. A possible biological mechanism to explain these findings is pathological changes to the brain resulting in structural permanent damage (Levitsky and Strupp, 1995). Yet, there is the possibility of reverse causality with educational traditions and coping ability (which may "run in the family") being important causes of PEM, thus the association suffers from the-causality dilemma of chicken-or-egg.

While our focus was on effects of PEM on adolescent cardiovascular disease risk and school achievements, female gender and alcohol consumption stood out as independent risk factors for both school attainment and cardiovascular diseases. Adolescent girls had a higher risk of cardiovascular disease and better school achievements than boys perhaps because of an earlier growth spurt resulting from hormonal changes in adolescence occurring earlier in girls and for the same reason girls had faster physical growth and cognitive development than boys. Thomas DiPrete and Claudia Buchmann provided compelling evidence based on large data bases of a multi-racial population in the US that girls perform better than boys especially in terms of grades over the life course (DiPrete and Buchmann, 2013).

Alcohol consumption negatively influenced schooling and increased cardiovascular disease risk. As observed earlier in the same population among adults, ethnic differences also showed influence on cardiovascular disease risk. Individuals from tribes that migrated into the study area had lower mean blood pressure compared to the indigenous Baganda perhaps due to genetic differences. We have previously observed ethnic differences for lipid profiles in the same population (Asiki et al., 2015a).

Integrated community based maternal and child health intervention

In the Lancet series, “Stillbirths: how can health systems deliver for mothers and babies?” it was estimated that if all women gave birth in health facilities offering high quality services, 27% of stillbirths, 46% of maternal deaths, and 18% of neonatal deaths could be averted (Pattinson et al., 2011). We therefore established an intervention to improve uptake of health facility delivery in rural Uganda through supporting community health workers with tailored health text messages to pregnant women relayed via mobile phones. The CHWs were able to deliver the messages to 60% of pregnant women registered in the study. An additional 40% of mothers accessed the messages from peers. A substantial reduction in home delivery was observed as a result of this intervention. Unlike the cluster randomized trial conducted in Zanzibar among mothers attending antenatal clinic (Lund et al., 2012a), we recruited pregnant women from their homes and sent text messages through the phones of the CHWs who in turn visited the mothers to deliver the message. This enabled us to reach women who did not own phones and the most vulnerable in rural communities. This adds to the dearth of literature for mHealth interventions targeting maternal, newborn and child health in low–and middle–income countries highlighted in a recent systematic review (Hurt et al., 2016). The pregnant women most likely attached more value to the gestational-age-relevant messages conveyed to them by the CHWs, than to general pregnancy health messages: thus the higher uptake of services. Although uptake of services improved, no difference in the first 24 hours’ mortality was discerned in this study. Besides lack of sufficient numbers of newborn deaths for this comparison, there is a high possibility that equipment and skills required to handle neonatal conditions are lacking in the facilities (Kruk et al., 2016).

One other important aspect of the study was that we were able to specifically demonstrate that CHWs could use a smartphone application (doForms, Cranford, USA) to register pregnant women. We have found no account of a digital questionnaire on a mobile phone being tested before as a tool for CHWs. When compared with paper forms, the quality of data collected onto the "smartphones" was within acceptable limits and it was very encouraging to find that numeric responses entered had a high level of agreement with paper form entries. Improvement in completeness and quality of data collected by CHWs is one important aspect of child health that requires continuous investments to improve child survival.

5.2 PUBLIC HEALTH IMPLICATIONS

Closing information gap on child mortality in rural population

This thesis has provided an opportunity to critically appraise and use data collected by lay community health workers for estimating under-five mortality in a rural population where data are scarce yet highly needed for planning public health interventions. According to the 2014 national census 80% of Uganda's population lives in rural areas and approximately 7 million are children under five years. Since health utilization is low in rural communities, facility reports are not representative of actual burden of mortality in the communities. Population level data on child mortality trends and determinants provides more relevant data for public health action.

We identified three modifiable maternal factors including non-attendance of professional health services during pregnancy and childbirth, high parity and short birth intervals as the major drivers of under-five mortality. This informed the design of a community based intervention that mainly targeted promotion of health services through community health workers. An increase in uptake of health services was demonstrated through an intervention that is scalable to improve child survival in rural populations.

Evidence of chronic effects of childhood PEM

Uganda is among the countries with the highest burden of childhood malnutrition. We did show that close to half the children in this rural population are exposed to some form of malnutrition before their fifth birthday and another one third experienced it later. Survival with malnutrition to adolescence is associated with development of cardiovascular disease especially following recovery. Meanwhile both wasting and stunting were associated with fewer years of schooling . We therefore stress the benefits of preventing malnutrition beyond child survival. The Uganda ministry of education and sports acknowledges the role of nutrition in promoting and improving physiological growth, school enrolment, learning and overall cognition and therefore issued guidelines for school feeding programs (MoES, 2015). Our findings provide further evidence to support these guidelines and it is important to highlight here that universal feeding programs will suffice since close to half of the children experience malnutrition in rural populations.

Role of community health workers in improving community health data

This thesis also highlights the successful engagement of community workers in community based registration of pregnancies, births and deaths that improved the establishment of population denominators and follow-up of mothers and children. This information is crucial for improvement of health programs in rural populations. Most districts in Uganda rely on projected populations to measure health indicators. This has often led to an overestimate of uptake of services. For example vaccination coverage estimated in the district where the study is located is much higher than the estimates from our population. Community health workers are available in almost every district in Uganda and could be a very good resource to improving community level data collection. The aspect that makes this very appealing is their ability to use phones for registration and to follow-up pregnant mothers.

5.3 METHODOLOGICAL CONSIDERATIONS

Generalizability

Generalizability refers to the extent to which results from a population studied are applicable to a larger population or other settings. These studies were conducted in a rural population in Uganda in a Health Demographic Surveillance System (HDSS). Study 1 used census, vital registration and survey data enrolling the entire population and all children. Study II enrolled all women of reproductive age in the study area. Study III followed all children from birth or entry into the study and below age of five years to adolescence. Meanwhile study IV followed all pregnant women in the study area. All the four studies had sufficient sample sizes to represent the study area. However, the study findings may not be representative of the national or a typical rural population in Uganda on two major grounds. First, the location of the study area in one part of the country with one major ethnic group, the Baganda. Uganda has more than 50 ethnic groups and the Baganda constitute 17% of the country's population. In our own studies we have shown that ethnicity is a determinant of disease outcomes or health services uptake. Secondly, the population has been surveyed for 27 years and repeated participation could bias findings through selective participation and improvement of health services.

Despite these, our findings are comparable to national estimates. For example for the period 2002-2012, we showed a mortality decline from 96 to 64 per 1000 which is close to the UN IGME national estimate of 147 to 69 per 1000 live births for the corresponding period 2000 to 2012 (UNICEF et al., 2013a). Stillbirth rate in our study was 26.2 per 1000 births compared to national estimate of 25 per 1000 (Blencowe et al., 2016). This comparison of HDSS findings with national data concurs with findings in Ethiopia, where child mortality data obtained from Butajira HDSS were comparable with national DHS data (Byass et al., 2007). Similar comparisons were done in Burkina Faso (Hammer et al., 2006), Mozambique (Nhacolo et al., 2006) and Bangladesh (Bairagi et al., 1997). The major challenge with these comparisons is that the national data were not empirical data and often based on modeling that uses data from various sources including that from the HDSS. A more reliable comparison of local data from counties in Sweden with national data in 1925; at a time when health indicators in Sweden were similar to current indicators in LMIC revealed that mortality data from each of the 19 out of 24 counties were highly correlated with the national data (Byass et al., 2011).

These findings give us the reassurance that HDSS produce results that may be representative nationally, thus the findings from our study could be used to guide national policy. Internationally, data from the study site have contributed to the ALPHA network (Maher et al., 2010) and INDEPTH network (Sankoh and Byass, 2012).

We also observed striking similarities in the age patterns of mortality, PEM, maternal risk factors for child mortality and uptake of health information as observed in several studies, thus our findings may be applicable to other settings.

Recall bias

Most low income countries rely on surveys to retrospectively document vital events. We examined data from several surveys to estimate stillbirths. Comparing stillbirths by asking mothers to recall their pregnancy experience in the past 12 months yielded a higher estimate than a life time experience recall (26 vs. 13). This clearly shows that a long period of recall could grossly lead to omission of stillbirths. The data from a shorter recall period was highly comparable with the national estimates. Some of our data on vaccinations based on maternal recall was subject to recall bias as well, but a high correlation between uptake of facility births and immunizations given to the newborn suggests some reliability of reported vaccinations.

Misclassification bias

It is possible that newborn deaths could have been classified as stillbirths by the CHWs. This could arise from lack of knowledge of CHW in differentiating stillbirths from newborn deaths. Our data shows that 47.2% of the deaths in the first week occurred the first 24 hours of birth, violating the two thirds rule where at least two thirds of deaths in the first week are expected to occur in the first 24 hours. Other possible reasons cited for misclassification of stillbirths include; avoidance of blame, extra work, or audit review for the birth attendant; or cultural reasons of perceived gain or loss for the family (Stanton et al., 2006). The under-reporting of early neonatal deaths is not unique to our population. Even in middle income countries such as Vietnam neonatal mortality rates are under reported by a wide margin of up to 4 times less than the expected rate (Målqvist, 2011).

Bias in registration of pregnancies and peri-neonatal mortality

Follow-up of the outcomes of pregnancies registered in a particular community, from pregnancy recognition, in principle, gives an unbiased account of peri-neonatal child mortality for a specified period of time. Maternal covariates with hypothetical influence can be interpreted in terms of their statistical effect on the survival of the fetus/newborn. This situation is approximated in the analysis of hazard and its covariates (Cox' regression) in paper I. The sources of bias here are mainly violation of the prospective principle (by including newborns who were the result of an unregistered pregnancy) and so called *informative sensoring* (e.g. the family regularly moving out as a social consequence of a child's death). We have not found evidence of any of these sources of error being important in these studies, nor have we found problems with the proportionality assumption underlying Cox' regression technique.

In registering pregnancy outcomes retrospectively, however, sampling bias may distort both size estimates and the statistical effect of covariates. In all societies there are different patterns of fecundity (even women with habitual abortions), and differences of sexual behavior and life-styles between couples. To simplify for the sake of clarity, there are couples who have one pregnancy every 4 years, each resulting in a live birth, and other couples where the woman will have had several pregnancies in the same period of time, some of them interrupted by fetal loss, soon followed by another pregnancy. Women of the latter kind will have a greater likelihood of being included when a researcher asks those of fertile age about their latest pregnancy or interviews the women who report they had a pregnancy that ended in the last 12 months (as we did for paper 2). This bias is hard to estimate numerically and all we can do is keep it in mind when we interpret the data.

Use of secondary data sources

Secondary data refers to data that was collected by someone other than the user, for other research purpose. Some of the secondary data sources include national censuses, DHS, HDSS, hospital records and administrative records. Availability of large sample sizes and low costs of obtaining the data are some of the advantages of using secondary data. However since the study design and methods of data collection are not under the control of the researcher, secondary data may not provide all the information required and accuracy of data is questionable.

Study I relied primarily on secondary data from the HDSS and these include birth and death registers, pregnancy register, census, health surveys and household living conditions including housing and socio-economic status collected over a decade through serial cross sectional surveys. We employed data linkage through use of a unique identification number. We were faced with missing data points especially for participants who were not consistently available in all the databases in the survey rounds. Some variables were not collected every year and sometimes variable names changed. We checked the data for quality and combined various sources before subjecting to analysis. Where data was missing, we imputed values based on available data. For study II, apart from extracting data for women of reproductive age from the adult survey, we also used census data collected in the same years. In 2013, we collected additional data on lifetime pregnancy outcome to compare with the 12 months recall data obtained between 1996 and 2013. This comparison was meant to validate the secondary data. Indeed we found the latter method grossly under estimated. In study III all data on anthropometric measurements were available but only those with an outcome measured in 2011 were included. We did not use secondary data for study IV.

The pitfalls of pragmatic intervention

In study IV we employed a pragmatic intervention to assess the effect of SMS delivered by CHWs to pregnant women on home births. Our original aim was a cluster randomized trial, but with the obvious effectiveness of the messages, this aim was abandoned and a pragmatic approach was preferred. Pragmatic trials approximate reality but are limited by internal validity. Internal validity is the extent to which differences between the intervention and control groups can be confidently attributed to the intervention and not due to some alternate explanation. Adjacent villages were grouped together assigned to the intervention for ease of implementation and to minimize contamination, but this caused an imbalance in the characteristics of the villages in intervention and control arms. For example women in intervention villages had better education and lived closer to health facilities. However, we collected data on these variables and adjusted for these factors during regression analysis to determine the independent effects of the intervention taking potential confounders into account.

Contamination

Contamination refers to receiving of some aspects of the intervention inadvertently by participants in the control group if they are in proximity to the intervention group. We attempted to minimize contamination by clustering adjacent villages together in the intervention arm but there was some leakage into the control arm. Up to 40% of pregnant women also reported receiving information similar to that sent by SMS to women in the intervention village. Information probably leaked through word of mouth from one village health worker to another or between women in some control villages which were adjacent to intervention villages through their social interactions in markets, places of worship (churches and mosques) or even during attendance of antenatal care. There is a high level of social interactions between villages in Uganda because they share social services and kin ties, thus avoiding contamination would require some reasonable geographical distance between intervention and control villages that may be logistically demanding on the study. Still, the exposure to the health messages, including the advice to give birth in the health center and not at home, was probably more widespread and intense in the intervention villages than in those referred to as "control". Leakage of information in this context is beneficial to women who do not own phones. The peer to peer spread of information could be explored further to complement the CHWs efforts.

Limited coverage with the intervention

Differences in terrain and size of village could have affected the ability of CHWs to follow all pregnant women in their own villages thus the modest coverage of 60%. Considering that 40% leakage of information occurred to the control villages, the leakage could have been more within the intervention villages, thus the possibility that the CHWs reached less than 60% of pregnant women in the intervention villages. This may be because only one CHW was assigned per village regardless of village size. However, considering that on average only 20 pregnant mothers were registered and followed per village within approximately one year, other factors such as motivating CHWs to perform better will require further investigation.

Measurement error

We excluded a small number of children who had biologically implausible anthropometric measurements due to either imprecise weight and height measurements or wrong age.

Clustering

A number of children shared the same households and in many instances there were more than one woman of reproductive age in a household. During analysis we addressed clustering through statistical methods such as Generalized Estimating Equations and Random effects model.

Self- reports for uptake of health services

We estimated uptake of antenatal care and facility deliveries based on a self-report. This could be exaggerated by the women. However we triangulated data sources on place of delivery by asking CHWs to also report on the place of delivery and two methods yielded very close figures. A more accurate way to assess uptake of health services should be through the review of health facility information to verify if women reach health facilities at all. However, since there was no linkage identifier between health facilities in the study area and the study population, it would not be possible to use health center records to verify uptake of referrals. The health facilities serving the study population do not use electronic patient records and do not have centralized patient administration.

5.4 CONCLUSION AND RECOMMENDATIONS

As the integrated approach to child health gains ground in both preventive and curative work, DSS such as Kyamulibwa serve as epidemiological field laboratories for formulating and monitoring population level changes. In such settings, the entire population is the sample as opposed to random samples and representativeness rests more on the characteristics of the study area than the statistical tests. The gains of in-depth understanding of population dynamics override the statistical nuances. Accordingly, studies I and II of this thesis did not rely on pre-formulated hypotheses and random samples, but rather research questions derived directly from existing empirical data based on following entire populations of children and women of reproductive age. Despite the inherent limitations of the studies, the findings in this thesis allow the following conclusions relevant for child survival in rural populations.

- Under- five mortality is high in rural Uganda and the age specific mortality pattern is reflective of national trends and closely associated with maternal factors such as short birth intervals, high parity and homebirths.

- While a secular trend seemed to have influenced post-neonatal survival positively in the studied environment, no substantial improvement over time was discerned for perinatal survival, denoting possibly distinct causes behind the observed mortality in the first week of life.

- PEM is widespread among children under five years with a negative association with school achievements in later in life ; calling for a need for special educational support to children with an early experience of PEM.

- The observed structures in the data on PEM in childhood on one hand and risk factors for future cardiovascular disease on the other hand, fit in with the hypothesis that some adaptive mechanisms in malnutrition being negative for the health of the individual after recuperation.

- The power of information technology in changing health seeking behavior of pregnant women towards increased uptake of facility delivery is one key observation that could significantly improve access to maternal and child health services in rural populations.

Lessons learnt

These studies were conducted in an environment of material scarcity and low literacy rate where some traditional ideas coexist with "modern" concepts concerning health, pregnancy and childbirth. Globally, a large proportion of child mortality happens in similar settings with limitations of valid vital statistics. Some of our practical experiences in handling scarce data and attempts to overcome the pitfalls in the process of data collection may therefore be of interest in the following ways.

- Prospective, community based registration of pregnancies, births and deaths by community health workers is feasible and has value
    - as a prerequisite for estimating perinatal mortality correctly and could be improved in low-resource rural setting with low literacy levels.
    - in enabling computation of up-to-date statistics for all age-groups under study (in the form of synthetic cohort life-tables), gives better guidance to interventions than do estimates based on anamnestic data (such as the Demographic and Health Surveys)
    - can be improved and facilitated with the use of modern technology (use of smart-phones with data upload to "the cloud" or local server)
- Health messages can be tailored according to population needs with a high potential to build more community confidence in health services.
- Engaging community health workers to use mobile phones for data collection has the potential to play a significant role in improving the quality and timeliness of community registration of events even in a community with low literacy rate.
- Communty health workers' registration of births should be based on as complete as possible registration and follow up of the pregnant women which could be achieved through an early home-visit and/or collaboration health facility personnel in order to avoid opportunistic or retrospective registration of events that could lead to gaps in death registation in the first 24 hours.
- The distinction between stillbirths and neonatal deaths in the first 24 hours is a challenge to community health workers, thus the need to focus efforts on their training in this area.
- Continuing with broad interventions not focusing on the perinatal period will not change the status of child survival in this critical period. A lacuna of population based data on perinatal outcomes inhibits appropriate policy formulation and planning of focused interventions.
- Ethical principles impose a limitation on controlled trials of interventions in the field; the well-being of the study participants takes priority and an obviously superior intervention must be made available even to the control group (Study IV).

Recommendations

- Establish systems of registration in other rural communities to be led by community health workers equipped with smart-phones making regular home visits to a manageable number of households.
- Develop the linkage of community registration of pregnancies to the ante-natal care services of health facilities in the area to support accurate health information

dissemnation by community health workers through mobile phones (via SMS reminders, showing “how-video clips”). Of particular interest in this aspect is the collection of data remotely and relaying via “the cloud” to a centralised data base.

- In consideration of mHealth for vital registration, electronic registration forms should be designed with minimal text entry to minimise entry errors by CHWs.
- Dissemination of health messages to women through mobile phones mediated by CHWs is feasible and may have a multiplicative effect through peer to peer dissemination. Further research evaluating the use of peer mothers to disseminate SMS health information for improving maternal and child health is needed and child nutrition could be a high priority for this sort of intervention.
- Continued family planning promotion to prevent frequent births and a high parity is a key strategy for prevention of child mortality.
- Alerting teachers to the special educational needs of children who experienced PEM in their early years is an important consideration for rural populations where PEM is highly prevalent.

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