EPIDEMIOLOGY AND IMPACT OF VACCINATION COVERAGE AND DELAYS IN KOROGOCHO AND VIWANDANI INFORMAL SETTLEMENTS, NAIROBI, KENYA

MARTIN KAVAO MUTUA

DOCTOR OF PHILOSOPHY

(Epidemiology)

JOMO KENYATTA UNIVERSITY OF

AGRICULTURE AND TECHNOLOGY

2017

Epidemiology and impact of vaccination coverage and delays in Korogocho and Viwandani informal settlements, Nairobi, Kenya

Martin Kavao Mutua

A thesis submitted in partial fulfilment for the degree of Doctor of Philosophy in Epidemiology in the Jomo Kenyatta University of Agriculture and Technology

2017

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University

Signature ……..... Date ...../……/……

Martin Kavao Mutua

This thesis has been presented for examination with our approval as University Supervisors

Signature ……..... Date ...../……/……

Prof. Peter Kabanya Mwaniki
JKUAT, Kenya.

Signature ……..... Date ...../……/……

Dr. Elizabeth Echoka
KEMRI, Kenya.

Signature ……..... Date ...../……/……

Dr. Henrik Ravn
Research Center for Vitamins and Vaccines (CVIVA),
Denmark.

DEDICATION

This thesis is dedicated to my late dear mother, Beatrice Munee.

ACKNOWLEDGEMENT

I thank my Supervisors Late Professor Peter Kabanya Mwaniki, Dr. Elizabeth Echoka and Dr. Henrik Ravn for their guidance and mentorship throughout the Ph.D. journey. I wish to acknowledge the Danish Development Agency (DANIDA) for funding the implementation of the project from data collection to data analysis and paying the stipend and tuition fee. The INDEPTH Network for financial support to attend the biennial INDEPTH Network scientific conference to present my Ph.D. work. African Population and Health Research Center (APHRC) for the research platform and allowing me to use part of their data to support my research work. The Kenya Medical Research Institute (KEMRI) and School of Public Health, Jomo Kenyatta University of Agriculture and Technology (JKUAT) for their support and guidance throughout my study. I also acknowledge the field research team who were involved in the process of data collection and the respondents for availing time to participate in this research. Lastly, I would like to acknowledge Dr. Elizabeth Kimani-Murage, Dr. Remare Ettarh, Nicholas Ngomi, and Shukri Mohamed, research staffs at APHRC for their support during the initial and subsequent stages of my research.

Special thanks to Peter Aaby, Dr. Christine Benn and Dr. Ane Fiskers, leaders of the vaccination working group under the INDEPTH Network for their support in general towards my Ph.D. program, especially in the organization of training workshops for data collection and data analysis. I would like to also acknowledge the DANIDA Fellowship Centre and the whole team of Statens Serum Institute (SSI) and Centre for Vitamins and Vaccines for the DANIDA Fellowship and hosting me in Copenhagen, Denmark, as part of my Ph.D. research work.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ACRONYMS AND ABBREVIATIONS

APHRC	African Population and Health Research Center
BCG	Bacillus Calmette–Guerin
CDC	Centre for Disease Control
CI	Confidence Interval
DHS	Demographic Health Surveys
DTP	Diphtheria Tetanus Pertussis Vaccine
ECDC	European Centre for Disease Prevention and Control
EPI	Expanded Program on Immunization
FIC	Fully Immunized Child (aged 12-23 months) by age of 12 months
FICm	Fully immunized child excluding measles vaccine
FICv	Fully Immunized Child (aged 12-23 months) at the time of interview
FIC-IS	FIC with all vaccines in-sequence
FIC-OS	FIC with some vaccines out-of-sequence
GACVS	Global Advisory Committee on Vaccine Safety
GEE	Generalized Estimating Equation
GIV	Global Immunization Vision and Strategy
GPEI	Global Polio Eradication Initiative
GVAP	Global Vaccine Action Plan
HAZ	Height-for-age z-scores
HBV	Hepatitis B Vaccine
HDSS	Health and Demographic Surveillance Systems
HTMV	High Titre-Measles Vaccine
IPV	Inactivated Polio Vaccine
IQR	Interquartile Range
KNBS	Kenya National Bureau of Statistics
MV	Measles Vaccine
NA	Nelson-Aalen estimator
NOTFIC	Not fully immunized child
NOTFICm	Not FICm

NOTFICv	Not FICv
NSE	Non-Specific Effects
NUHDSS	Nairobi Urban Health and Demographic Surveillance System
OPV	Oral Polio Vaccine
PCA	Principal Component Analysis
PCV	Pneumococcal Conjugate Vaccine
PR	Prevalence Ratio
RCT	Randomized Clinical Trials
RI	Routine Immunization
UN	United Nations
UNICEF	United Nations Children's Fund
UNSCN	United Nations System Standing Committee on Nutrition
VAS	Vitamin A Supplementation
VPD	Vaccine Preventable Diseases
WAZ	Weight-for-age z-scores
WHO	World Health Organization
WHZ	Weight-for-height z-scores

DEFINITION OF OPERATIONAL TERMS

Child under-nutrition	An outcome of a combination of undernourishment, poor absorption and poor biological use of nutrients consumed as a result of repeated infectious disease
Fully immunized child (FIC)	A child seen alive with a vaccination card and aged 12-23 months who has received eight routine childhood vaccines (1 dose of BCG, 3 doses of polio, 3 doses of pentavalent and 1 dose of measles vaccines) as recommended by the World Health Organization before attaining the age of one year.
Fully immunized child excluding measles (FICm)	A child seen alive with a vaccination card and aged 12-23 months who has received seven routine childhood vaccines (1 dose of BCG, 3 doses of polio and 3 doses of pentavalent) before attaining the age of one year.
Fully immunized child at the time of visit (FICv)	A child seen alive with a vaccination card and aged 12-23 months who has receive eight routine childhood vaccines (1 dose of BCG, 3 doses of polio, 3 doses of pentavalent and 1 dose of measles vaccines) as at the time of interview visit.
Fully immunized child in sequence (FIC-IS)	A child who is FIC (as defined above) and has been immunized with BCG first, then polio 1 and pentavalent 1 on the same day, then polio 2 and pentavalent 2 on the same day, then polio 3 and pentavalent 3 on the same day and then measles vaccine in that order.
Fully immunized child out-of-sequence (FIC-OS)	A child who is FIC (as defined above) and but has not been immunized as defined below has been immunized with BCG first then polio 1 and pentavalent 1 on the same day, then polio 2 and pentavalent 2 on the same day, then polio 3 and pentavalent 3 on the same day and then measles vaccine in that order.
NOTFIC	A child who is not FIC i.e. has missed at least one of the eight vaccines needed to be FIC
NOTFICm	A child who is not FICm i.e. has missed at least one of the seven vaccines needed to be FICm

NOTFICv	A child who is not FIC i.e. has missed at least one of the eight vaccines needed to be FICv
Pentavalent	Diphtheria-Tetanus-Pertussis (DTP), Haemophilus influenza type B and Hepatitis B virus antigens vaccine

ABSTRACT

Childhood Immunization has been identified as the most cost-effective health intervention in the last century. It is estimated to save more than two millions lives annually. Completion, timeliness and sequencing of routine vaccination as recommended by the World Health Organization is very crucial for maximum protection of children against specific infections. Existence of non-specific effects-effects other than prevention of specific infection–have been documented and could be linked to vaccination timeliness and sequencing. The objective of the study was to determine the prevalence and determinants of vaccination coverage and delays among children aged 12-23 months and establish the relationship with subsequent morbidity, anthropometry and, mortality in two Nairobi informal settlements. The study targeted households with children aged 12-23 months. Data from the Maternal and Child Health longitudinal study run by Nairobi Health and Demographic Surveillance System and collected between 2007 and 2014 was used. Structured data collection tools were used to collect data from mothers or guardians with children aged between 12 and 23 months. Proportions and medians were used to determine vaccination coverage and levels of delays respectively. Logistic regression models were used to identify determinants of full immunization and delays. Cox regression and Generalized Estimation Equation models were used to assess relationship between immunization patterns and morbidity, anthropometry and mortality respectively. The findings indicated that 67% of the children were fully immunized and 22% received their vaccinations out-of-sequence. Mother's education level, post-natal care, and health facility delivery were identified as the determinants of being fully immunized. Place of delivery was identified as the determinant of out-of-sequence. A significant 58% ($p=0.017$) and 64% ($p<0.001$) decreases in child mortality was observed for being fully immunized and immunized in recommended sequence respectively. A non-significant 35% ($p=0.159$) reduction in hospitalization cases was observed for being fully immunized. Vaccine completion was significantly associated with 0.13 ($p=0.002$) and 0.12 ($p=0.006$) increase in weight-for-age and weight-for-height z-scores respectively. More focus is needed on making sure all children are immunized on time and as per schedule. The low immunization coverage and age-specific vaccination can easily be

improved by targeting disadvantaged groups. Particular attention is needed on the uptake of the measles and the third doses of polio and pentavalent vaccines. Further research is needed to determine the effects of each routine vaccine other than preventing the specific infection.

CHAPTER ONE

1 INTRODUCTION

1.1 Background information

The routine immunizations which are vaccines given for children aged below one year have been used in the prevention of the main childhood infections such as tuberculosis, diphtheria, pertussis, tetanus, and polio for the last couple of decades. The World Health Organization (WHO) estimates that 2.5 million lives are saved annually by vaccinating children (WHO, 2008). Each of the vaccines is for prevention of specific infection, and implementation has been successful to a point of complete eradication of smallpox and elimination of poliovirus transmissions in nearly all regions of the world (GPEI, 2013) with the exception of Pakistan and Afghanistan which have outbreaks of a few cases (WHO, 2016). Thus the overall result of full immunization coverage is a reduction in child mortality and morbidity.

The WHO through the Expanded Program on Immunization (EPI), recommends specific schedules of the recommended vaccines; Bacillus Calmette Guérin (BCG) and oral polio vaccine (OPV) at birth, pentavalent (Diphtheria-Tetanus-Pertussis (DTP), Haemophilus influenza type B and Hepatitis B virus antigens vaccine) and OPV at 6, 10, and 14 weeks and measles vaccine (MV) at 9 months of age. More recently, new vaccines have been added to the schedule, for instance, the Pneumococcal Conjugate Vaccine (PCV) at 6, 10 and 14 weeks were also added to the Kenya vaccination schedule (Moszynski, 2011). For vaccine effectiveness, high coverage is required for both individual and herd immunity (Anderson, 1992). Immunization coverage has

been low especially in low-income countries as compared to the developed countries (WHO, 2014). The WHO has been in the forefront in strategizing on ways of improving the coverage levels and over the years coverage has been increasing for most developing countries.

The improvement in immunization coverage of the last decade is commendable, but in measuring the full immunization coverage, timeliness and sequencing of immunization have not been taken into account, yet they are an integral part of the success of the immunization program. A lot of children especially in the developing countries, receive their immunization much later than the recommended schedule and to some extent, they get their vaccines in an out-of-sequence manner (ECDC, 2009). Few studies have documented the levels of early, delayed and out-of-sequence of the routine childhood vaccination and their consequences on child health (Aaby, Ibrahim, *et al.*, 2006; Benn *et al.*, 2012).

Recent studies have demonstrated that failure to adhere to recommended schedule can result in non-specific effects (NSE) – effects that go beyond protection against the specific infection (Hirve *et al.*, 2012; Kabir *et al.*, 2005; A. Roth *et al.*, 2005; Welaga *et al.*, 2012). The NSEs can be either beneficial or detrimental and are more pronounced depending on the sequencing and timing of vaccines administration (Aaby, Ibrahim, *et al.*, 2006; Hornshoj *et al.*, 2012). Such NSEs may have major implications for child morbidity and mortality in high-mortality areas. Therefore, understanding these effects will go a long way in maximizing the benefits of the routine vaccination and thereby help to address the third goal of the 2030 agenda for

sustainable development (UN, 2014) of "Ensuring healthy lives and promoting well-being for all at all ages."

Just like the overall global full immunization coverage hides the disparity existing between the developed and developing countries, there exist disparities in full immunization coverage within countries, when comparing the rural and urban areas and even within the urban areas, immunization coverage differs between formal and informal settlements. Many studies have documented the characteristics of children who get fully immunized by the age of twelve months in different settings. On the other hand, very few studies have documented the characteristics of children who have delays in their immunizations. For the success of the immunization programs in improving the immunization uptake and full coverage, it is important to identify, both the determinants of full and delayed immunization. The identification will help the government and other vaccination program implementers to know and target a specific group of children who are disadvantaged.

Most of the vaccines developed over the years involved development and testing of specific vaccines for a particular infectious disease. Interactions between vaccines and other interventions have rarely been examined. Efficacy of a vaccine against a specific infection is assumed to lead to similar effectiveness even though the effectiveness may be influenced by other interventions and individual level factors.

Administration of two vaccines simultaneously may modify the effect of the same vaccines in sequence (P. Aaby *et al.*, 2007; Aaby, Ibrahim, *et al.*, 2006; Aaby, Jensen, *et al.*, 2006; Aaby, Vessari, *et al.*, 2006; Benn *et al.*, 2008). Vaccines are sometimes

not available and may therefore not be given as recommended; the sequence is often delayed, or many vaccines maybe all given at the same time, for instance, BCG and DTP or DTP and MV may be administered simultaneously. In most developing countries, more than half of the children are getting such out-of-sequence combined vaccinations (Benn *et al.*, 2009). There is little scientific justification for the current recommendations; e.g. OPV is given at birth, but no study was conducted to examine interactions between OPV and BCG when OPV was introduced. Studies have consistently shown that MV and DTP simultaneously are associated with higher mortality than MV alone (Agergaard *et al.*, 2011; Benn *et al.*, 2012; J.E. Veirum *et al.*, 2005). On the other hand, beneficial effects have been reported when combining BCG and DTP in reducing the negative effect of DTP (Aaby *et al.*, 2009; Aaby *et al.*, 2004).

Hence, the estimates on which current policies are developed on may be underestimating or overestimating the effects of vaccination/immunization. Randomized control trials (RCTs) are the most appropriate methods to test these effects scientifically as compared to the observational studies, but given the importance of the vaccines in the prevention of these childhood infections, it would be unethical to deny a child of a known therapy that can prevent illness. Therefore, observational studies are the only options for assessing these effects. More observational studies are needed to get evidence-based policies for most important interventions to improve the monitoring of interventions in different regions, examine interactions between interventions and study the effects of different variations in the implementation of current policy.

Alternatively, natural experiments offer a different avenue for assessing the effects of vaccinations programs on child health. If there are sudden changes in program implementation due to vaccines lacking or stopped during a war, effects of missing certain vaccines or receiving vaccine later than scheduled can be assessed. Such "natural experiments" have shown strong NSEs of vaccines, for example, vaccinations stopped during the war (Aaby *et al.*, 2002), and when OPV could not be administered with BCG due to a shortage of OPV (Sartono *et al.*, 2010).

If observational studies and the 'natural experiments' suggest consistent patterns it may be justified to conduct new RCTs (Prentice *et al.*, 2009) to test different variations in current practice, e.g. giving or not giving DTP and MV simultaneously or giving or not giving Vitamin A supplements (VAS) with DTP. This study intent is to contribute to this process by providing evidence of the NSEs from an urban poor settlement population's perspective.

Locally there are substantial variations in how vaccinations are implemented that provide many possibilities for assessing the likely importance of NSEs. From a long-term perspective, the potential modifications in policies and practices which appear to have the largest impact on child health will have to be tested in randomized studies. This study aimed at measuring the level of vaccination coverage, the frequency of delay and sequencing of the routine vaccinations in an urban poor settlement and compare child health indicators between children who receive their vaccine late and in an out-of-sequence manner to those who receive vaccines on time with the correct sequence of administration. The study used longitudinal data routinely collected in the Nairobi Urban Health and Demographic Surveillance System (NUHDSS)

implemented in two informal urban settlements, Korogocho, and Viwandani, in Nairobi City by the African Population and Health Research Center (APHRC).

1.1 Problem statement

The Demographic Health Surveys (DHS) (Murray *et al.*, 2003) has been used to estimate the vaccination coverage in many countries over the years. These estimates have shortcomings, given the surveys are based on retrospective data collection which is prone to both recall and selection biases. The Health and Demographic Surveillance Systems (HDSS) offers alternative methods of validating the DHS estimates (Ettarh *et al.*, 2012; Mutua *et al.*, 2011) with the limitation on population coverage.

Most developing countries lag behind the developed countries with regards to vaccination coverage. Even within the countries with overall low coverages, there is disparity within the country regarding different factors such as education level, wealth status, area of residence, distance to a health centre, vial opening policies, availability of vaccines, and ethnic group among other factors. The WHO set Immunization coverage targets for all countries as part of 'decade of vaccine' initiative. Through the global vaccines action plan (GVAP), the strategy aims at a coverage of 90% for all the childhood routine immunizations and more than 80% in each the districts for all countries.

The disparities and difficulties in access to vaccination leads to many children being disadvantaged and ending up not getting fully immunized, and when they are immunized, they may not have been vaccinated as per the recommended schedule. Children end up getting their vaccines earlier or later than the recommended age and

sometimes getting vaccines together or after another vaccine which is recommended to be given later and not before or together. Few studies in Kenya have tried to quantify the levels of vaccination delays and sequencing and their effects on childhood health.

While studies have documented the determinants of lack of RI completion among infants, very few have looked at the determinants of lack of completion among the disadvantaged groups, for example, children in informal urban settlements. Worryingly none has looked at the determinants of delayed or out-of-sequence immunization. The second aim of this study looks at determinants of lack of completion of the RI in disadvantaged urban poor settlement area of Nairobi as well as identifying the determinants of delayed immunization among children aged 12-23 in the study area.

Evidence from studies conducted in West African countries have shown DTP to have detrimental effects (P. Aaby *et al.*, 2007; Agergaard *et al.*, 2011; Benn *et al.*, 2012; Sankoh *et al.*, 2014) and BCG and measles to have beneficial effects on child health (Aaby, Martins, Garly, *et al.*, 2010; Aaby *et al.*, 2015; Kabir *et al.*, 2005; A. Roth *et al.*, 2005; Sankoh *et al.*, 2014). There is no information available on vaccination delays among the urban poor living in informal settlements and how they impact on child health. Therefore, there is need to evaluate and test formally the different interactions of the RI to ascertain their effectiveness in prevention of the targeted infections. Studies have documented the existence of the NSEs of the RI (Agergaard *et al.*, 2011; Higgins *et al.*, 2014; Sankoh *et al.*, 2014). The NSEs so far have only been documented in a few regions or countries. This study examined the relationship between

vaccination coverage and the probability of a child being hospitalized or child survival in an urban informal settlement setting.

1.2 Justification

The focus of the vaccination programs has been on immunization coverage with little attention on the process in term of timeliness and sequencing. There is evidence that delays in vaccinating children or vaccinating children in different sequence than recommended may lead to a change in the effectiveness of the vaccines. The delays increases the time a child is at risk of the targeted infections (specific effects) and/or missing out on the protective effects against other unrelated infections (non-specific effects). Very few studies in Kenya have looked at the timeliness of vaccines given to children and almost none has looked at the effects of the different immunization patterns on child health. Most of the evidence so far have come from West African countries, and in particular from Guinea Bissau. Therefore, more evidence is needed from other parts of the world and in particular from developing countries where immunization coverages are low and vaccination delays are high. This evidence will help to ascertain levels of vaccination delays and sequencing and the effect on child health. This need, formed the basis of this study which will add to the body of knowledge on immunization process and its benefits in developing countries and also provide a basis for recommendations to inform policy and practice towards immunization coverage. The two sites, Korogocho and Viwandani were chosen due to the already existing structures of a demographic surveillance system with defined population.

1.3 Objectives

1.3.1 General objective

To determine vaccination coverage and delay, determinants and outcomes among children aged 12-23 months in Korogocho and Viwandani informal settlements.

1.3.2 Specific objectives

The specific objectives of this study were be as follows;

i. To determine vaccination coverage and delays among children aged 12-23 months in Korogocho and Viwandani urban informal settlements.
ii. To establish the determinants of vaccination coverage and delays among children aged 12-23 months in Korogocho and Viwandani urban informal settlements.
iii. To determine the relationship between vaccination coverage and delays and child health outcome among children aged 12-23 months in Korogocho and Viwandani urban informal settlements.

1.4 Research questions

The study sought to answer the following research questions:

i. What are the vaccination coverage and delays among children aged 12-23 months in Korogocho and Viwandani urban informal settlements?
ii. What are the determinants of vaccination coverage and delays among children aged 12-23 months in Korogocho and Viwandani urban informal settlements?
iii. How are vaccination coverage and delays associated with child health outcomes?

CHAPTER TWO

2 LITERATURE REVIEW

2.1 History and successes

Since the first discovery of the vaccines more than a century ago, great strides have been made in discovering new vaccines for major infectious diseases in the world (CDC, 1999). The vaccination program has led to the aversion of millions of childhood deaths every year (Bustreo *et al.*, 2015) and it is also thought to be the most cost-effective medical interventions for reducing under-five morbidity and mortality worldwide (CDC, 1999). The success of the immunization programs includes containment of the infectious diseases and complete eradication of some – smallpox and soon poliomyelitis (Fenner *et al.*, 1988). The WHO in its effort to improve immunization coverage among children in developing countries launched EPI in 1974 (Chan, 2014). The immunization coverages improved during that period in many developing countries, but millions of children worldwide still did not receive their routine vaccine during their first year of life (WHO, 2002a) by 2000. The so-called 'decade of vaccination' started in 2005 with the formation of the Global Immunization Vision and Strategy (GIVs) (Bilous *et al.*, 2006; WHO, 2005) by the World health assembly. The GIV's mandate was to reduce vaccine-preventable disease morbidity and mortality by two-thirds by 2015 (UNICEF, 2002). The GIVs targeted to immunize more people against more diseases and targeted the world poorest countries (WHO, 2005).

In compacting the common vaccine-preventable diseases, WHO came up with specific immunization schedule which is common to all settings. The immunization schedule could vary from time to time with the addition of new vaccines (Duclos *et al.*, 2011; Moszynski, 2011) , and may differ from region to region depending prevalence of the specific vaccines-preventable diseases for instance yellow fever which is mainly limited to West and Central Africa, South America, and Panama (Brenzel *et al.*, 2006). The basic Routine Immunization (RI) (Steinglass, 2013) covers all vaccines recommended for children within the first year of life. RI has been the focal point in evaluating immunization programs (WHO, 2014). The WHO classifies a child as fully immunized with all basic vaccinations if the child has received; BCG vaccine against tuberculosis at birth, three doses of polio vaccine against poliomyelitis virus at six, ten, and fourteen weeks of age, three doses of pentavalent vaccines against diphtheria, tetanus, pertussis, hepatitis B, Haemophilus influenza B infections at six, ten, and fourteen weeks of age and measles vaccine at nine months of age (WHO, 2013).

The importance of monitoring performance of vaccination programs can never be overstated. Identifying countries with lower vaccines coverage, and the disadvantaged groups within countries that are under-served is critical. Global vaccination coverage has been on the increase with 86% of all infants worldwide being vaccinated with three doses of DTP/pentavalent vaccine in 2014 (WHO, 2014). Similarly, in the last decade, there has been a marked improvement in access to the routine childhood vaccines and also the development of new vaccines which has led to more children being vaccinated (Kyaw *et al.*, 2006). This improvement has greatly improved child survival by reducing the under-five mortality from 9.6 million in 2000 to 6.3 million in 2013

(WHO, 2015). Despite the progress, significant coverage gaps between countries and also within countries still exists. The average coverage for pentavalent 3/DTP 3 and measles-containing vaccines in developing countries is estimated at 16% and 15% below that of developed countries in 2010, respectively (WHO, 2011b). In Kenya, the difference is more pronounced when comparing urban and rural areas (KNBS, 2015). The coverage in urban areas is significantly different among the urban poor as compared to the affluent and the middle-income areas (Mutua *et al.*, 2011). Currently, immunization coverage in Kenya stands at 79.4%, with regional proportions varying from 55.6% in North Eastern to 93.3% in the Central Province (KNBS, 2015). The proportion of under two year old children in Nairobi who are fully vaccinated stands at 81.2% (KNBS, 2015), which is much higher compared to the estimate (68.5%) for the urban poor settlement areas also within Nairobi (Egondi *et al.*, 2015). This low level is also observed in facilities serving the informal settlements in Nairobi (Borus, 2004).

2.2 Timeliness and sequencing

The timing of vaccine is important for effectiveness and safety of the vaccine. Timely administration of vaccines has implications for the success of childhood immunization programs and a timely start of immunization is important in the first year of life as the transplacental immunity declines rapidly (Heininger *et al.*, 1992). In practice, although a few children might be vaccinated early, many are vaccinated late (Ndiritu *et al.*, 2006) reducing the impact of vaccine programs on disease burden especially in high-risk groups (Heininger *et al.*, 2006). The routine vaccines administered to children before the age of six weeks (excluding BCG and polio at birth) have shown poor

response and in some cases could be detrimental to infants as they reduce the immune response of subsequent doses (ECDC, 2009). Similarly there is need to observe the minimum recommended age for different vaccines which are normally based on the youngest age group at risk for the specific infections where vaccine safety and efficacy have been demonstrated. Therefore giving doses earlier than scheduled or given closer to each other may lead to less optimal immune response (ECDC, 2009). On the other hand, when a child's vaccine is delayed, the interval between doses/vaccines is increased, and the optimal vaccine protection may not be attained (ECDC, 2009). Simultaneous vaccination (pentavalent, polio and PCV doses) increases the chance that a child will be fully vaccinated on time and hence improve age specific vaccines coverage (Kroger *et al.,* 2012; National Vaccine Advisory Committee, 2003). However, the out-of-sequencing, early or delays of vaccines may affect child survival. Several studies have documented various reasons causing delays in the administration of vaccines and its impact. Measles and BCG vaccines are known to have NSEs when given on time. DTP containing vaccines, on the other hand, does not seem to have beneficial NSEs (Aaby, Ibrahim, *et al.*, 2006; Benn *et al.*, 2012; Kabir *et al.*, 2005; A. Roth *et al.,* 2005; J.E. Veirum *et al.,* 2005; Welaga *et al.,* 2012).

Few studies have documented timeliness and sequencing of routine vaccinations in Sub-Saharan Africa. A study done in Ghana in 2010 revealed that 44% of children aged 12-23 months had their measles vaccine delayed (Gram *et al.*, 2014). In Burkina Faso, approximately 40% of children aged 12-23 months had their polio, and pentavalent doses delayed (Schoeps *et al.,* 2013). In an earlier study in the same study area as the current study, delays in MV was estimated at 20% among boys and 24%

among girls (Ettarh *et al.*, 2012). Timely immunization have been documented in several studies (Clark *et al.*, 2009; Ettarh *et al.*, 2012; Fadnes, Jackson, *et al.*, 2011; Laryea *et al.*, 2014; Mutua *et al.*, 2015; Sadoh *et al.*, 2009), however almost none of these studies have looked at the levels of out-of-sequence.

2.3 Determinants of immunization coverage

Despite the effectiveness of the routine childhood vaccines in preventing and eradicating diseases, the uptake remains suboptimal. It is estimated that 17% of children are not fully immunized worldwide (WHO, 2011a). A large number of non-vaccinated children represent a risk to the resurgence of infectious diseases under control for example measles (Sugerman *et al.*, 2010) and pertussis (Atwell *et al.*, 2013) and re-emergence of infectious diseases already eliminated (Rainey *et al.*, 2011). Vaccination completion and timeliness of vaccination is much lower in developing countries compared to the developed world (WHO, 2014). Immunization coverage gaps exist within countries, depicting the inequities in the provision of health services (WHO, 2014). Several studies have documented factors influencing vaccination completion (Akmatov *et al.*, 2007; Bondy *et al.*, 2009; Butler *et al.*, 2015; Cui *et al.*, 2007; Danis *et al.*, 2010; Fatiregun *et al.*, 2012; Rainey *et al.*, 2011; Rocha *et al.*, 2015; Tauil Mde *et al.*, 2016) and timeliness (Fadnes, Nankabirwa, *et al.*, 2011; Gibson *et al.*, 2015; Hutchings *et al.*, 2016; Lernout *et al.*, 2014; Moisi *et al.*, 2010; Schoeps *et al.*, 2013; Tauil Mde *et al.*, 2016). These factors can broadly be classified into factors related to the child, parental attitude, and knowledge, family social context and health care services (Tauil Mde *et al.*, 2016). The main determinant of vaccine completion

and timeliness is the low households' social-economic status which is mainly concentrated in rural and urban informal settlements.

2.4 Immunization status and child health

2.4.1 Child nutrition status

Child under-nutrition is a major health problem in developing countries (WHO, 2002b). Even with the modest progress made in the last decade (UNSCN, 2011), under-nutrition, estimated at 17%, 33%, and 8% for underweight, stunting and wasting of under five-year children respectively (McGuire, 2015) is still very high. Under-nutrition increases one's susceptibility to infections and contributes immensely to illness and death from disease with an estimated 45% of deaths of children under-five can be linked to malnutrition (Black *et al.*, 2013). The deaths are mainly due to the increased risk due to infectious diseases (Black *et al.*, 2008). Studies have linked child under-nutrition to infectious disease (De Romana *et al.*, 1989; Martorell *et al.*, 1980) and hence any health measures which reduces the burden of an infectious disease leads to improved child nutrition, this includes water and sanitation (Behrman *et al.*, 1987) and maternal education (Barrera, 1990).

Immunization programs have been successful in compacting many infectious diseases over the years and by extension it can be linked to improved child growth (Anekwe *et al.*, 2012). Fully immunized children are less likely to get infections which mean their growth will not be impeded and hence less likely to be undernourished. Frongillo et al. (Frongillo *et al.*, 1997) and Milman (Milman *et al.*, 2005; Thomas *et al.*, 1996) in cross-country studies, showed a significant association between immunization coverage and prevalence of wasting and stunting respectively. Another study

conducted in Kwale district, Kenya, child immunization status was found to be a significant predictor of linear growth (Adeladza, 2009). in a study to evaluate the impact of the immunization program in India, Anekwe et al. (Anekwe *et al.*, 2012) found immunization status of a child helped to increase the height-for-age and weight-for-age Z-scores of the child. These growth benefits may not be directly from vaccination but rather from the vaccination program as a whole. This study explores the relationship between vaccination status as a proxy for vaccination program and under-nutrition levels in Nairobi urban informal settlement in Kenya.

2.4.2 Childhood hospitalization

Routine childhood immunizations have tremendously reduced the risk of vaccine-preventable infections globally. The WHO estimates up to two and a half million under-five children die every year due to vaccine-preventable infections (WHO, 2014). More children could be saved from severe infections, cost of hospitalization, and deaths by increasing coverage and optimizing the use of the RI (WHO, 2005). Several studies have documented how vaccination status, timing, and sequencing affects the severity of infections and mortality (P. Aaby *et al.*, 2007; Aaby, Martins, Bale, *et al.*, 2010; Biai *et al.*, 2011; Rodrigues *et al.*, 2006; Valentiner-Branth *et al.*, 2007). In a study conducted in Guinea-Bissau looking at the risks of hospitalization by vaccination status and sequence of vaccinations, Biai sidu (Biai *et al.*, 2011) found out that having measles vaccine only as the most recent vaccination was associated significantly with the lowest risk of hospitalization. The risk of hospitalization depended on adherence to the immunization schedule with children receiving DTP with or after MV being associated with higher risk.

2.4.3 Childhood mortality

Studies conducted in Guinea-Bissau, have demonstrated that; live, attenuated vaccines (BCG, measles, and polio vaccines) have beneficial effects particularly for girls (Aaby, Jensen, *et al.*, 2006) in terms of child survival. Measles vaccine has been shown to have a beneficial effect on child survival in many studies, an effect which cannot be explained by prevention of measles. A 30-40% reduction in mortality is found in most studies that have looked at effects of measles vaccine on child mortality (P. Aaby *et al.*, 2003; Aaby, Martins, *et al.*, 2012; Aaby *et al.*, 1995; Sorup *et al.*, 2014). The beneficial effect has also been documented in randomized control trials showing similar or even stronger effects, (Aaby, Martins, Garly, *et al.*, 2010; Martins *et al.*, 2014). Observational studies have also suggested a non-specific beneficial effect of BCG (Adam Roth *et al.*, 2006; A. Roth *et al.*, 2005; Adam Roth *et al.*, 2004). BCG has been shown to reduce neonatal mortality by 45% (12%-65%) among low birth weight children who do not receive BCG at birth (Biering-Sorensen *et al.*, 2012).

Inactivated vaccines such as DTP, hepatitis B (HBV), and inactivated polio vaccine (IPV) may have negative effects for girls. For all three vaccines, girls have higher mortality than boys (Aaby *et al.*, 2002; Garly *et al.*, 2004; J. E. Veirum *et al.*, 2005). The DTP vaccine studies in Africa have shown a consistent pattern of higher female-to-male mortality when DTP vaccine is the most recent vaccine. Female-to-male mortality is increased in the age in which DTP is the predominant vaccine, and declines once the children get MV (Aaby, Ibrahim, *et al.*, 2006; Aaby, Vessari, *et al.*, 2006).

All the studies conducted so far suggests that the most recent vaccination affects the immune system (P. Aaby *et al.*, 2007; Knudsen *et al.*, 1996; Sankoh *et al.*, 2014; Sorup

et al., 2014) and changing the sequence of vaccinations may affect how the immune system reacts to an infection and the overall mortality (P. Aaby *et al.*, 2007; Aaby, Ibrahim, *et al.*, 2006; Sankoh *et al.*, 2014). The World Health Organization recommends BCG and OPV vaccines at birth, DTP or pentavalent and OPV vaccines at 6, 10 and 14 weeks and MV at nine months old. Changing the sequence of vaccination may have important consequences on child health. For instance, the high-titre measles vaccine (HTMV) introduced by the WHO was withdrawn in 1992 after studies showed it was associated with higher mortality for girls in Guinea-Bissau and Senegal (Peter Aaby *et al.*, 2003) and Haiti (Holt *et al.*, 1993). But after the data was reanalysed, MV was the most recent vaccine for most girls after nine months of age and MV had a beneficial effect (Aaby *et al.*, 1995). HTMV was introduced at 4-5 months of age and most children received DTP/IPV after HTMV. The change was associated with a two-fold increase in mortality for girls but mattered little to boys(Peter Aaby *et al.*, 2003). Therefore, the high mortality for girls was not due to HTMV as such but due to receiving DTP/IPV rather than MV as the most recent vaccine. Changing the sequence of DTP and standard MV, i.e. providing DTP after standard MV, has similar effects (Peter Aaby *et al.*, 2007). However, changing the sequence of BCG and DTP, i.e. providing BCG after DTP, has a beneficial effect for girls, but the effects were not significant in boys (Aaby *et al.*, 2009; Aaby *et al.*, 2004). Additionally, BCG-revaccination after booster DTP was associated with a strong reduction in mortality in an RCT (A. E. Roth *et al.*, 2010).

2.5 Conceptual framework

The World Health Organization through its EPI program targets to improve RI coverages globally in order to reduce or completely eradicate major childhood infections. Vaccines program has been hugely successful in the prevention of the specific targeted infections. Studies have also shown vaccines to be having NSEs with BCG, MV and OPVs demonstrating beneficial effects while DTP or pentavalent exhibiting detrimental effects (Sankoh *et al.*, 2014). NSEs can be maximized by optimizing the use of the RI by improving coverage and timeliness. Developing countries still lag behind with low immunization coverage and poor timeliness (WHO, 2014). Several factors have been identified as determinants of a child being fully immunized. Studies have documented the determinants of a child being fully immunized by 12 months of age, but few have looked at factors contributing to delayed or out-of-sequence vaccination. By identifying the determinants of vaccination delays and out-of-sequence, vaccination programs implementers will be able to identify the disadvantaged group for targeted interventions.

The conceptual framework presented in Figure 2.1 summarizes potential demographic, socioeconomic, and cultural factors which could be possible determinants of a child being fully immunized (FIC) by the age of twelve months and also being fully immunized with the correct sequence (FIC-IS) in the study setting. The framework summarizes the potential linkages between FIC or FIC-IS and childhood nutrition status, hospitalization, and mortality.

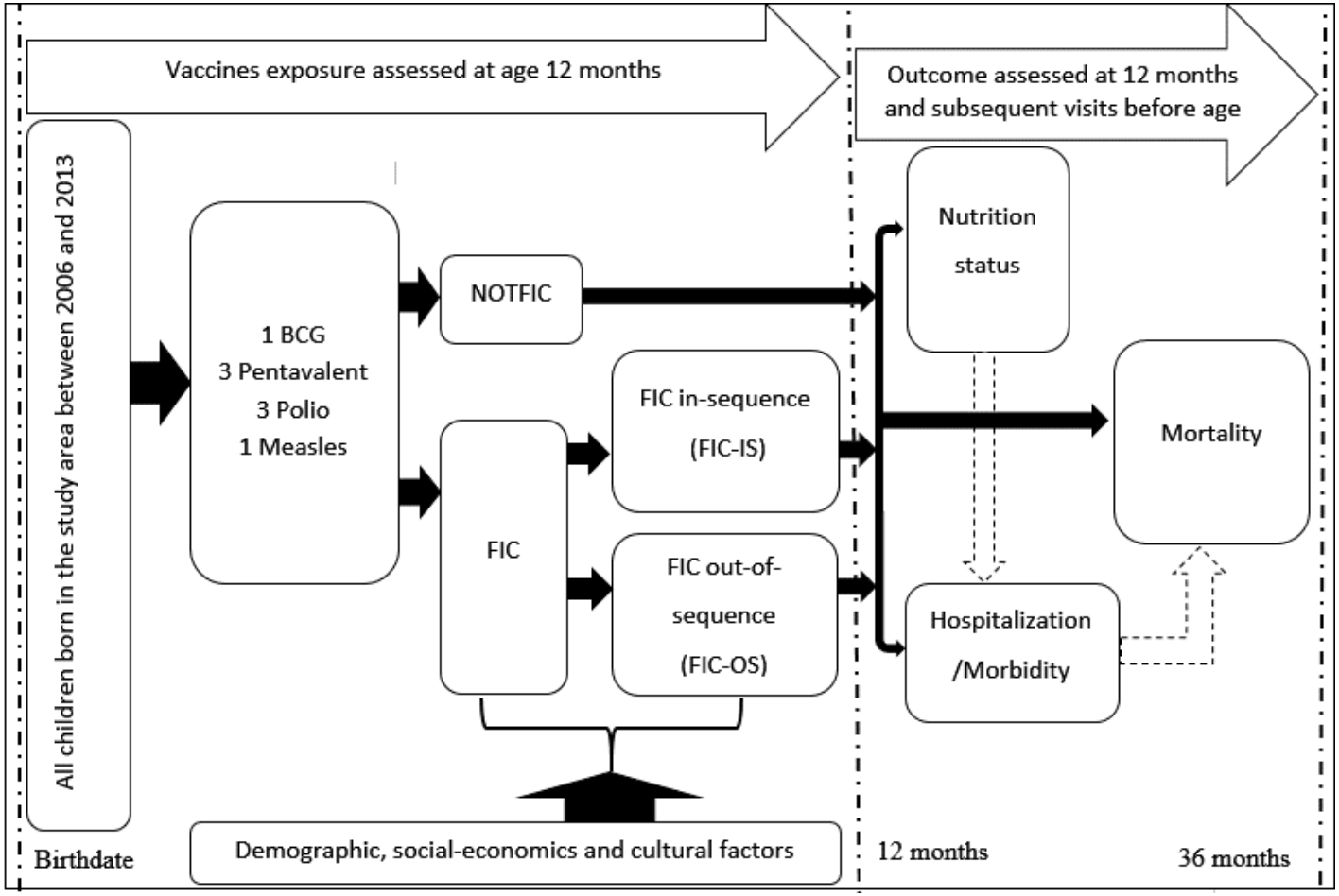


Figure 2.1: Hypothetical model for the study of the epidemiology and impact of vaccination coverage among children aged 12-23 months

Adapted from (Mosley *et al.*, 1984)

CHAPTER THREE

3 MATERIALS AND METHODS

3.1 Study design

Ambi-directional cohort study design was used to evaluate the three study objectives. Exposure to routine immunization was evaluated when the child was between 12 and 23 months of age. The study outcomes of interest were assessed when the child was between age 12 and 36 months. Some of the study outcomes had occurred prior to the start of the study or the children were already older than 3 months, hence their records were evaluated retrospectively. The rest of the children had either not yet experience the outcomes of interest or they were not yet 36 months of age and children were followed until they attained the age of 36 months or the end of study. Immunization coverage, timing and out-of-sequence and associated risk factors (objective #1 & #2) were determined at the start of the study for children aged between 12 and 23 months at the first visit after attaining the age of one year. Relationship between immunization exposure (full coverage, delays, and sequencing) and child health (hospitalization, anthropometry and mortality) (Objective #3) were assessed at the end of the study. In ambi-directional cohort studies, both aspects of prospective and retrospective studies are present. Subjects are selected by exposure which has already occurred. Some of the study outcomes have occurred prior to the start of the study (retrospective cohort study) but some outcomes have not yet occurred and subjects will be followed into the future (prospective cohort study). The common features of cohort designs are that

subjects are selected by exposure and followed over time (real or past) to identify outcomes in the future.

3.2 Study area

The study was conducted in two informal settlements of Nairobi (Korogocho and Viwandani) as shown by the map in Figure 3.1, where the APHRC run the NUHDSS. The two communities had an estimated population of about 75,922 in approximately 30,000 households as of the end of 2012. These settlements have high unemployment, poverty, poor sanitation, crime and poorer health indicators as compared to Nairobi in general (APHRC, 2002; Emina *et al.*, 2011). The informal settlements normally have limited health services as there is no single public health facility within the area, they can only access health services at the public health facilities in the neighboring communities: Six health facilities are located in the neighborhood of the two settlements. Several private and non-governmental health facilities located within or near the settlements offer health services to the residents. The area was chosen because of the existing NUHDSS which has been running in Korogocho and Viwandani settlement areas for over ten years. The NUHDSS has been following up the population every four months collecting both background factors, health status and movement of the population under surveillance. A maternal and child health project within the NUHDSS has been collection information on the vaccination status of all children in the two settlements area since September 2006. The project has been described in detail elsewhere (Mutua *et al.*, 2016; Mutua *et al.*, 2015).

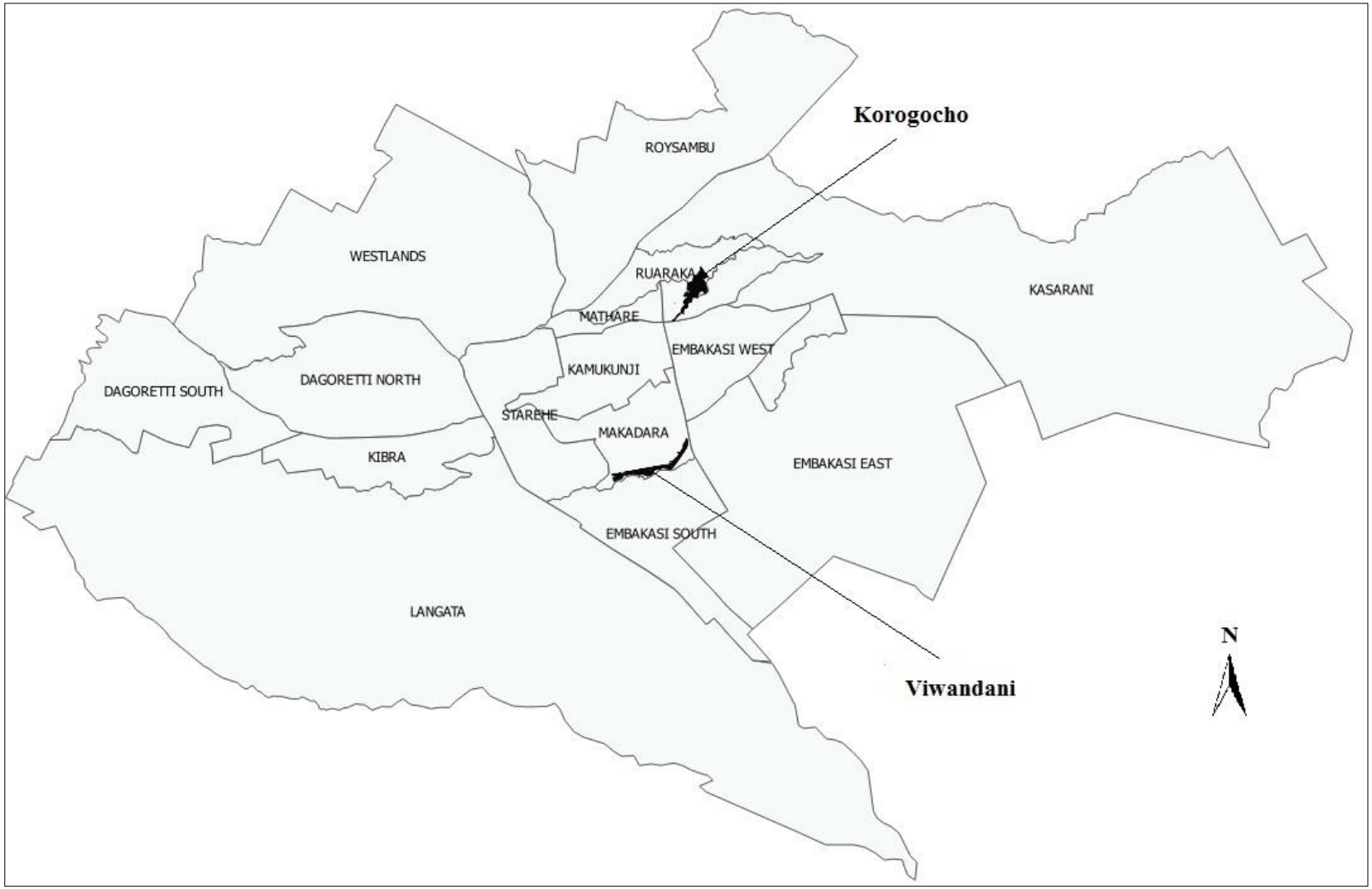


Figure 3.1: Map of the study areas

3.3 Study population

The target population was mothers with children age between 12 and 23 months and living in the study area. Children aged 12-23 months were targeted because that is the age when children are expected to have received all the childhood routine immunization as recommended by WHO as well as the age used to evaluate immunization coverage.

3.4 Inclusion criteria

- Women with children aged 12-23 months at the time of the interview living in the study area
- Had a vaccination card seen by the research assistant.
- Women who read the informed consent and agreed to be interviewed

3.5 Exclusion criteria

- Children with no vaccination card at the time of interview
- Children who were sick at the time of interview
- Children whose mother did not consent to be interviewed.

3.6 Sampling

3.6.1 Sample size

The study took advantage of the NUHDSS framework which had collected information on immunization, anthropometry, morbidity, hospitalization and mortality on children in the study area for the period 2007 to 2013. This study used all the available data in the existing NUHDSS database and collected additional data for those

whose information was not yet collected because they had not attained the age or they were due for follow up visits.

3.6.2 Sampling frame

The sampling frame was all women with children aged 12 to 23 months and lived in the study area between September 2006 and January 2013, and their records existing in the NUHDSS database. The study area, Korogocho, and Viwandani has an approximate 1,500 births each year and totalled to approximately 10,500 children during the period under consideration. This study used all available data on children recruited in the NUHDSS study from February 2007 to December 2013. This frame provides a perfect platform to use the readily available data to answer our research question in the current study. Additional follow-up data was collected for children who were below the age of 36 months at the start of the current study.

3.7 Data collection tools

The maternal and child health component of the NUHDSS used structured data collection tool (appendices III and IV) to collect information from mothers with children aged 12 to 23 months and lived in the study area. The data collection tool was divided into different sections collecting information about the health of child, mother and household characteristics. The information collected included, background characteristics, pregnancy, anti-natal, delivery, postnatal, parity, child feeding, morbidity, routine childhood vaccination and anthropometric measures. Childhood hospitalization was introduced in 2011. The data collection tool was translated into Kiswahili before being administered in the field. Data collection tools were piloted

before the full data collection exercise was conducted. The data collection tool was adapted for this study to collect additional data from mothers with children recruited in the current study and needed more follow up data collection visits.

3.8 Data Collection

Mothers with children aged 12 to 23 months were identified from the database and inclusion and exclusion status established. For mothers who met the inclusion and exclusion criteria and had follow-up data up to three years of age no additional data was collected. For mothers with children who met inclusion criteria but did not have follow-up data up to three years of age in the NUHDSS database, additional data was collected every fourth month until they attained the age of three years or the end of the study. Anthropometry measurements, including weight and height, were collected during each time a child was visited for an interview. The weight and height data were used to compute the weight-for-age, height-for-age, and weight-for-height Z-scores. Data collection was done by trained research assistants recruited within the participating community and with a minimum secondary level education. The research assistants were trained on good research skills, data collection, and data management practices.

3.9 Data processing

Data were captured from the data collection tools (Appendix III and IV) using data entry screens developed using Visual Basics software and stored in a SQL server database hosted at APHRC. All data processing, management and analysis were conducted using STATA statistical software version 13.1.

3.9.1 Fully immunized child (FIC)

A child was classified as FIC if the child had received within the first 12 months of life, eight doses of the routine immunization (one BCG vaccine dose immediately after birth, three polio vaccine doses given at 6, 10 and 14 weeks, three pentavalent vaccine doses vaccines which are given at 6, 10 and 14 weeks and one measles vaccine dose given at nine months of age) as recommended by WHO. To establish the effect of receiving measles vaccine as the last vaccine on child health, an indicator fully immunized child excluding the measles vaccine (FICm) was used. A child was classified as FICm if the child had received within the first 12 months of life, seven doses of the routine immunization (one BCG vaccine dose, three polio vaccine doses, three pentavalent vaccine doses vaccines. An indicator, fully vaccinated child at the time interview visit (FICv) was also considered for analyses for children receiving some of their vaccines past 12 months of age. A child was classified as FICv if the child had received eight doses of the routine immunization (one BCG vaccine dose, three polio vaccine doses, three pentavalent vaccine doses vaccines and one measles vaccine dose) by the time of the first visit between ages 12 to 23 months.

3.9.2 Timeliness of Immunization (early and delayed)

The timeliness of each vaccine was assessed by comparing the date the vaccine was administered with the recommended age for administration of each vaccine. Delayed immunization was defined as any vaccine given to a child two or more weeks later than the recommended age and one month later for measles vaccine. Early immunization was defined as vaccine/dose (polio, pentavalent or measles) given more than four days before the recommended age.

3.9.3 Immunization sequence

Fully immunized children were further assessed and classified based on the recommended sequence of administering the routine vaccines. A child was classified as FIC in-sequence (FIC-IS) if the child was fully vaccinated by the age of 12 months and all the vaccines were in-sequence and FIC out-of-sequence (FIC-OS) if the child was fully immunized by the age of 12 months but some vaccines were out-of-sequence. A vaccine was classified as FIC-OS if any of the following scenarios was satisfied:

i. BCG given together with any pentavalent, second, third or fourth doses of polio or measles vaccines
ii. Pentavalent and polio doses not being given together respectively
iii. BCG, pentavalent or polio doses given after measles vaccine.

3.9.4 Childhood nutrition status

Anthropometric z-scores - height-for-age (chronic malnutrition), weight-for-age (acute malnutrition) and weight-for-height (chronic and acute malnutrition) were computed and used to assess nutrition status. Child's weight, height, sex, and age at every visit were used in the computations. The WHO Anthro software version 3.2.2 and the STATA 'igrowup' macro (WHO, 2011c) were used to calculate the indicators of the attained growth standards. The exact z-score of a child was computed using the formula:

$$\frac{\text{Measured value - Average value in the reference population}}{\text{Standard deviation of the reference population}}$$

The value is then compared to the values of average from the reference group minus two and minus three standard deviations. The child is then classified stunted/wasted/underweight if the respective z-scores (height-for-age, weight-for-height or weight-for-age) is less than minus two (two standard deviations below the average)

3.9.5 Childhood hospitalization

All cases of hospitalization were recorded during each visit for each child. Reasons, date and duration the child was hospitalized were recorded. The number of hospitalization cases occurring between the age of 12 months and 36 months of age were assessed. Hospitalizations due to injuries were excluded from the analysis.

3.9.6 Childhood mortality

All deaths occurring in the study area are recorded during the routine household visits by the NUHDSS data collection team. The dates when the death occurred, and the cause of death were recorded. Childhood mortality between the ages of 12 and 36 months were assessed. Deaths due to accidents were excluded from analysis.

3.9.7 Household wealth status

Principal component analysis method was used to generate a wealth index for each household using different household possessions and ammenities. The household possessions included ownership of motor vehicle, motorcycle, cooking stove, television, refrigerator, livestock, bed, bicycle, video player, iron, lamp, phone, radio, sewing machine, sofa, table, torch, wall clock, phone source of water toilet type, floor type, wall type, cooking place, fuel cook. The wealth index was then used to classify

the households in the study area into three (tertiles) distinct and equal groups, lower (with lowest wealth indices), middle (with wealth indices in the middle) and upper (with highest wealth indices)

3.10 Data analysis

3.10.1 Descriptive statistics

Proportions were used to summarize categorical variables while the mean, median, and standard deviation were used to summarize continuous variables. Individual vaccine coverage was computed by dividing the number of children who received a particular antigen by the total number of children in the study. The FIC coverage by 12 months of age was computed by dividing the number of children who had all the eight recommended antigens by the total number of children in the study. Vaccination delay/early was computed for each antigen by dividing the number of children whose vaccination was delayed or given earlier by the total number of children in the study. The proportion of children receiving vaccines in out-of-sequence was computed by dividing the number of children whose vaccines were given out-of-sequence by the total number of FIC children. Chi-square test of independence was used to test the association between the outcomes of interest by the different categorical factors of interest. The median test was used to compare the median age by different factors of interest. The median test performs a nonparametric K-sample test on the equality of medians. It tests the null hypothesis that the K-samples were drawn from populations with the same median.

3.10.2 Logistic regression models

Potential factors associated with coverage and timing of immunization were assessed using logistic regression. The outcome variables of interest were binary FIC or not FIC for immunization coverage and FIC-OS or FIC-IS for the timing of immunization. First, logistic regressions for each of the available factors were fitted. The unadjusted p-values were then used to select variables to be included in the multiple logistic model. All variables from the bivariate logistic models with a p-value less than 0.25 were included in the multiple model. estimated margins were then used to estimate both the unadjusted and adjusted prevalence ratio (PR) and their corresponding 95% Confidence Interval (CI) of the strength of association between an independent variable and the dependent variable (Deddens *et al.*, 2008; Thompson *et al.*, 1998). The PR indicates how large the prevalence of an outcome in one group of individuals is with a given attribute compared to another group without the attribute.

3.10.3 Kaplan-Meier curves, Cox proportion hazards regression models

Survival analysis modeling techniques were used to assess the time-to-event (death or hospitalization) data. This analysis focusses on the time elapsing before an event is experienced. In this study, our events of interest are death and hospitalization cases. The observations for each child in the study noting the length of time when no event was observed and an indicator at the end of the study of whether the event occurred or not were assessed. Individuals who by the end of the study period did not experience the event of interest are ‘censored’. Hazard ratio to measure the effect of a factor on the time to the event of interest was used. Hazard ratio can be interpreted as a ratio of two instantaneous risks. Kaplan-Meier curves were used to describe the survival data

and compare the FIC versus Not FIC, FIC-IS versus FIC-OS survival curves. Unadjusted and adjusted Cox proportional hazards regression were used to assess the relationship between vaccination patterns (FIC, FICm, FICv and FIC-IS) and time-to-hospitalization, and time-to-death. Schoenfeld residuals were used to test the proportional hazards assumption in the Cox models (Fisher *et al.*, 1999).

Multiple failure-time data or multivariate survival data occur when either more than two events (failures) occur for the same individual, or when same events occur to related individual such in a family. The failure times are correlated within an individual which violates the independence of failure times (Kelly *et al.*, 2000). Therneau (Therneau *et al.*, 1997) suggestion that for analyses that failure events should be classified according to whether they have a natural order, and that they are recurrences of the same types of events was followed. In this study, the hospitalizations fit the description; the hospitalizations cases are ordered from first hospitalization, second hospitalization and so on. Data was analysed by excluding the dependencies between failure times and use the covariance matrix of the estimators adjusting to account for the additional correlation, which gives robust standard errors. For repeated events (hospitalizations cases) Nelson-Aalen (NA) estimator was used to describe the failure data. Children did not have any follow-up visit after the first visit between 12-23 months where a vaccination card was observed were excluded from analysis.

3.10.4 Generalized estimating equation

Generalized estimating equation (GEE) was used to assess the relationship between immunization patterns and child growth between the ages of one to three years in the study area. The generalized estimating equation is very useful when analyzing data

which has correlated observations such as data with repeated measures on the same individuals or clustered data (Liang *et al.*, 1986). GEE models produce correct standard errors and p values for the regression coefficients by using a robust estimation of standard errors to allow for the clustering or correlation. The model makes use of a working correlation matrix reflecting the average dependence among the correlated/clustered observations. GEE models give the odds of having an outcome of interest (e.g. higher z-scores) between two distinct groups (e.g. vaccinated versus non-vaccinated)

CHAPTER FOUR

4 RESULTS

4.1 Background characteristics

A total of 3,827 out of 10,035 (38%) children met the inclusion criteria and were included in the analysis for the first and second objectives. Sixty-two percent of the children were excluded due to lack of an interview visit where a vaccination card was seen between 12-23 months of age. A further 610 children were excluded from the mortality analysis due to luck of at least one follow-up visit to access the outcome of interest. A total of 34 deaths were recorded during the period of study, 1,694 children were followed up to the maximum of follow up time (36 months). A total of 1,489 children did not attained the maximum age of follow up by the end of the study and hence were censored. A further half of the children (1,681) were excluded from the time-to-hospitalization analysis because data on hospitalization was not collected prior to 2011. A total of 54 hospitalizations were recorded between 2011 and 2014 from 26 children.

Figure 4.1 show a histogram of age at visits for all visits superimposed with age at first visit with a card seen between 12-23 months (and child is alive) and visits used for full immunization coverage analysis.

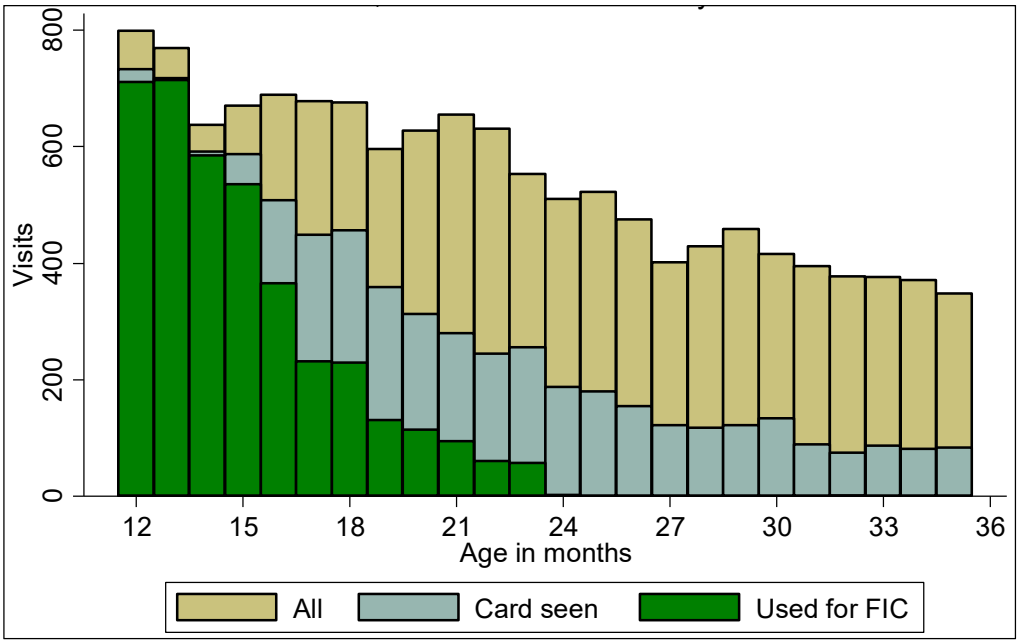


Figure 4.1: Histogram of age of the child at all visits

The study population had slightly more males (50.4%) overall, there were more males in Korogocho (51.6%) and slightly more females in Viwandani location (50.6%). Majority of children were delivered in health facilities (83.1% overall, 84.2% in Korogocho and 82.1% in Viwandani). Slightly higher proportion of the mothers were aged below 25 years (54.4%), 84.3% were married or living together with a spouse, 92.1% attended post-natal care, 69.1% had attained primary or less level of education overall, with a higher proportion of mothers in Viwandani with secondary or above (35.3%) compared with Korogocho at 15.4% (Figure 4.1).

Table 4.1: Background characteristics for children aged 12-23 months

Background Characteristic	Korogocho %	Viwandani %	Total %
Childs gender			
Male	51.6	49.4	50.4
Female	48.4	50.6	49.6
Mothers age			
11-20	27.5	20.7	23.9
21-24	27.0	33.6	30.5
25-29	23.1	25.4	24.3
30-55	19.5	16.8	18.1
Mothers education level			
Primary	79.3	60.2	69.1
Secondary+	15.4	35.3	26.1
Mothers parity			
One	27.3	36.7	32.3
Two	28.3	32.9	30.7
Three and above	44.1	30.1	36.6
Mothers ethnicity			
Kikuyu	30.8	20.0	25.0
Luhya	21.8	15.1	18.2
Luo	24.6	8.2	15.9
Kamba	6.3	35.2	21.7
Other	13.9	17.8	16.0
Household wealth status			
Lower	64.2	4.8	32.5
Middle	21.6	40.1	31.5
Upper	10.8	50.7	32.1
Year of visit			
2008	22.9	25.7	24.4
2009	6.6	9.1	7.9
2010	11.3	10.4	10.8
2011	17.1	14.6	15.8
2012	25.7	23.6	24.6
2013	12.8	10.3	11.5
2014	3.5	6.4	5.0
% attended post-natal care	86.4	97.0	92.1
% delivered from Health Facility	84.2	82.1	83.1
% who were married	79.0	88.8	84.3
N	1784	2043	3827

A higher proportion of mothers in Korogocho were classified in the lower wealth tertile (64%) compared to Viwandani where the majority were classified in the upper wealth tertile (50%), 44.1% of the mothers had a parity of three or more in Korogocho compared 30.1% in Viwandani.

4.2 Vaccination coverage by 12 months of age

Overall FIC coverage by age 12 months was estimated to be 66.6% in this study. FIC coverage in Korogocho was estimated at 58.1%, significantly lower than that of Viwandani at 74.1%. Coverage of the different antigens/doses were all above 90% apart from polio dose at birth (78.6%), measles (81.2%), second dose of PCV (87.2%) and third doses of pentavalent (87.2%), polio (85.7%) and Pneumococcal conjugate vaccines (74.0%). All the specific antigens coverages were significantly different between Viwandani and Korogocho apart from BCG and OPV 1. FIC at the time of visit was estimated slightly higher than FIC at 12 months 68.1% overall (59.7% in Korogocho and 75.5% in Viwandani). Overall FICm was estimated at 78.3% (71.2% in Korogocho and 84.5% in Viwandani). Significant differences were observed in coverage of all the routine vaccines apart from BCG, polio at birth, and first doses of polio and pentavalent. The overall coverages (FIC, FICm, and FICv) were significantly different between the two locations, p-values <0.001 for each (Table 4.2)

Table 4.2: Vaccination coverage by 12 months of age by location and FIC status

Type of vaccine	Korogocho	Viwandani		NOTFIC	FIC	Total
	%	%	p-value	%	%	%
	N=1784	N=2043		N=1277	N=2550	N=3827
BCG	97.1	97.2	0.889	**91.4**	100	97.1
OPV1	98.8	99.3	0.080	**97.2**	100	99.1
OPV2	**94.6**	**98.4**	0.000	**89.8**	100	96.6
OPV3	**80.6**	**90.3**	0.000	**57.2**	100	85.7
Penta1	98.8	99.2	0.214	**97.1**	100	99.0
Penta2	**95.2**	**97.8**	0.000	**89.7**	100	96.6
Penta3	**82.5**	**91.3**	0.000	**61.7**	100	87.2
MV	**75.3**	**86.3**	0.000	**43.5**	100	81.2
FIC	**58.1**	**74.1**	0.000		100	66.6
FICm	**71.2**	**84.5**	0.000	**35.1**	100	78.3
FICv	**59.7**	**75.5**	0.000	**4.5**	100	68.1
	N=751	N=823		N=563	N=1011	N=1574
PCV1	**87.6**	**97.8**	0.000	84.6	97.6	93.0
PCV2	**78.6**	**95.1**	0.000	73.7	94.8	87.2
PCV3	**61.8**	**85.2**	0.000	52.6	86.0	74.0

Proportions significantly different at 5% level of significance are highlighted in bold

Kaplan-Meier coverage curves for each antigen ranged from 75% and above (Figure 4.2). The curves are not touching the 100% mark since children who are not FIC are included. The coverage curves for BCG, OPV 1, OPV 2, pentavalent 1 and pentavalent 2 are very close to the 100% mark showing most of the children received the vaccines. The curves for the third doses of pentavalent and polio vaccines rises slightly above the 75% mark which means around 25% of the children were not vaccinated with the third doses of pentavalent and polio. The curve for the measles vaccine rises up to 75% mark indicating that 75% of the children received their measles vaccine between the ages of 9-12 months. The curves also shows that overall, most children receive their vaccination on time as the curves are more upright. The respective pentavalent and polio curves reveals a proportion of children are not receiving their pentavalent and

polio doses on the same day. The curves also reveals a number of children are receiving their vaccines earlier than the recommended age as the curves are not starting exactly at the recommended age.

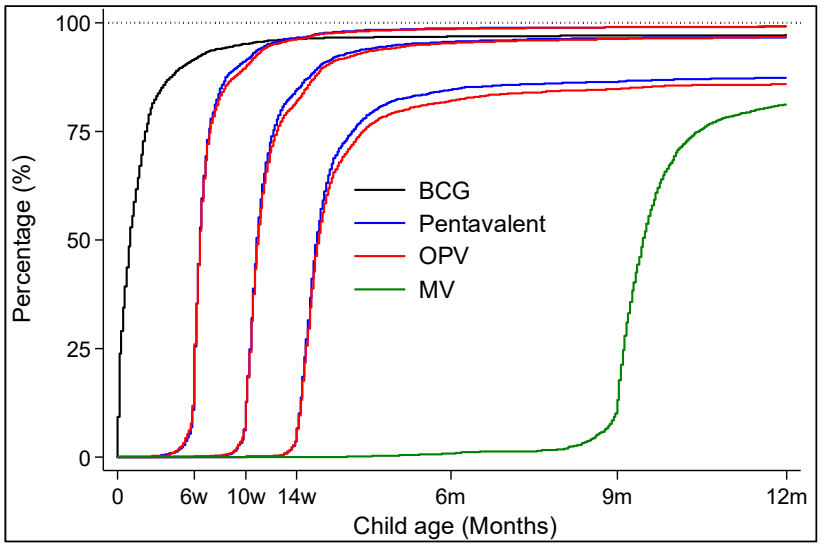


Figure 4.2: Vaccination coverage curves by each antigen by 12 months of age

Immunization coverage curves for each vaccine by FIC status for the whole period are shown in Figure 4.3. The curves for each vaccine by definition end at 100% for FIC children. Vaccination timing among FIC are remarkable especially for the polio and pentavalent doses almost upright apart from a few children who received them a bit later. The MV and BCG coverage curves appear less upright. The coverage curves among the NOTFIC children does not reach 100% and are less upright compared to FIC children which show that more NOTFIC children have their vaccines delayed compared to FIC. Results from Log-rank tests showed significant differences in Kaplan–Meier curves between third doses of polio and pentavalent (P-value 0.004) and non-significant differences between the first doses (P-values=0.242) and second doses (P-value=0.054) of polio and pentavalent vaccines respectively. Significant

differences (P-value <.001) in Kaplan-Meier curves of each antigen by FIC status were observed from log-rank tests. The curves also reveals children receiving vaccines earlier than the recommended age as the curves are not starting exactly at the recommended age for both FIC and NOTFIC children. The NOTFIC curves shows that more than half missed measles vaccination and more than a third of the children missed the third doses of pentavalent and polio.

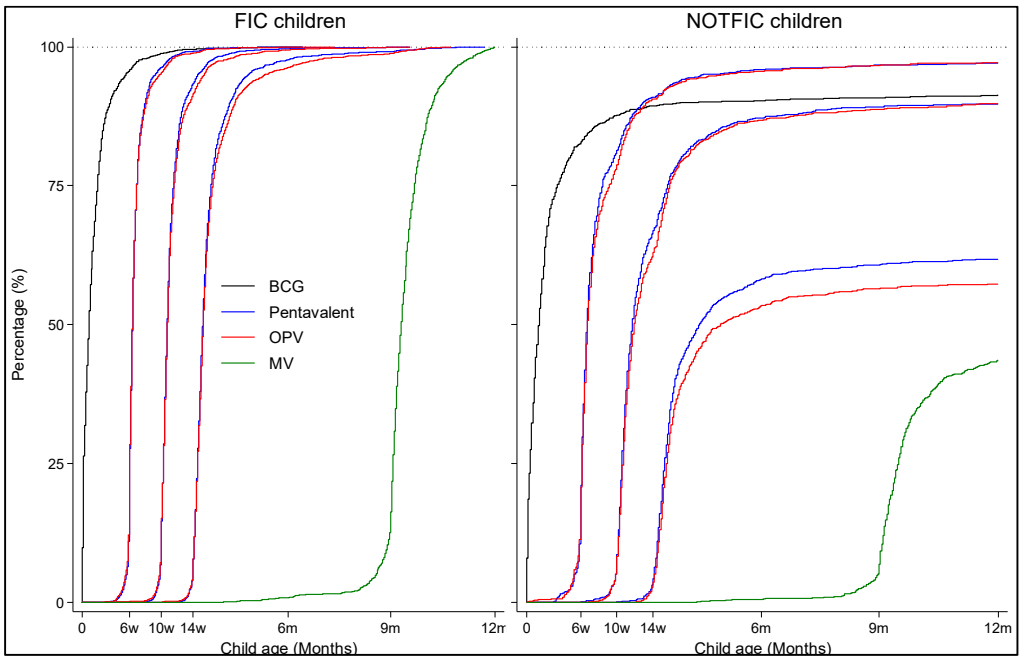


Figure 4.3:Vaccination coverage curves by each vaccine and FIC status by 12 months of age

4.3 Timeliness of immunization

4.3.1 Median age of immunization

The median age and Interquartile range (IQR) of each antigen are summarized in Table 4.3. The overall median age for BCG was estimated at six days (IQR 1-14) for FIC, significantly lower than eight days (IQR 2-17) for NOTFIC children. The median age for the third dose of pentavalent was estimated at 107 (102-114) and 110 (103-126)

days for FIC and NOTFIC children respectively. The median age for the third dose of polio was estimated at 111 (104-129) days for NOTFIC and 107 (102-116) days for FIC children. The median age for the MV was estimated at 282 (275-294) days among FIC children and 290 (277-323) days for NOTFIC children. Overall median age for all vaccines were significantly lower for FIC compared to NOTFIC children. There was an overall decreasing trend in the median age of immunization for all the routine vaccine over the years.

Table 4.3: Median age and interquartile range (in days) of the routine immunizations by FIC status and year of visit

FIC status & Year of visit	BCG	OPV1	OPV2	OPV3	Penta1	Penta2	Penta3	Measles
	M (IQR)	M (IQR)	M (IQR)	M (IQR)	M (IQR)	M (IQR)	M (IQR)	M (IQR)
NOTFIC 2008	12 (4;22)	50 (44;69)	85 (75;110)	115 (106;150)	47 (43;61)	82 (73;105)	112 (102;135)	290 (277;339)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001
2009	10 (3;17)	46 (43;67)	82 (73;104)	109 (103;135)	45 (42;55)	79 (73; 95)	109 (105;127)	288 (275;313)
p-value	0.064	0.055	0.002	0.060	0.674	0.084	0.029	0.126
2010	11 (5;26)	47 (43;59)	82 (73;99)	112 (104;126)	47 (43;59)	82 (74;102)	109 (103;120)	287 (277;301)
p-value	0.237	0.002	0.002	0.126	0.005	0.002	0.232	0.009
2011	6 (1;13)	50 (43;73)	84 (74;111)	112 (104;140)	47 (43;57)	80 (73; 96)	113 (104;125)	286 (276;318)
p-value	0.497	<0.001	<0.001	0.335	0.013	<0.001	0.033	0.078
2012	5 (2;13)	47 (43;53)	81 (75;101)	111 (105;126)	47 (43;55)	81 (75;101)	110 (104;132)	293 (279;341)
p-value	0.048	<0.001	<0.001	<0.001	<0.001	<0.001	0.003	0.002
2013	7 (2;16)	46 (42;51)	77 (73;91)	108 (103;116)	46 (42;53)	78 (74; 90)	108 (103;116)	291 (280;310)
p-value	0.030	0.140	.014	0.283	0.621	0.010	0.121	0.033
2014	10 (3;23)	45 (42;71)	77 (73;102)	110 (104;123)	46 (42;58)	77 (73; 96)	108 (102;117)	286 (277;367)
p-value	0.029	0.943	0.931	0.414	0.373	0.930	0.886	0.353
2008-2014	8 (2;17)	47 (43;61)	81 (74;104)	111 (104;129)	47 (43;57)	80 (74;99)	110 (103;126)	290 (277;323)
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
FIC 2008	8 (2;17)	45 (42;50)	75 (72;84)	108 (102;120)	45 (42;49)	75 (72;81)	106 (101;115)	282 (275;295)
2009	7 (1;16)	45 (42;47)	75 (71;80)	106 (102;115)	45 (42;48)	75 (72;81)	106 (102;118)	282 (274;294)
2010	9 (2;17)	45 (42;49)	75 (72;82)	107 (102;115)	45 (42;49)	75 (72;81)	107 (102;114)	280 (274;293)
2011	6 (1;13)	45 (43;49)	77 (72;85)	109 (103;123)	45 (43;49)	76 (72;81)	108 (102;116)	281 (275;295)
2012	4 (1;10)	44 (42;47)	75 (72;79)	106 (102;112)	44 (42;48)	75 (72;80)	106 (102;113)	284 (276;294)
2013	5 (1;12)	45 (42;48)	75 (72;79)	106 (102;112)	45 (42;49)	76 (72;79)	107 (103;112)	285 (276;295)
2014	5 (2;10)	45 (42;50)	77 (74;83)	108 (104;119)	45 (42;50)	77 (73;81)	108 (104;116)	283 (275;292)
2008-2014	6 (1;14)	45 (42;48)	75 (72;81)	107 (102;116)	45 (42;48)	75 (72;81)	107 (102;114)	282 (275;294)

Penta1,2,3 = Pentavalent 1,2,3 vaccines doses, M=Media, IQR= interquartile range

4.3.2 Immunization delays

Overall, a quarter of the children received BCG more than two weeks after birth. In each of the vaccines administered at least 14% of the children got it more than two weeks later than scheduled with the third doses of OPV (34.5%), pentavalent (32.3%) and, measles (38.5%) vaccines recording highest proportions of delays. The magnitude of delays increased with subsequent doses for polio and pentavalent vaccines. The first dose of the polio had 16% of the children with delayed vaccination, a further 10% had their second polio dose delayed and 8% had their third polio dose delayed. The first dose of the pentavalent had 14% of the children with delayed vaccination, a further 9% delayed their second pentavalent dose and 9% more delayed their third dose. A further 18% and 4% of the children received measles vaccine more than one and three months late respectively. The levels of vaccination delays were significantly higher among children from Korogocho area for OPV 1, 2, 3 (p-values <0.001), pentavalent 1, 2, 3 (p-values <0.001) and measles (p-values <0.002) vaccines compared to Viwandani area. Levels of vaccination delays were significantly high among the NOTFIC children for all routine vaccination compared to FIC children (p-values <0.001) (Table 4.4).

Table 4.4: Vaccination delays by vaccine type, location and FIC status

Type of vaccine	Korogocho	Viwandani		NOTFIC	FIC		Total
	%	%	P-value	%	%	P-value	% (N)
BCG	24.4	26.2	0.211	30.5	23.0	0.000	25.4 (3717)
OPV0	19.9	19.3	0.688	23.4	17.9	0.000	19.6 (3008)
OPV1	22.0	11.3	0.000	28.7	10.2	0.000	16.3 (3791)
OPV2	34.7	19.2	0.000	43.1	18.6	0.000	26.2 (3697)
OPV3	45.6	25.9	0.000	45.1	31.5	0.000	34.5 (3281)
Penta1	18.4	11.0	0.000	25.1	9.2	0.000	14.4 (3790)
Penta2	30.8	17.5	0.000	38.9	16.8	0.000	23.6 (3696)
Penta3	40.7	25.7	0.000	41.6	29.4	0.000	32.3 (3338)
Measles	41.6	36.1	0.002	51.3	35.1	0.000	38.5 (3106)
Measles (1 month)	22.2	14.7	0.000	34.1	13.7	0.000	18.0 (3106)
Measles (3 months)	5.7	2.6	0.000	18.7	0.0	0.000	4.0 (3106)
PCV1	49.7	27.6	0.000	45.0	33.9	0.023	37.6 (1463)
PCV2	58.2	32.5	0.000	52.1	39.8	0.002	43.6 (1373)
PCV3	61.9	38.2	0.00	53.4	45.9	0.132	47.8 (1165)

Penta1,2,3 = Pentavalent 1,2,3 vaccines doses. Vaccination delays define as vaccine given more than two weeks after recommended date

4.3.3 Early immunization

Overall, 3.3%, 2.7% and 8.4% of the children received their polio 1, pentavalent 1 and measles vaccines earlier than recommended age respectively. Approximately 4.9% of the children received MV more than 14 days before the recommended age. The proportion of early immunization was significantly higher among the NOTFIC compared to FIC children for pentavalent doses (P-values, 0.005, 0.029 and 0.001 for first, second and third doses respectively) and the first polio dose (P-value=0.010). Early immunization was significantly higher among children in Korogocho compared to Viwandani for all polio and pentavalent doses and the third PCV dose (P-values<0.05) (Table 4.5).

Table 4.5: Early vaccination by vaccine type and location and FIC status

Type of vaccine	Korogocho % (N)	Viwandani % (N)	p-value	NOTFIC % (N)	FIC % (N)	Total % (N)
OPV1	4.3 (1762)	2.4 (2029)	0.001	**4.3** (1241)	**2.8** (2550)	3.3 (3791)
OPV2	2.3 (1687)	0.9 (2010)	0.001	1.7 (1147)	1.5 (2550)	1.6 (3697)
OPV3	1.3 (1437)	0.6 (1844)	0.030	1.1 (731)	0.9 (2550)	0.9 (3281)
Penta1	3.3 (1763)	2.2 (2027)	0.043	**3.8** (1240)	**2.2** (2550)	2.7 (3790)
Penta2	1.9 (1699)	1.0 (1997)	0.016	**2.0** (1146)	**1.1** (2550)	1.4 (3696)
Penta3	1.6 (1472)	0.7 (1866)	0.016	**2.2** (788)	**0.8** (2550)	1.1 (3338)
Measles	7.5 (1343)	9.2 (1763)	0.092	7.0 (556)	8.8 (2550)	8.4 (3106)
Measles (2 weeks earlier)	4.8 (1343)	4.9 (1763)	0852	4.8 (556)	4.9 (2550)	4.9 (3106)
Measles (1 month earlier)	2.3 (1343)	1.8 (1763)	0.324	1.9 (556)	2.1 (2550)	2.0 (3106)
PCV1	1.8 (658)	1.4 (805)	0.392	1.9 (476)	1.4 (987)	1.6 (1463)
PCV2	1.3 (590)	0.5 (783)	0.070	1.2 (415)	0.7 (958)	0.9 (1373)
PCV3	1.9 (464)	0.3 (701)	0.003	1.0 (296)	0.9 (869)	0.9 (1165)

Proportions significantly different at 5% level of significance are highlighted in bold. Early vaccination defined as vaccine given more than four day before recommended age

4.3.4 Immunization sequencing

Proportion of children fully immunized with all recommended routine childhood vaccines but in a different sequence from the recommendations (FIC-OS) is summarised in Table 4.6. Overall, 21.8% of FIC children were FIC-OS. The levels of FIC-OS were significantly higher among mothers from Korogocho location at 30.6% compared to Viwandani at 15.8% (p-value <0.001). The main cause of being FIC-OS was not receiving pentavalent and polio doses together at 18.3% overall, with significantly higher proportion in Korogocho at 27.0% compared to Viwandani at 12.3% (p-value <0.001). Four percent of the children received their BCG vaccine together or after pentavalent or measles vaccine.

Table 4.6: Out-of-sequence vaccination for FIC children by location

	Vaccination pattern	Korogocho %	Viwandani %	P-value	Total %
1	BCG together or after Pentavalent/Measles	4.3	3.8	0.464	4.0
2	Pentavalent and Polio doses NOT given together	27.0	12.3	0.000	18.3
3	Pentavalent given together or after Measles	1.1	0.7	0.271	0.8
4	Fully immunized children in out-of-sequence (1 or 2 or 3)	30.6	15.8	0.000	21.8
	N (FIC only)	1,036	1,514		2,550

Approximately 60% and 17% of children who were not FIC were missing only one or two vaccines respectively. A significantly higher proportion of NOTFIC children in Viwandani (65.6%) were missing one vaccine compared to Korogocho (56.7%). A significantly higher proportion of NOTFIC children in Korogocho (6.0%) were missing five or more vaccines compared to Viwandani at 2.5%. About 6.6% became fully vaccinated after 12 months of age. The main vaccines missing were OPV3 (41.8%), MV (46.4%) and pentavalent 3 (38.2%). Korogocho location had significantly higher number of children missing the second (12.2%, P-value <0.05) and third (45.7%, P-value<0.05) doses of polio and third dose (41.6%, P-value<0.05) of pentavalent compared to Viwandani. Significantly higher numbers of children from Viwandani location were missing BCG vaccine compared to Korogocho (9.8% vs. 6.6, P-value <0.05). Overall, majority (46.4%) of the NOTFIC children were missing the measles vaccine (Table 4.7).

Table 4.7: Number of missing vaccines and type of vaccines missing by location

Vaccines missing	Korogocho	Viwandani	Total	p-value
	%	%	%	
N	748	529	1277	
By number of vaccine missing				
None (FIC after 12 months)	**5.8**	7.8	6.6	0.001
One vaccine	**56.7**	65.6	60.4	
Two vaccines	**19.1**	14.2	17.1	
Three vaccines	**7.6**	7.0	7.4	
Four vaccines	**4.8**	3.0	4.1	
Five and above vaccines	**6.0**	2.5	4.5	
By type of vaccine missing				
BCG	**6.6**	9.8	7.9	0.032
OPV1	2.3	1.7	2.0	0.476
OPV2	**12.2**	5.3	9.3	<0.001
OPV3	**45.7**	36.3	41.8	0.001
Pentavalent1	2.7	3.0	2.8	0.709
Pentavalent2	11.2	8.7	10.2	0.140
Pentavalent3	**41.6**	33.5	38.2	0.003
Measles	48.1	44.1	46.4	0.150
OPV3 & Measles	**15.4**	9.5	12.9	0.002
Pentavalent3 & Measles	**17.3**	7.2	13.1	<0.001
OPV3 & Penta3	**22.7**	17.2	20.4	0.016
OPV3, Penta3 & Measles	**11.4**	6.1	9.2	0.001

Proportions significantly different at 5% level of significance are highlighted in bold

4.3.5 Determinants of vaccination coverage

4.3.5.1 Determinants of FIC

Results from logistic regression analyses of potential determinants of FIC (Table 4.8), shows children from mothers attending post-natal care were 24% more likely to be fully immunized compared children from mothers who did not attend for the unadjusted model. From the adjusted model, mothers who attends postnatal care (PR 1.12, CI: 1.02:1.23), aged above 20 years (21-24 years (PR 1.08, CI: 1.00:1.16), 25-29 years (PR 1.13, CI: 1.05:1.22) and 30+ years (PR 1.12, CI: 1.02:1.21)) and residents of Viwandani (PR 1.22, CI: 1.15:1.30) were statistically associated with higher FIC coverages (8-22%). In contrast, mothers with higher parity (Parity 2 (PR 0.89, CI: 0.82:0.95) and Parity 3+ (PR 0.84, CI: 0.76:0.92)) and those not from Kikuyu or Kamba ethnic groups (Luhya (PR 0.93, CI: 0.85:1.00), Luo (PR 0.88, CI: 0.80:0.96) and others (PR 0.89, CI: 0.81:0.97)) were statistically associated with (7-16%) lower FIC coverages adjusting for all other factors.

Table 4.8:Unadjusted and adjusted logistic regression of association between background factors and FIC coverage

Background factors		Unadjusted	Adjusted	
		PR [95% CI]	PR [95% CI]	p-values
Child sex	Male	1.00	1.00	
	Female	1.02 [0.97;1.06]	1.03 [0.98;1.08]	0.200
Postnatal care	No	1.00	1.00	
	Yes	**1.24** [1.13;1.35]	**1.12** [1.02;1.23]	**0.019**
Mothers age	11_20	1.00	1.00	
	21_24	1.05 [0.99;1.12]	**1.08** [1.00;1.16]	**0.023**
	25_29	1.06 [1.00;1.13]	**1.13** [1.05;1.22]	
	30_55	1.03 [0.95;1.10]	**1.12** [1.02;1.21]	
Marital status	Married	1.00	1.00	
	Not married	0.95 [0.88;1.02]	0.98 [0.90;1.05]	0.536
Mothers education	Primary	1.00	1.00	
	Secondary+	**1.12** [1.07;1.16]	1.04 [0.98;1.09]	0.210
Health facility delivery	Yes	1.00	1.00	
	No	**0.92** [0.86;0.99]	0.96 [0.90;1.03]	0.311
Parity	Parity 1	1.00	1.00	
	Parity 2	**0.92** [0.87;0.97]	**0.89** [0.82;0.95]	**<0.001**
	Parity 3+	**0.86** [0.80;0.91]	**0.84** [0.76;0.92]	
Ethnic group	Kikuyu	1.00	1.00	
	Luhya	**0.88** [0.81;0.95]	**0.93** [0.85;1.00]	**0.006**
	Luo	**0.81** [0.73;0.89]	**0.88** [0.80;0.96]	
	Kamba	**1.05 [**0.99;1.10]	**0.97** [0.90;1.04]	
	Other	**0.89** [0.82;0.96]	**0.89** [0.81;0.97]	
Wealth tertile	Lower	1.00	1.00	
	Middle	**1.14** [1.08;1.20]	0.97 [0.90;1.03]	0.079
	Upper	**1.13** [1.07;1.19]	0.91 [0.84;0.99]	
Location	Korogocho	1.00	1.00	
	Viwandani	**1.24** [1.20;1.29]	**1.22** [1.15;1.30]	**<0.001**

Estimates significantly different at 5% level of significance are highlighted in bold
PR=Prevalence ratio CI=Confidence interval

4.3.5.2 Determinants of FIC-OS

Regression analyses were also conducted considering only the fully immunized children. The FIC-out-of-sequence (FIC-OS) children were compared to those who received their vaccines as recommended (FIC in-sequence). Mothers who did not deliver from a health facility (PR 1.53, CI: 1.34:1.72) were statistically associated with a 53% higher FIC-OS compared to mothers who delivered in a health facility adjusted for all other factors. In contrast, mothers' residents of Viwandani were statistically associated with a 69% (46-91%) lower prevalence of FIC-OS compared to mothers' resident of Korogocho adjusting for all other factors. Post-natal attendance, mother's education level, ethnicity, and wealth status were significant in the unadjusted model but insignificant after controlling for other factors in the model. All other factors considered were not statistically significant when controlling for other factors (Table 4.9).

Table 4.9: Unadjusted and adjusted logistic regression of association between background factors and FIC-OS coverage

Factors		Unadjusted	Adjusted	
		PR [95% CI]	PR [95% CI]	p-value
Child sex	Male	1.00	1.00	
	Female	1.03 [0.89;1.18]	1.06 [0.90;1.22]	>0.05
Postnatal care	No	1.00	1.00	
	Yes	**0.68** [0.43;0.94]	0.86 [0.56;1.16]	>0.05
Mothers age	11_20	1.00	1.00	
	21_24	0.82 [0.62;1.02]	0.89 [0.66;1.13]	>0.05
	25_29	0.80 [0.59;1.01]	0.88 [0.60;1.15]	
	30_55	0.94 [0.72;1.17]	0.98 [0.68;1.29]	
Marital status	Married	1.00	1.00	
	Not married	1.17 [0.97;1.37]	1.02 [0.78;1.26]	>0.05
Mothers education	Primary	1.00	1.00	
	Secondary+	**0.81** [0.63;0.99]	1.04 [0.86;1.23]	>0.05
Health facility delivery	Yes	1.00	1.00	
	No	**1.45** [1.28;1.61]	**1.53** [1.34;1.72]	**<0.001**
Parity	Parity 1	1.00	1.00	
	Parity 2	0.96 [0.78;1.15]	1.04 [0.82;1.27]	>0.05
	Parity 3+	1.07 [0.89;1.24]	1.02 [0.76;1.29]	
Ethnic group	Kikuyu	1.00	1.00	
	Luhya	**1.12** [0.91;1.34]	1.10 [0.86;1.34]	>0.05
	Luo	**1.20** [0.98;1.42]	1.04 [0.79;1.30]	
	Kamba	**0.79** [0.57;1.01]	1.06 [0.82;1.31]	
	Other	**0.76** [0.51;1.02]	0.85 [0.55;1.14]	
Wealth tertile	Lower	1.00	1.00	
	Middle	**0.62** [0.45;0.79]	1.02 [0.80;1.25]	>0.05
	Upper	**0.45** [0.27;0.64]	0.95 [0.69;1.21]	
Location	Korogocho	1.00	1.00	
	Viwandani	**0.34** [0.19;0.49]	**0.31** [0.09;0.54]	**<0.001**

- **Estimates significantly different at 5% level of significance are highlighted in bold**
- **PR=Prevalence ratio, CI=confidence interval**

4.4 Relationship between vaccination coverage and child health

4.4.1 Child survival

A total of 34 deaths were recorded during the period under consideration excluding deaths from accidents. Kaplan-Meier survival curves (Figure 4.4) compared the survival probabilities of a child dying after the age of 12 months for a child who is FIC or FICm, FICv, and FIC-IS or FIC-OS compared to NOTFIC children. From the survival curves, the NOTFIC children group have consistently steeper curves compared to children who are FIC or FICm or FICv or FIC-IS which mean they are dying quicker.

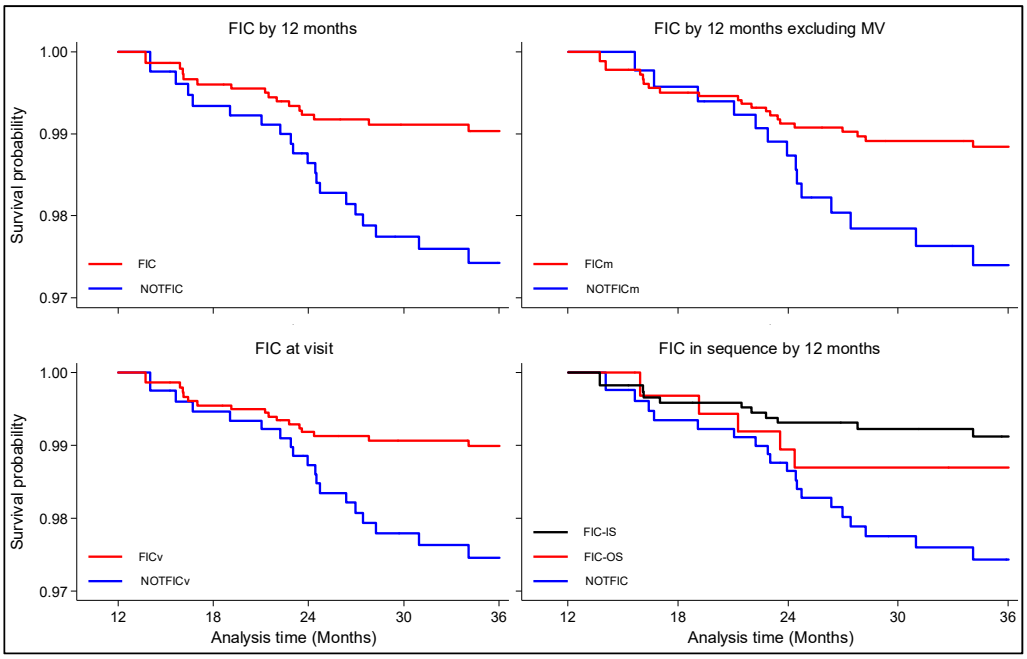


Figure 4.4: Kaplan-Meier survival curves by immunization patterns

The survival analyses for the relationship between being FIC at 12 months, FIC excluding measles vaccine (FICm) and FIC out-of-sequence (Not FIC, FIC-IS and FIC-OS) and child mortality are summarized in Table 4.10. The results from the

unadjusted and adjusted Cox regression models pointed towards positive relationships between FIC, FICm, FICv, FIC-IS and FIC-OS and child survival compared to NOTFIC children. Being FIC was statistically associated with a 63% lower mortality (HR 0.37, 95% CI: 0.19:0.72) between age one and three years compared to NOTFIC children. When excluding the measles vaccine in the classification of fully immunized or not, being FIC (FICm) was statistically associated with 60% lower mortality (HR 0.40, 95% CI: 0.20:0.79) compared to NOTFIC children. Considering the sequence in which the vaccines were administered to the children, being FIC in-sequence (FIC-IS) was statistically associated with a 69% (HR 0.31, 95% CI: 0.15:0.67) lower mortality compared to NOTFIC children. When adjusted for other background factors, there was statistically significant 58% (HR 0.42, 95% CI: 0.20:0.85), 51% (HR 0.49, 95% CI: 0.24:1.00) and 64% (HR 0.36, 95% CI: 0.16:1.80) lower mortality for FIC, FICm and FIC-IS respectively compared to NOTFIC children.

Table 4.10: Cox proportional hazards regression models for time-to-death controlling for other factors

Vaccination status	Rate	No. deaths	N	Unadjusted	Adjusted[1]
				HR [95% CI]	HR [95% CI] [p-value]
1.FIC status					
NOTFIC	14.0	19	1,030		
FIC	5.1	15	2,187	**0.37** [0.19;0.72]	**0.42** [0.21;0.85] [0.017]
2.FICm status					
NOTFICm	14.8	14	696	1.00	1.00
FICm	6.0	20	2,521	**0.40** [0.20;0.79]	**0.49** [0.24;1.00] [0.049]
3. FICv status					
NOTFICv	13.8	18	985	1.00	1.00
FICv	5.3	16	2,232	**0.39** [0.20;0.76]	**0.45** [0.22;0.91] [0.027]
4. FIC-IS status					
NOTFIC	14.0	19	1,030	1.00	1.00
FIC-OS	7.6	5	471	**0.55** [0.21;1.48]	**0.61** [0.23;1.66] [0.042]
FIC-IS	4.4	10	1,716	**0.31** [0.15;0.67]	**0.36** [0.16;0.80] [0.001]

- [1]controlled for child sex, mother's postnatal attendance, age, marital status, health facility delivery, education level, ethnicity, wealth status and location
- Estimates significantly different at 5% level of significance are highlighted in bold
- HR=Hazards ratio, CI=confidence interval
- FIC (model 1), FICm (model 2), FICv (model 3) and FIC-IS (model 4)

4.4.2 Child hospitalization

The number of episodes, dates and duration of hospitalization of the children in the study area were used to evaluate hospitalization rates between 12-36 months of age. A total of 54 hospitalizations were reported during the period of follow-up. Six and four children reported two and three number of hospitalizations during the whole period of follow-up respectively. Kaplan-Meier survival curves in Figure 4.5 below compares the survival probabilities of a child being hospitalized after the age of 12 months for a child who is FIC or FICm, FICv, and FIC-IS or FIC-OS compared to NOTFIC children.

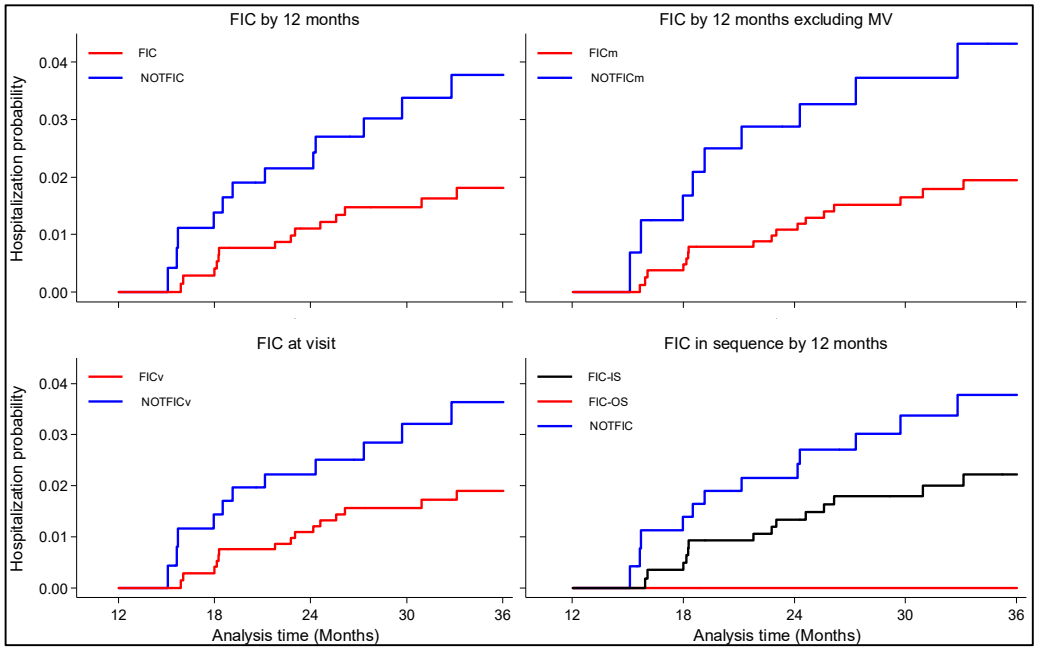


Figure 4.5: Nelson-Allen survival curves for time-to-hospitalization by different immunization patterns

The survival analyses for the relationship between immunization patterns (FIC, FICm, and FIC-IS) and time to hospitalization are summarized in Table 4.11. All the estimates shown have been controlled for child's sex, postnatal care attendance, mother's age, marital status, education level, delivery place, parity, ethnicity, wealth status and household location. Sex of the child was statistically associated with 46% lower hospitalization cases in males (HR 0.54, 95% CI: 0.20:0.79) in the unadjusted Cox regression model as compared to females. Though not significant, results pointed towards lower hospitalization cases among fully immunized 35% (HR 0.65, 95% CI: 0.35:1.19) reduction, fully immunized excluding measles 24% (HR 0.76, 95% CI: 0.39:1.47) reduction and fully immunized and in sequence 26% (HR 0.74, 95% CI: 0.40:1.38) reduction respectively compared to NOTFIC.

Table 4.11: Cox proportional hazards regression models for time-to-hospitalization controlling for other factors

Vaccination status	Rate	No. hospitalizations	Unadjusted	Adjusted[1]	p-value
			HR [95% CI]	HR [95% CI]	
1. FIC status					
NOTFIC	36.8	21			
FIC	23.2	31	0.63 [0.36;1.1]	0.65 [0.35;1.19]	0.159
2. FICm status					
NOTFICm	36.6	14	1.00	1.00	
FICm	25.0	38	0.68 [0.37;1.26]	0.76 [0.39;1.47]	0.411
3. FICv status					
NOTFICv	31.0	17	1.00	1.00	
FICv	25.8	35	0.84 [0.47;1.49]	0.90 [0.48;1.69]	0.378
4. FIC-IS status					
NOTFIC	36.8	21	1.00	1.00	
FIC-OS	11.7	3	0.32 [0.09;1.08]	0.33 [0.10;1.15]	0.196
FIC-IS	26.0	28	0.70 [0.40;1.24]	0.74 [0.40;1.38]	

- [1]controlled for child sex, mother's postnatal attendance, age, marital status, health facility delivery, education level, ethnicity, wealth status and location
- Estimates significantly different at 5% level of significance are highlighted in bold
- HR=Hazards ratio, CI=confidence interval
- FIC (model 1), FICm (model 2), FICv (model 3) and FIC-IS (model 4)

4.4.3 Child anthropometry measurements

4.4.3.1 Height-for-age z-scores

From the bivariate regression analysis, there were significant positive associations between FIC (B 0.13, CI: 0.041:0.22), FICm (B 0.11, CI: 0.01:0.21), FIC-OS (B 0.04, CI: -0.09:0.16) and FIC-IS (B 0.15, CI: 0.07:0.24) and height for age z-scores respectively. Controlling for all background factors, only FICv was significantly associated with an increase in height-for-age Z-scores. Fully immunized children, FICm, and FIC-IS were positively associated with an increase in height for age z-scores though the results were not statistically significant.

Table 4.12: Unadjusted and adjusted GEE models for height-for-age controlling for other factors

Immunization patterns		Unadjusted	Adjusted[1]	
		Coefficient. [95% CI]	Coefficient. [95% CI]	p-value
1.FIC	NOTFIC			
	FIC	**0.13** [0.04;0.22]	0.08 [-0.01;0.17]	0.067
2.FICm	NOTFICm			
	FICm	**0.11** [0.01;0.21]	0.05 [-0.05;0.15]	0.300
3.FICv	NotFICv			
	FICv	**0.15** [0.06;0.23]	**0.10** [0.01;0.20]	**0.023**
4.FIC-IS	NOTFIC			
	FIC-OS	**0.04** [-0.09;0.16]	0.05 [-0.08;0.18]	0.102
	FIC-IS	**0.15** [0.07;0.24]	0.09 [0.00;0.19]	

- [1]controlled for child sex, mother's postnatal attendance, age, marital status, health facility delivery, education level, ethnicity, wealth status and location
- Estimates significantly different at 5% level of significance are highlighted in bold. GEE=Generalized Estimating Equation, CI=Confidence interval
- FIC (model 1), FICm (model 2), FICv (model 3) and FIC-IS (model 4)

4.4.3.2 Weight-for-age z-scores

Results from bivariate regression analysis between weight for ages z-scores and FIC patterns showed statistically positive associations between FIC (B 0.14, CI: 0.07:0.22), FICm (B 0.16, CI: 0.07:0.25), FIC-OS (B 0.05, CI: 0.06:-0.17) and FIC-IS (B 0.17, CI: 0.09:0.25) and weight for age z-scores respectively. Controlling for all background factors, being FIC was associated with 0.13 increase (B 0.13, CI: 0.05:0.21), being FICm was associated with 0.15 increase (B 0.15, CI: 0.06:0.24) and being FIC-IS was associated with 0.14 increase (B 0.14, CI: 0.06:0.23) in weight-for-age z-score respectively.

Table 4.13: Unadjusted and adjusted GEE models for weight-for-age controlling for other factors

Immunization patterns		Unadjusted Coefficient. [95% CI]	Adjusted[1] Coefficient. [95% CI]	p-value
1.FIC	NOTFIC			
	FIC	**0.14** [0.07;0.22]	**0.13** [0.05;0.21]	**0.002**
2.FICm	NOTFICm			
	FICm	**0.16** [0.07;0.25]	**0.15** [0.06;0.24]	**0.001**
3.FICv	NotFICv			
	FICv	**0.14** [0.06;0.22]	**0.13** [0.05;0.22]	**0.001**
4.FIC-IS	NOTFIC			
	FIC-OS	**0.05** [-0.06;0.17]	**0.07** [-0.05;0.19]	**0.004**
	FIC-IS	**0.17** [0.09;0.25]	**0.14** [0.06;0.23]	

- [1]controlled for child sex, mother's postnatal attendance, age, marital status, health facility delivery, education level, ethnicity, wealth status and location
- Estimates significantly different at 5% level of significance are highlighted in bold. GEE=Generalized Estimating Equation, CI=Confidence interval
- FIC (model 1), FICm (model 2), FICv (model 3) and FIC-IS (model 4)

4.4.3.3 Weight-for-Height z-scores

Results from bivariate regression analysis between weight for height z-scores and FIC patterns showed statistically positive associations between FIC (B 0.13, CI: 0.04:0.22), FICm (B 0.11, CI: 0.01:0.21), FIC-OS (B 0.04, CI: -0.09:0.16) and FIC-IS (B 0.15, CI: 0.07:0.24) and weight for age z-scores respectively. Controlling for all background factors, being FIC was associated with 0.12 increase (B 0.12, CI: 0.03:0.20), being FICm was associated with 0.17 increase (B 0.17, CI: 0.08:0.27) and being FIC-IS was associated with 0.13 increase (B 0.13, CI: 0.05:0.22) in weight for age z-score respectively.

Table 4.14: Unadjusted and adjusted GEE models for weight-for-height controlling for other factors

Immunization patterns		Unadjusted	Adjusted[1]	
		Coefficient. [95% CI]	Coefficient[95%CI]	p-value
1.FIC	NOTFIC			
	FIC	**0.13** [0.04;0.22]	**0.12** [0.03;0.20]	**0.006**
2.FICm	NOTFICm			
	FICm	**0.11** [0.01;0.21]	**0.17** [0.08;0.27]	**0.001**
3.FICv	NotFICv			
	FICv	**0.15** [0.06;0.23]	**0.12** [0.03;0.20]	**0.006**
4.FIC-IS	NOTFIC			
	FIC-OS	**0.04** [-0.09;0.16]	**0.07** [-0.05;0.19]	**0.011**
	FIC-IS	**0.15** [0.07;0.24]	**0.13** [0.05;0.22]	

- [1]controlled for child sex, mother's postnatal attendance, age, marital status, health facility delivery, education level, ethnicity, wealth status and location
- Estimates significantly different at 5% level of significance are highlighted in bold. GEE=Generalized Estimating Equation, CI=Confidence interval
- FIC (model 1), FICm (model 2), FICv (model 3) and FIC-IS (model 4)

CHAPTER FIVE

5 DISCUSSION

This study describes the level of immunization coverage of Fully Immunized Children, timing of immunization (early and delays) and sequencing of the routine childhood vaccination by 12 months of age in children aged 12-23 months in informal urban settlements in Nairobi, Kenya. The study further identifies the determinants of a - 12-23 months of age child - being fully immunized by 12 months and the determinants of a fully immunized 12-23 months of age child being immunized in out-of-sequence for vaccines given by 12 months of age. The study also describes the association between immunization patterns and childhood health (nutrition status, morbidity, and mortality) for children followed from the age of one year to three years old.

5.1 Immunization coverage

The overall FIC coverage was estimated at 66.6% in this study. Coverages for the specific vaccine antigens were above 90% apart from measles and third doses of polio and pentavalent vaccines. Overall FIC coverage was shown to depend on postnatal care attendance, mother's age, parity, ethnicity, and location. The unadjusted model showed FIC coverage also depended on mother's education and household wealth status.

The overall FIC coverage in this study are similar to results (68%) obtained from a cross-sectional study targeting approximately all informal settlements in Nairobi (Egondi *et al.*, 2015) conducted in 2012 which is an increase from the result (44%)

estimated in a previous study conducted in same area (APHRC, 2002) in 2002. The FIC coverage in this study still lags behind Nairobi (81%) and national estimates (79%). This increase in FIC coverage in the study area may be attributed to efforts made by the ministry of health and other stakeholders to improve the uptake of health services and awareness from interventions conducted in the study area, even though more needs to be done to reduce the gap existing between informal settlements and other parts of Nairobi. Increases in immunization coverage have been reported in other low and middle-income countries over the years (WHO, 2011a). The study showed an initial increase of FIC coverage between 2008 and 2010 followed by a decrease between 2011 and 2014. Further investigation is needed in the study area to understand this scenario. Even with the increase in FIC coverage, the figure is still lower in urban poor settlements as compared to estimates from other urban areas and Nairobi in particular (KNBS, 2015).

This study showed higher coverage for vaccines given during infants' early part of life and lower for vaccines given later in life specifically measles and third doses of polio, pentavalent and pneumococcal vaccines. This resonates well with previous findings in the study area (KNBS, 2011; Mutua *et al.*, 2011) and other studies conducted in Burkina Faso, Nigeria and South Africa (Fadnes, Jackson, *et al.*, 2011; Sadoh *et al.*, 2009; Schoeps *et al.*, 2013). Children missing measles and third doses of polio and pentavalent vaccines were identified in this study as the main reasons of not being fully immunized. Similar observations were made by other studies conducted in other settings (Fadnes, Jackson, *et al.*, 2011). The issue of not completing recommended doses of a vaccine is a big concern. A child is protected optimally from specific

infections if the child received all the three doses. When a dose is skipped, delayed or missed altogether the child becomes vulnerable from specific infections and also 'herd' immunity is compromised (Fine, 1993). The low coverage of measles vaccine poses similar concerns. Studies have shown measles and BCG vaccines to be having non-specific beneficial effects on child survival (Sankoh *et al.*, 2014; Welaga *et al.*, 2012). The high number of infant missing out on MV vaccines could be missing out on these benefits.

The coverage of fully immunized children was higher among mothers who attended postnatal care in the study, and this is expected as their children have more chances of getting immunized than those who do not make any follow-up contact with a health centre after delivery. Coverage of fully immunized children by 12 months of age was higher among mothers with lower parity compared to mothers with higher parity, which has been found in other settings (Rahman *et al.*, 2010). The more children a mother has, the more constraints on the little resources available especially in informal settlements where levels of poverty are high and affects healthcare utilization (Ndiritu *et al.*, 2006). Ethnicity also played a role in determining coverage of fully immunized children by 12 months of age. Coverage of fully immunized children by 12 months of age was significantly higher among Kikuyu and Kamba ethnic groups compared to other ethnic groups. Similar results were found in other studies done in Kenya, and this has been linked to cultural differences in addition to education and income disparities among the different ethnicities (Egondi *et al.*, 2015; Ettarh *et al.*, 2012; Mutua *et al.*, 2011). Coverage of fully immunized children by 12 months of age was found to be higher in Viwandani compared to Korogocho study area in line with earlier

studies (Mutua *et al.*, 2011). Viwandani area is next to an industrial area, and residents here are better off than Korogocho residents. Additionally, from the unadjusted models, children delivered in a health facility, from households with higher wealth status and mothers with higher education status were associated with higher coverage of fully immunized children by 12 months of age. Similar results have been documented in other studies done in Kenya (Egondi *et al.*, 2015; Mutua *et al.*, 2011), and India (Lauridsen *et al.*, 2011) where health outcomes are better off among the wealthier in the community compared to the less wealthy households. Apart from geographical inequality, studies done in the informal settlement areas have identified the parental level of education, age, and marital status to be associated with non-completion of the vaccine uptake (Borus, 2004, Mutua et al., 2011).

5.2 Immunization timeliness

This study estimated the prevalence of fully immunized children who received at least one vaccine in a different sequence than the recommended one at 22%. The prevalence differed significantly by delivery place and location.

A substantial number of children were immunized much earlier than the recommended age. This early immunization has been documented elsewhere in Nigeria, Mozambique and Guinea (Cutts *et al.*, 1991; Sadoh *et al.*, 2009). Studies have shown that those vaccines given more than four days earlier than the recommended age may not be optimally effective (Kroger *et al.*, 2012) and one may need to re-vaccinate. The median age of the different vaccines revealed significant delays in immunization among children not fully immunized compared to fully immunized children. The delay was

substantial for BCG, measles and third doses of polio and pentavalent vaccines. This delay is consistent with other studies in sub-Saharan Africa (Sadoh *et al.*, 2009).

This study provides evidence of children receiving vaccines in a different sequence than recommended. The main cause of the fully immunized children not adhering to recommended schedules was identified as not receiving the pentavalent and corresponding polio doses together. This result highlights the levels of missed opportunities in immunization programs in the disadvantaged areas as the child had a contact with a health care person and was only given one vaccine instead of all recommended vaccines. The missed opportunity may be occasioned by vaccine stock-outs. Similar results have been documented in other studies as determinants of vaccine delays (Ouédraogo *et al.*, 2013; Schoeps *et al.*, 2013).

Children who were not delivered in a health centre or children from Korogocho study area were significantly associated with being FIC out-of-sequence, this is true as mother who deliver away from a health centre may take a while before taking the child for vaccination and may decide to take the child to receive all the vaccinations at same time instead of making several trips to the health centre. However, this study found no association between not being fully immunized in the recommended sequence and post-natal care, education level, ethnicity and wealth status. Results from the unadjusted models indicated a significant association with postnatal care, education level, ethnicity and wealth status.

5.3 Immunization and childhood health

5.3.1 Childhood nutrition status

This study has demonstrated a positive relationship between completion of childhood immunization schedule and childhood growth for children under three years of age. Children who were either fully immunized with the eight recommended routine vaccinations, fully immunized excluding measles vaccine and fully immunized and in proper sequence had significantly higher z-scores (height-for-age, weight-for-age, and weight-for-height) compared to children missing at least one of the recommended vaccines or children receiving immunization in an out-of-sequence manner respectively. Better childhood nutrition status could be attributed to the fact that fully immunized children have better immunity against the major illnesses hence child growth is not interrupted (Greenberg *et al.*, 2005). Apart from prevention of measles infections, measles vaccination have been shown to prevent many other infections which determine the nutrition status of a child (Stephensen, 1999; Victora *et al.*, 1990). The better nutrition status can also be attributed to the fact that fully immunized children have more visits to health center hence they are more likely to receive more information on nutrition than the children who make fewer visits to a health center.

5.3.2 Childhood hospitalization

Results from this study showed no significant relationship between childhood immunization patterns and hospitalization cases even though the statistical estimates direction indicated children who miss at least one of the recommended vaccines had higher hospitalization rates. Other studies conducted in England and Wales found an association between hospitalizations and lack of vaccination (Van Buynder *et al.*,

1999). Another study conducted in Germany showed higher hospitalization cases among unvaccinated children 6-24 months of age as compared to those partially or fully immunized (Stojanov *et al.*, 2000). The lack of significance in the relationship between immunization patterns and hospitalization cases could be due to fewer numbers of hospitalizations cases in the study which affected the power of the study to detect any significant result. More follow-up time would be needed for more power.

5.3.3 Child mortality

The study found significantly lower childhood mortality among children who were FIC or FICm compared to children who are not fully immunized respectively. Childhood survival was even better among children who were fully immunized and followed the recommended vaccine sequence compared to children not fully vaccinated.

This excess mortality can be attributed to children who are missing the measles vaccine which was identified in this study as one of the main cause of not being fully vaccinated which meant pentavalent vaccine was the last vaccine for the children not fully vaccinated. Studies examining immunization sequence with DTP versus measles vaccinations as the last vaccine have demonstrated that DTP administered with or after measles vaccine are associated with considerably higher mortality than receiving measles vaccine alone after DTP3 (Welaga *et al.*, 2012). The slightly higher childhood survival observed for FIC-IS vs. Not FIC compared to FIC vs. Not FIC can be explained by the presence of more out-of-sequence vaccinated children in the FIC-group than in the NOTFIC groups which would have diminished the mortality disparity estimated for FIC versus NOTFIC children. Live attenuated vaccines (BCG,

polio and measles vaccines) have been shown in randomized trials to be associated with non-specific beneficial effects, i.e. reducing mortality more than can be explained by prevention of tuberculosis, polio or measles infections (Aaby, Martins, Garly, *et al.*, 2010; Lund *et al.*, 2015). In the last 15 years, there have been a lot of polio and measles vaccines campaigns conducted in most low-income countries which has led to huge reductions in child mortality rate. These campaigns have also diminished the difference between groups with different vaccination status e.g. between FIC and not FIC. On the other hand, inactivated vaccines (DTP-containing vaccines) have been shown in randomized trials to be associated with detrimental non-specific effects, i.e. increasing mortality more than can be explained by prevention of diphtheria, tetanus or pertussis infections (P. Aaby *et al.*, 2007; Aaby, Ravn, *et al.*, 2012; Agergaard *et al.*, 2011).

The non-specific beneficial effects of measles vaccine have now been documented in many observational and randomized studies (Aaby *et al.*, 2015; Welaga *et al.*, 2012). The World Health Organization strategic advisory group of experts (SAGE), in a review of all studies done on non-specific effects of the routine childhood vaccination, found that measles vaccination was associated with close to 50% reduction in childhood mortality which could not be explained entirely by prevention of measles infection (Higgins *et al.*, 2014). The difference found in childhood survival between FIC and not FIC groups in the current study is quite consistent with what the SAGE review found without prevention of measles infection being an important component of the effect.

CHAPTER SIX

6 CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

The overall coverage in the study was estimated at 67%. Coverage for specific antigens were all above 75% with low coverages observed for the third pentavalent vaccine dose, third polio vaccine dose and measles vaccine dose. High coverages were observed among BCG, first and second doses of polio and pentavalent vaccines. Vaccination delays of 15% to 39% were observed for the different vaccines and doses given to children in the study. Vaccination delays were higher in Korogocho compared to Viwandani. Early immunization was higher for the first doses of polio and pentavalent vaccines at 3.3% and 2.&% respectively. A fifth of children who were fully immunized by the age of 12 months had received their immunization in a different sequence from the recommended. The main source of out-of-sequence was identified as not receiving the respective pentavalent doses together as it is recommended.

The main determinants of not being fully vaccinated by the end of one year of life were identified as children from mothers with lower education level, who did not attend post-natal care, did not deliver in a health center and from Korogocho area. Determinants of out-of-sequence among the fully immunized child were established as being from Korogocho area and not delivered in a health center.

Better child health outcome have been shown to be associated with not only a child being fully immunized but there is an additional benefit for getting immunized in the recommended sequence.

6.2 Recommendations

The following recommendations and further research work are derived from this study:

6.2.1 Policy and action

1. New strategies are needed to enable health care providers and parents/guardians to work together to increase the levels of completion of all required vaccines and in recommended schedule, especially measles vaccine which was the main reason for children not being fully immunized.
2. Particular attention is needed from the health care provider, parents and guardians on the uptake and completion of the three doses of polio, pentavalent and pneumococcal vaccines. Additionally, the health care providers should make sure a child is given all the antigens that are supposed to be given on the same day when a child is brought to a health centre. This was identified as the main cause of immunization delays and out-of-sequence
3. The low immunization coverage and age-specific vaccination can easily be improved by targeting disadvantaged groups through specific programmes.

6.2.2 Further research

1. Further research is needed to properly determine the effects of each routine vaccine other than preventing the specific infection.

2. This study has shown existence of non-specific effects of vaccination and the importance of being fully immunized and being immunized on time. Other studies have shown that boys and girls immunity responds differently to the routine vaccines. This sex differential effect need to be investigated in the urban informal settlement setting with the available data.
3. Similar study should be conducted in rural and urban formal settlement areas to see whether similar results will be obtained.
4. Work is needed to find out from mothers why they are unable to complete the vaccination of their children. There is a possibility of other demographic characteristics affecting immunization coverage by preventing mothers from taking children for immunization.

6.3 Study limitations

This study was conducted in an urban informal settlement, and therefore, the estimated coverages, levels of delays and out-of-sequence may only represent similar populations. A major limitation of this study was that vaccination card for a large number (62%) of those recruited during the visits between 12 and 23 months of age were not seen and hence they were excluded from the analysis. However, on the positive side, the exclusion eliminated the possibility of introducing recall and survival bias in the analysis. Despite the exclusion, the analysis still included a reasonable sample size for the cross-sectional study. However, excluding children without an observed vaccination card may impact the internal validity of the results within the target population as vaccine coverage among these children may differ in substantial ways from children with an observed vaccination card. The other limitation was the

shorter follow-up time for the analysis for the third objective and also some children were excluded due lack of follow-up visits.

REFERENCES

Aaby, P., Benn, C. S., Nielsen, J., Lisse, I. M., Rodrigues, A., & Jensen, H. (2007). DTP vaccination and child survival in observational studies with incomplete vaccination data. *Tropical Medicine & International Health, 12*(1), 15-24.

Aaby, P., Benn, C. S., Nielsen, J., & Ravn, H. (2009). Sex-differential non-specific effects of BCG and DTP in Cebu, The Philippines. *Int J Epidemiol, 38*(1), 320-323; author reply 323-324.

Aaby, P., Bhuiya, A., Nahar, L., Knudsen, K., de Francisco, A., & Strong, M. (2003). The survival benefit of measles immunization may not be explained entirely by the prevention of measles disease: a community study from rural Bangladesh. *International Journal of Epidemiology, 32*(1), 106-115.

Aaby, P., Biai, S., Veirum, J. E., Sodemann, M., Lisse, I., Garly, M. L., . . . Rodrigues, A. (2007). DTP with or after measles vaccination is associated with increased in-hospital mortality in Guinea-Bissau. *Vaccine, 25*(7), 1265-1269.

Aaby, P., Garly, M.-l., Bale, C., Martins, C., Jensen, H., Lisse, I., & Whittle, H. (2003). Survival of previously measles-vaccinated and measles-unvaccinated children in an emergency situation: an unplanned study. *The Pediatric Infectious Disease Journal, 22*(9), 798-805.

Aaby, P., Ibrahim, S. A., Libman, M. D., & Jensen, H. (2006). The sequence of vaccinations and increased female mortality after high-titre measles vaccine: trials from rural Sudan and Kinshasa. *Vaccine, 24*(15), 2764-2771.

Aaby, P., Jensen, H., Garly, M. L., Bale, C., Martins, C., & Lisse, I. (2002). Routine vaccinations and child survival in a war situation with high mortality: effect of gender. *Vaccine, 21*(1-2), 15-20.

Aaby, P., Jensen, H., Rodrigues, A., Garly, M. L., Benn, C. S., Lisse, I. M., & Simondon, F. (2004). Divergent female-male mortality ratios associated with different routine vaccinations among female-male twin pairs. *Int J Epidemiol, 33*(2), 367-373.

Aaby, P., Jensen, H., & Walraven, G. (2006). Age-specific changes in the female-male mortality ratio related to the pattern of vaccinations: an observational study from rural Gambia. *Vaccine, 24*(22), 4701-4708.

Aaby, P., Martins, C., Bale, C., Garly, M. L., Rodrigues, A., Biai, S., . . . Benn, C. S. (2010). Sex differences in the effect of vaccines on the risk of hospitalization due to measles in Guinea-bissau. *Pediatr Infect Dis J, 29*(4), 324-328.

Aaby, P., Martins, C. L., Garly, M. L., Bale, C., Andersen, A., Rodrigues, A., . . . Whittle, H. C. (2010). Non-specific effects of standard measles vaccine at 4.5 and 9 months of age on childhood mortality: randomised controlled trial. *BMJ, 341*, c6495.

Aaby, P., Martins, C. L., Garly, M. L., Rodrigues, A., Benn, C. S., & Whittle, H. (2012). The optimal age of measles immunisation in low-income countries: a secondary analysis of the assumptions underlying the current policy. *BMJ Open, 2*(4), e000761.

Aaby, P., Martins, C. L., Ravn, H., Rodrigues, A., Whittle, H. C., & Benn, C. S. (2015). Is early measles vaccination better than later measles vaccination? *Transactions of The Royal Society of Tropical Medicine and Hygiene, 109*(1), 16-28.

Aaby, P., Ravn, H., Roth, A., Rodrigues, A., Lisse, I. M., Diness, B. R., . . . Benn, C. S. (2012). Early diphtheria-tetanus-pertussis vaccination associated with higher female mortality and no difference in male mortality in a cohort of low birthweight children: an observational study within a randomised trial. *Arch Dis Child, 97*(8), 685-691.

Aaby, P., Samb, B., Simondon, F., Seck, A. M., Knudsen, K., & Whittle, H. (1995). Non-specific beneficial effect of measles immunisation: analysis of mortality studies from developing countries. *BMJ, 311*(7003), 481-485.

Aaby, P., Vessari, H., Nielsen, J., Maleta, K., Benn, C. S., Jensen, H., & Ashorn, P. (2006). Sex differential effects of routine immunizations and childhood survival in rural Malawi. *Pediatr Infect Dis J, 25*(8), 721-727.

Adeladza, A. (2009). The influence of socio-economic and nutritional characteristics on child growth in Kwale District of Kenya. *African Journal of Food, Agriculture, Nutrition and Development, 9*(7).

Agergaard, J., Nante, E., Poulstrup, G., Nielsen, J., Flanagan, K. L., Ostergaard, L., . . . Aaby, P. (2011). Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls. A randomised trial from Guinea-Bissau. *Vaccine, 29*(3), 487-500.

Akmatov, M. K., Kretzschmar, M., Kramer, A., & Mikolajczyk, R. T. (2007). Determinants of childhood vaccination coverage in Kazakhstan in a period of societal change: implications for vaccination policies. *Vaccine, 25*(10), 1756-1763.

Anderson, R. M. (1992). The concept of herd immunity and the design of community-based immunization programmes. *Vaccine, 10*(13), 928-935.

Anekwe, T. D., & Kumar, S. (2012). The effect of a vaccination program on child anthropometry: evidence from India's Universal Immunization Program. *J Public Health (Oxf), 34*(4), 489-497.

APHRC. (2002). *Population and health dynamics in Nairobi's informal settlements : Report of the Nairobi Cross-sectional Slums Survey (NCSS) 2000*. Nairobi, Kenya: African Population and Health Research Center.

Atwell, J. E., Van Otterloo, J., Zipprich, J., Winter, K., Harriman, K., Salmon, D. A., . . . Omer, S. B. (2013). Nonmedical vaccine exemptions and pertussis in California, 2010. *Pediatrics, 132*(4), 624-630.

Barrera, A. (1990). The role of maternal schooling and its interaction with public health programs in child health production. *Journal of Development Economics, 32*(1), 69-91.

Behrman, J. R., & Wolfe, B. L. (1987). How does mother's schooling affect family health, nutrition, medical care usage, and household sanitation? *Journal of econometrics, 36*(1-2), 185-204.

Benn, C. S., & Aaby, P. (2012). Diphtheria-tetanus-pertussis vaccination administered after measles vaccine: increased female mortality? *Pediatr Infect Dis J, 31*(10), 1095-1097.

Benn, C. S., Aaby, P., Nielsen, J., Binka, F. N., & Ross, D. A. (2009). Does vitamin A supplementation interact with routine vaccinations? An analysis of the Ghana Vitamin A Supplementation Trial. *The American Journal of Clinical Nutrition, 90*(3), 629-639.

Benn, C. S., Fisker, A. B., Rodrigues, A., Ravn, H., Sartono, E., Whittle, H., . . . Aaby, P. (2008). Sex-differential effect on infant mortality of oral polio vaccine administered with BCG at birth in Guinea-Bissau. A natural experiment. *PLoS One, 3*(12), e4056.

Biai, S., Rodrigues, A., Nielsen, J., Sodemann, M., & Aaby, P. (2011). Vaccination status and sequence of vaccinations as risk factors for hospitalisation among outpatients in a high mortality country. *Vaccine, 29*(20), 3662-3669.

Biering-Sorensen, S., Aaby, P., Napirna, B. M., Roth, A., Ravn, H., Rodrigues, A., . . . Benn, C. S. (2012). Small randomized trial among low–birth-weight children receiving Bacillus Calmette-Guérin vaccination at first health center contact. *The Pediatric Infectious Disease Journal, 31*(3), 306-308.

Bilous, J., Eggers, R., Gasse, F., Jarrett, S., Lydon, P., Magan, A., . . . Wolfson, L. (2006). A new global immunisation vision and strategy. *Lancet, 367*(9521), 1464-1466.

Black, R. E., Allen, L. H., Bhutta, Z. A., Caulfield, L. E., de Onis, M., Ezzati, M., . . . Child Undernutrition Study, G. (2008). Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet, 371*(9608), 243-260.

Black, R. E., Victora, C. G., Walker, S. P., Bhutta, Z. A., Christian, P., de Onis, M., . . . Child Nutrition Study, G. (2013). Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet, 382*(9890), 427-451.

Bondy, J. N., Thind, A., Koval, J. J., & Speechley, K. N. (2009). Identifying the determinants of childhood immunization in the Philippines. *Vaccine, 27*(1), 169-175.

Borus, P. K. (2004). Missed opportunities and inappropriately given vaccines reduce immunisation coverage in facilities that serve slum areas of Nairobi. *East Afr Med J, 81*(3), 124-129.

Brenzel, L., Wolfson, L. J., Fox-Rushby, J. A., Miller, M., & Halsey, N. A. (2006). Vaccine-preventable diseases. *Disease control priorities in developing countries, 2*, 389-412.

Bustreo, F., Okwo-Bele, J. M., & Kamara, L. (2015). World Health Organization perspectives on the contribution of the Global Alliance for Vaccines and Immunization on reducing child mortality. *Arch Dis Child, 100 Suppl 1*, S34-37.

Butler, R., & MacDonald, N. E. (2015). Diagnosing the determinants of vaccine hesitancy in specific subgroups: The Guide to Tailoring Immunization Programmes (TIP). *Vaccine, 33*(34), 4176-4179.

CDC. (1999). Ten great public health achievements, United States, 1900-1999. *Morbidity and mortality weekly report, 48*(12), 241.

Chan, M. (2014). Beyond expectations: 40 years of EPI. *Lancet, 383*(9930), 1697-1698.

Clark, A., & Sanderson, C. (2009). Timing of children's vaccinations in 45 low-income and middle-income countries: an analysis of survey data. *Lancet, 373*(9674), 1543-1549.

Cui, F. Q., & Gofin, R. (2007). Immunization coverage and its determinants in children aged 12-23 months in Gansu, China. *Vaccine, 25*(4), 664-671.

Cutts, F. T., Zell, E. R., Soares, A. C., & Diallo, S. (1991). Obstacles to achieving immunization for all 2000: missed immunization opportunities and inappropriately timed immunization. *Journal of tropical pediatrics, 37*(4), 153-158.

Danis, K., Georgakopoulou, T., Stavrou, T., Laggas, D., & Panagiotopoulos, T. (2010). Socioeconomic factors play a more important role in childhood vaccination coverage than parental perceptions: a cross-sectional study in Greece. *Vaccine, 28*(7), 1861-1869.

De Romana, G. L., Brown, K. H., Black, R. E., & Kanashiro, H. C. (1989). Longitudinal studies of infectious diseases and physical growth of infants in Huascar, an underprwileged peri-urban community in Lima, Peru. *American journal of epidemiology, 129*(4), 769-784.

Deddens, J. A., & Petersen, M. R. (2008). Approaches for estimating prevalence ratios. *Occup Environ Med, 65*(7), 481, 501-486.

Duclos, P., Okwo-Bele, J. M., & Salisbury, D. (2011). Establishing global policy recommendations: the role of the Strategic Advisory Group of Experts on immunization. *Expert Rev Vaccines, 10*(2), 163-173.

ECDC. (2009). Scientific panel on childhood immunisation schedule: Diphtheria-tetanus-pertussis (DTP) vaccination, ECDC Guidance, Stockholm, Sweden.

Egondi, T., Oyolola, M., Mutua, M. K., & Elung'ata, P. (2015). Determinants of immunization inequality among urban poor children: evidence from Nairobi's informal settlements. *International Journal for Equity in Health, 14*(1), 24.

Emina, J., Beguy, D., Zulu, E. M., Ezeh, A. C., Muindi, K., Elung'ata, P., . . . Ye, Y. (2011). Monitoring of health and demographic outcomes in poor urban settlements: evidence from the Nairobi Urban Health and Demographic Surveillance System. *J Urban Health, 88 Suppl 2*, S200-218.

Ettarh, R. R., Mutua, M. K., & Kyobutungi, C. (2012). Ethnicity and delay in measles vaccination in a nairobi slum. *Trop Med Health, 40*(2), 59-62.

Fadnes, L. T., Jackson, D., Engebretsen, I. M., Zembe, W., Sanders, D., Sommerfelt, H., . . . Group, P.-E. S. (2011). Vaccination coverage and timeliness in three South African areas: a prospective study. *BMC Public Health, 11*(1), 404.

Fadnes, L. T., Nankabirwa, V., Sommerfelt, H., Tylleskar, T., Tumwine, J. K., Engebretsen, I. M., & Group, P.-E. S. (2011). Is vaccination coverage a good indicator of age-appropriate vaccination? A prospective study from Uganda. *Vaccine, 29*(19), 3564-3570.

Fatiregun, A. A., & Okoro, A. O. (2012). Maternal determinants of complete child immunization among children aged 12-23 months in a southern district of Nigeria. *Vaccine, 30*(4), 730-736.

Fenner, F., Henderson, D. A., Arita, I., Ježek, Z., & Ladnyi, I. D. (1988). *Smallpox and its eradication*: World Health Organization.

Fine, P. E. (1993). Herd immunity: history, theory, practice. *Epidemiol Rev, 15*(2), 265-302.

Fisher, L. D., & Lin, D. Y. (1999). Time-dependent covariates in the Cox proportional-hazards regression model. *Annu Rev Public Health, 20*(1), 145-157.

Frongillo, E. A., Jr., de Onis, M., & Hanson, K. M. (1997). Socioeconomic and demographic factors are associated with worldwide patterns of stunting and wasting of children. *J Nutr, 127*(12), 2302-2309.

Garly, M. L., Jensen, H., Martins, C. L., Bale, C., Balde, M. A., Lisse, I. M., & Aaby, P. (2004). Hepatitis B vaccination associated with higher female than male mortality in Guinea-bissau: an observational study. *Pediatr Infect Dis J, 23*(12), 1086-1092.

Gibson, D. G., Ochieng, B., Kagucia, E. W., Obor, D., Odhiambo, F., O'Brien, K. L., & Feikin, D. R. (2015). Individual level determinants for not receiving immunization, receiving immunization with delay, and being severely underimmunized among rural western Kenyan children. *Vaccine, 33*(48), 6778-6785.

GPEI. (2013). Polio eradication and endgame strategic plan (2013–2018). Geneva, Switzerland: World Health Organization, Global Polio Eradication Initiative; 2013.

Gram, L., Soremekun, S., ten Asbroek, A., Manu, A., O'Leary, M., Hill, Z., . . . Kirkwood, B. R. (2014). Socio-economic determinants and inequities in coverage and timeliness of early childhood immunisation in rural Ghana. *Trop Med Int Health, 19*(7), 802-811.

Greenberg, D. P., von Konig, C. H., & Heininger, U. (2005). Health burden of pertussis in infants and children. *Pediatr Infect Dis J, 24*(5 Suppl), S39-43.

Heininger, U., Stehr, K., & Cherry, J. D. (1992). Serious pertussis overlooked in infants. *Eur J Pediatr, 151*(5), 342-343.

Heininger, U., & Zuberbuhler, M. (2006). Immunization rates and timely administration in pre-school and school-aged children. *Eur J Pediatr, 165*(2), 124-129.

Higgins, J., Soares-Weiser, K., & Reingold, A. (2014). *Systematic review of the non-specific effects of BCG, DTP and measles containing vaccines*. Retrieved from http://www.who.int/immunization/sage/meetings/2014/april/3_NSE_Epidemiology_review_Report_to_SAGE_14_Mar_FINAL.pdf?ua=1.

Hirve, S., Bavdekar, A., Juvekar, S., Benn, C. S., Nielsen, J., & Aaby, P. (2012). Non-specific and sex-differential effects of vaccinations on child survival in rural western India. *Vaccine, 30*(50), 7300-7308.

Holt, E. A., Moulton, L. H., Siberry, G. K., & Halsey, N. A. (1993). Differential mortality by measles vaccine titer and sex. *Journal of Infectious Diseases, 168*(5), 1087-1096.

Hornshoj, L., Benn, C. S., Fernandes, M., Rodrigues, A., Aaby, P., & Fisker, A. B. (2012). Vaccination coverage and out-of-sequence vaccinations in rural Guinea-Bissau: an observational cohort study. *BMJ Open, 2*(6), e001509.

Hutchings, H. A., Evans, A., Barnes, P., Healy, M. A., James-Ellison, M., Lyons, R. A., . . . Dunstan, F. (2016). Does frequent residential mobility in early years affect the uptake and timeliness of routine immunisations? An anonymised cohort study. *Vaccine, 34*(15), 1773-1777.

Kabir, Z., & Aaby, P. (2005). Non-specific effect of measles vaccination on all-cause child mortality: revisited. *Indian Pediatr, 42*(6), 541-544.

Kelly, P. J., & Lim, L. L. (2000). Survival analysis for recurrent event data: an application to childhood infectious diseases. *Stat Med, 19*(1), 13-33.

KNBS. (2011). *Kenya 2008-09: results from the demographic and health survey* (0039-3665 (Print)

0039-3665 (Linking)). Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21834415

KNBS. (2015). *Kenya Demographic and Health Survey 2014*. Retrieved from

Knudsen, K. M., Aaby, P., Whittle, H., Rowe, M., Samb, B., Simondon, F., . . . Fine, P. E. (1996). Child mortality following standard, medium or high titre measles immunization in West Africa. *International Journal of Epidemiology, 25*(3), 665-673.

Kroger, A., Sumaya, C., Pickering, L., & Atkinson, W. (2012). Centers of Disease Control and Prevention. General Recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations Report, 60*, 3-60.2011.

Kyaw, M. H., Lynfield, R., Schaffner, W., Craig, A. S., Hadler, J., Reingold, A., . . . Active Bacterial Core Surveillance of the Emerging Infections Program, N. (2006). Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant Streptococcus pneumoniae. *N Engl J Med, 354*(14), 1455-1463.

Laryea, D. O., Parbie, E. A., & Frimpong, E. (2014). Timeliness of childhood vaccine uptake among children attending a tertiary health service facility-based immunisation clinic in Ghana. *BMC Public Health, 14*(1), 90.

Lauridsen, J., & Pradhan, J. (2011). Socio-economic inequality of immunization coverage in India. *Health Econ Rev, 1*(1), 11.

Lernout, T., Theeten, H., Hens, N., Braeckman, T., Roelants, M., Hoppenbrouwers, K., & Van Damme, P. (2014). Timeliness of infant vaccination and factors related with delay in Flanders, Belgium. *Vaccine, 32*(2), 284-289.

Liang, K.-Y., & Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika, 73*(1), 13-22.

Lund, N., Andersen, A., Hansen, A. S. K., Jepsen, F. S., Barbosa, A., Biering-Sørensen, S., . . . Benn, C. S. (2015). The effect of oral polio vaccine at birth on infant mortality: a randomized trial. *Clinical Infectious Diseases*, civ617.

Martins, C. L., Benn, C. S., Andersen, A., Bale, C., Schaltz-Buchholzer, F., Do, V. A., . . . Whittle, H. (2014). A randomized trial of a standard dose of Edmonston-Zagreb measles vaccine given at 4.5 months of age: effect on total hospital admissions. *Journal of Infectious Diseases, 209*(11), 1731-1738.

Martorell, R., Yarbrough, C., Yarbrough, S., & Klein, R. E. (1980). The impact of ordinary illnesses on the dietary intakes of malnourished children. *Am J Clin Nutr, 33*(2), 345-350.

McGuire, S. (2015). FAO, IFAD, and WFP. The State of Food Insecurity in the World 2015: Meeting the 2015 International Hunger Targets: Taking Stock of Uneven Progress. Rome: FAO, 2015. *Adv Nutr, 6*(5), 623-624.

Milman, A., Frongillo, E. A., de Onis, M., & Hwang, J.-Y. (2005). Differential improvement among countries in child stunting is associated with long-term development and specific interventions. *The Journal of nutrition, 135*(6), 1415-1422.

Moisi, J. C., Kabuka, J., Mitingi, D., Levine, O. S., & Scott, J. A. (2010). Spatial and socio-demographic predictors of time-to-immunization in a rural area in Kenya: Is equity attainable? *Vaccine, 28*(35), 5725-5730.

Mosley, W. H., & Chen, L. C. (1984). An Analytical Framework for the Study of Child Survival in Developing Countries. *Population and Development Review, 10*, 25-45.

Moszynski, P. (2011). A pneumococcal vaccine is launched in Africa to cut child deaths. *BMJ, 342*.

Murray, C. J., Shengelia, B., Gupta, N., Moussavi, S., Tandon, A., & Thieren, M. (2003). Validity of reported vaccination coverage in 45 countries. *Lancet, 362*(9389), 1022-1027.

Mutua, M. K., Kimani-Murage, E., & Ettarh, R. R. (2011). Childhood vaccination in informal urban settlements in Nairobi, Kenya: who gets vaccinated? *BMC Public Health, 11*(1), 6.

Mutua, M. K., Kimani-Murage, E., Ngomi, N., Ravn, H., Mwaniki, P., & Echoka, E. (2016). Fully immunized child: coverage, timing and sequencing of routine immunization in an urban poor settlement in Nairobi, Kenya. *Trop Med Health, 44*(1), 1.

Mutua, M. K., Ochako, R., Ettarh, R., Ravn, H., Echoka, E., & Mwaniki, P. (2015). Effects of low birth weight on time to BCG vaccination in an urban poor settlement in Nairobi, Kenya: an observational cohort study. *BMC Pediatr, 15*(1), 45.

National Vaccine Advisory Committee. (2003). Standards for child and adolescent immunization practices. *Pediatrics, 112*(4), 958-963.

Ndiritu, M., Cowgill, K. D., Ismail, A., Chiphatsi, S., Kamau, T., Fegan, G., . . . Scott, J. A. G. (2006). Immunization coverage and risk factors for failure to immunize within the Expanded Programme on Immunization in Kenya after introduction of new Haemophilus influenzae type b and hepatitis b virus antigens. *BMC Public Health, 6*(1), 132.

Ouédraogo, N., Kagoné, M., Sié, A., Becher, H., & Müller, O. (2013). Timeliness and Out-of-Sequence Vaccination among Young Children in Burkina Faso–Analysis of Health and Demographic Surveillance System (HDSS) Data.

Prentice, A. M., Savy, M., Darboe, M. K., & Moore, S. E. (2009). Commentary: Challenging public health orthodoxies—prophesy or heresy? *International Journal of Epidemiology, 38*(2), 591-593.

Rahman, M., & Obaida-Nasrin, S. (2010). Factors affecting acceptance of complete immunization coverage of children under five years in rural Bangladesh. *Salud Publica Mex, 52*(2), 134-140.

Rainey, J. J., Watkins, M., Ryman, T. K., Sandhu, P., Bo, A., & Banerjee, K. (2011). Reasons related to non-vaccination and under-vaccination of children in low and middle income countries: findings from a systematic review of the published literature, 1999-2009. *Vaccine, 29*(46), 8215-8221.

Rocha, H. A., Correia, L. L., Campos, J. S., Silva, A. C., Andrade, F. O., Silveira, D. I., . . . Cunha, A. J. (2015). Factors associated with non-vaccination against measles in northeastern Brazil: Clues about causes of the 2015 outbreak. *Vaccine, 33*(38), 4969-4974.

Rodrigues, A., Fischer, T. K., Valentiner-Branth, P., Nielsen, J., Steinsland, H., Perch, M., . . . Aaby, P. (2006). Community cohort study of rotavirus and other enteropathogens: are routine vaccinations associated with sex-differential incidence rates? *Vaccine, 24*(22), 4737-4746.

Roth, A., Garly, M., Jensen, H., Nielsen, J., & Aaby, P. (2006). Bacillus Calmette-Guerin vaccination and infant mortality. *Expert review of vaccines, 5*(2), 277-293.

Roth, A., Gustafson, P., Nhaga, A., Djana, Q., Poulsen, A., Garly, M. L., . . . Aaby, P. (2005). BCG vaccination scar associated with better childhood survival in Guinea-Bissau. *Int J Epidemiol, 34*(3), 540-547.

Roth, A., Jensen, H., Garly, M.-L., Djana, Q., Martins, C. L., Sodemann, M., . . . Aaby, P. (2004). Low birth weight infants and Calmette-Guerin bacillus vaccination at birth: community study from Guinea-Bissau. *The Pediatric Infectious Disease Journal, 23*(6), 544-550.

Roth, A. E., Benn, C. S., Ravn, H., Rodrigues, A., Lisse, I. M., Yazdanbakhsh, M., . . . Aaby, P. (2010). Effect of revaccination with BCG in early childhood on mortality: randomised trial in Guinea-Bissau. *BMJ, 340*, c671.

Sadoh, A. E., & Eregie, C. O. (2009). Timeliness and completion rate of immunization among Nigerian children attending a clinic-based immunization service. *J Health Popul Nutr, 27*(3), 391-395.

Sankoh, O., Welaga, P., Debpuur, C., Zandoh, C., Gyaase, S., Poma, M. A., . . . Aaby, P. (2014). The non-specific effects of vaccines and other childhood interventions: the contribution of INDEPTH Health and Demographic Surveillance Systems. *Int J Epidemiol, 43*(3), 645-653.

Sartono, E., Lisse, I. M., Terveer, E. M., van de Sande, P. J., Whittle, H., Fisker, A. B., . . . Benn, C. S. (2010). Oral polio vaccine influences the immune response to BCG vaccination. A natural experiment. *PLoS One, 5*(5), e10328.

Schoeps, A., Ouedraogo, N., Kagone, M., Sie, A., Muller, O., & Becher, H. (2013). Socio-demographic determinants of timely adherence to BCG, Penta3, measles, and complete vaccination schedule in Burkina Faso. *Vaccine, 32*(1), 96-102.

Sorup, S., Benn, C. S., Poulsen, A., Krause, T. G., Aaby, P., & Ravn, H. (2014). Live vaccine against measles, mumps, and rubella and the risk of hospital admissions for nontargeted infections. *JAMA, 311*(8), 826-835.

Steinglass, R. (2013). Routine immunization: an essential but wobbly platform. *Glob Health Sci Pract, 1*(3), 295-301.

Stephensen, C. B. (1999). Burden of infection on growth failure. *J Nutr, 129*(2S Suppl), 534S-538S.

Stojanov, S., Liese, J., & Belohradsky, B. H. (2000). Hospitalization and complications in children under 2 years of age with Bordetella pertussis infection. *Infection, 28*(2), 106-110.

Sugerman, D. E., Barskey, A. E., Delea, M. G., Ortega-Sanchez, I. R., Bi, D., Ralston, K. J., . . . Lebaron, C. W. (2010). Measles outbreak in a highly vaccinated

population, San Diego, 2008: role of the intentionally undervaccinated. *Pediatrics, 125*(4), 747-755.

Tauil Mde, C., Sato, A. P., & Waldman, E. A. (2016). Factors associated with incomplete or delayed vaccination across countries: A systematic review. *Vaccine, 34*(24), 2635-2643.

Therneau, T. M., & Hamilton, S. A. (1997). rhDNase as an example of recurrent event analysis. *Statistics in medicine, 16*(18), 2029-2047.

Thomas, D., Lavy, V., & Strauss, J. (1996). Public policy and anthropometric outcomes in the Cote d'Ivoire. *Journal of public Economics, 61*(2), 155-192.

Thompson, M. L., Myers, J. E., & Kriebel, D. (1998). Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: what is to be done? *Occupational and environmental medicine, 55*(4), 272-277.

UN. (2014). *Proposal for Sustainable Development Goals*. Retrieved from https://sustainabledevelopment.un.org/content/documents/1579SDGs%20Proposal.pdf.

UNICEF. (2002). *A world fit for children: Millenium Development Goals.* Paper presented at the Special Session on Children Documents, and The Convention on the Rights of the Child.

UNSCN. (2011). Sixth Report on the World Nutrition Situation. Progress in Nutrition: Lavanham Press Sudbury.

Valentiner-Branth, P., Perch, M., Nielsen, J., Steinsland, H., Garly, M. L., Fischer, T. K., . . . Aaby, P. (2007). Community cohort study of Cryptosporidium parvum infections: sex-differential incidences associated with BCG and diphtheria-tetanus-pertussis vaccinations. *Vaccine, 25*(14), 2733-2741.

Van Buynder, P. G., Owen, D., Vurdien, J. E., Andrews, N. J., Matthews, R. C., & Miller, E. (1999). Bordetella pertussis surveillance in England and Wales: 1995-7. *Epidemiol Infect, 123*(3), 403-411.

Veirum, J. E., Sodemann, M., Biai, S., Jakobsen, M., Garly, M. L., Hedegaard, K., . . . Aaby, P. (2005). Routine vaccinations associated with divergent effects on female and male mortality at the paediatric ward in Bissau, Guinea-Bissau. *Vaccine, 23*(9), 1197-1204.

Veirum, J. E., Sodemann, M., Biai, S., Jakobsen, M., Hedegaard, K., Jensen, H., & Aaby, P. (2005). Diphtheria-tetanus-pertussis and measles vaccinations associated with divergent effects on female and male mortality at the paediatric ward in Bissau, Guinea-Bissau. *Vaccine, 23*(9), 1197-1204.

Victora, C. G., Barros, F. C., Kirkwood, B. R., & Vaughan, J. P. (1990). Pneumonia, diarrhea, and growth in the first 4 y of life: a longitudinal study of 5914 urban Brazilian children. *Am J Clin Nutr, 52*(2), 391-396.

Welaga, P., Nielsen, J., Adjuik, M., Debpuur, C., Ross, D. A., Ravn, H., . . . Aaby, P. (2012). Non-specific effects of diphtheria-tetanus-pertussis and measles vaccinations? An analysis of surveillance data from Navrongo, Ghana. *Trop Med Int Health, 17*(12), 1492-1505.

WHO. (2002a). State of the World's Vaccines and Immunizations. *JAMA, 288*(20), 2532.

WHO. (2002b). *The world health report 2002: reducing risks, promoting healthy life*: World Health Organization.

WHO. (2005). Global immunization vision and strategy: 2006-2015. Retrieved from http://www.who.int/immunization/givs/en/

WHO. (2008). Global Immunization Data. Retrieved from http://www.who.int/immunization/newsroom/Global_Immunization_Data.pdf

WHO. (2011a). Expanding Immunization Coverage. Retrieved from http://www.unicef.org/immunization/index_coverage.html

WHO. (2011b). Global Vaccine Action Plan 2011-2020. Retrieved from www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/

WHO. (2011c). WHO Anthro (version 3.2. 2, January 2011) and macros. *World Health Organization.* Retrieved from http://www.who.int/childgrowth/software/en

WHO. (2013). WHO recommendations for routine immunization-summary tables. *WHO*. Retrieved from http://www.who.int/immunization/policy/immunization_tables/en/

WHO. (2014, July 2014). Global Immunization Data. Retrieved from http://www.who.int/immunization/monitoring_surveillance/global_immunization_data.pdf

WHO. (2015). Global health observatory (GHO) data. Retrieved from http://www.who.int/gho/tb/en

WHO. (2016). Global Polio Eradication Initiative. Retrieved from http://www.who.int/mediacentre/factsheets/fs114/en/

APPENDICES

Appendix I: Informed Consent Form-English

Childhood Vaccination Delays: Prevalence, Determinants and Association with Childhood Morbidity and Growth in Korogocho and Viwandani Informal Settlements, Nairobi, Kenya

Consent form

INVESTIGATORS AND THEIR INSTITUTIONS

Dr Peter Mwaniki, Jomo Kenyatta University of Agriculture and Technology (JKUAT)
Dr Elizabeth Echoka, Kenya Medical Research Institute (KEMRI)
Dr Catherine Kyobutungi, African Population and Health Research Centre (APHRC)

The study will be led by Martin Kavao Mutua. His contacts are, PO BOX 10787-00100, Nairobi. Tel +254 20 4001000

PURPOSE OF STUDY:

Hello, my name is _____ and I work with the African Population and Health Research Center (APHRC). The purpose of this interview is to assess the level of uptake of the routine childhood vaccination among children in this community
The APHRC and Jomo Kenyatta University of Agriculture and Technology, with funding from DANIDA, is undertaking this study.
All women who delivered a live birth in Korogocho and Viwandani in the last three years and previously agreed to participate in the Maternal and Child Health Project conducted by APHRC are eligible to participate in the study

PROCEDURES:

You are among **1050** women who will be interviewed. If you agree to take part in this study and agree to the use of your previously collected information for the purpose of this study, you will be asked questions about yourself, and the health of your child.
This interview will take about 45 minutes of your time. We shall also take height and weight measurements of you and your child
You will not be paid any money by taking part in this study.

VOLUNTARY PARTICIPATION:

Your participation is voluntary and you have the right to stop the interview at any time without any problem

RISKS/DISCOMFORTS:

This interview is not expected to cause you any harm but if you feel uncomfortable with some of the questions you can choose not to answer any question(s) but can decide to continue with the interview.

BENEFITS:

There are no direct benefits from this study but results may help the Government of Kenya and other organisations to improve health services in this and other districts. The chiefs and the community will be informed of the findings when the study is completed.

CONFIDENTIALITY:

Your responses will be private and confidential. They will not be made available to other persons that are not part of the project.

WHOM TO CONTACT:

This research has been reviewed and approved by the Ethical Review Committee of the Kenya Medical Research Institute (KEMRI). If you have any questions about your rights as a research participant you may contact

The Secretary of the KEMRI ERC (a team of professionals who review the research to protect your rights)
P.O. Box 54840-00200 Nairobi
E mail: erc@kemri.org
Tel: 020-2722541, 020-2726781, 0722 205 901 or 0733 400 003
or
The Principal,
College of Health Sciences (CoHES), Jomo Kenyatta University of Agriculture and Technology,
P.O. Box 62000, 00200 Nairobi, Kenya.
Tel: 254-67-52711/52181-4.
Email: director@itromid.jkuat.ac.ke

YOUR STATEMENT OF CONSENT AND SIGNATURE

If you have read the informed consent, or had it read and explained to you, and you understand the information and voluntarily agree to join this study, please carefully read the statements below and think about your choice before signing your name or making your identification mark below. No matter what you decide, it will not affect anything:

I have been given the chance to ask any questions I may have and I am content with the answers to all of my questions.
I know that my records will be kept confidential and that I may leave his study at any time.
I have been told the name, phone number and address of the person to contact in case of an emergency, and this information has also been given to me in writing.
I agree for the use of my previously collected information for the purpose of this study
I agree to take part in this study as a volunteer, and will be given a copy of this informed consent form to keep.

_____	_____
Subject's signature or fingerprint	*Witness to Consent Procedure*
_____	_____
Signature of Investigator	*Date*

Appendix II: Informed Consent Form-Swahili

Childhood Vaccination Delays: Prevalence, Determinants and Association with Childhood Morbidity and Growth in Korogocho and Viwandani Informal Settlements, Nairobi, Kenya

Fomu ya idhini

WATAFITI NA MASHIRIKA WANAYOHUSIANA NAYO

Dr Peter Mwaniki, Jomo Kenyatta University of Agriculture and Technology (JKUAT)

Dr Elizabeth Echoka, Kenya Medical Research Institute (KEMRI)

Dr Catherine Kyobutungi, African Population and Health Research Centre (APHRC)

Uchunguzi/Utafiti huu utaongozwa na Martin Kavao Mutua. Anwani yake ni, SLP 10787-00100, Nairobi. Simu +254 20 4001000

MADHUMUNI YA UTAFITI:

Hujambo, Jina langu ni _____; na ninafanya kazi na shirika la utafiti la African Population and Health Research Center (APHRC). Lengo la utafiti huu ni kuelewa kiwango cha matumizi ya chanjo muhimu za watoto katika jamii hii mara baada ya kuzaliwa. Shirika la APHRC, kupitia ufadhili wa DANIDA linatekeleza utafiti huu. Kina mama wote ambao wamejifungua watoto walio hai hapa Korogocho/Viwandani katika miaka mitatu kwenda chini iliyopita na ambao walikuwa wamekubali kushiriki katika utafiti uliopita wa afya ya watoto uliofanywa na APHRC watajumuishwa kwenye utafiti huu.

TARATIBU ZA UTAFITI HUU:

Wewe ni miongoni mwa wanawake 1050 ambao watahojiwa. Iwapo utakubali kushiriki katika utafiti huu na unakubali habari zako za awali zitumiwe katika utafiti wa sasa, utaulizwa maswali kuhusu wewe mwenyewe na afya ya mtoto wako. Mahojiano haya yatachukua muda wa dakika arobaini na tano hivi.

Pia tutachukua vipimo vya kimo na uzito wako na wa mtoto wako. Hautalipwa chochote kwa kushiriki katika utafiti huu.

HIARI/KUJITOLEA:

Kushiriki kwako ni kwa hiari na uko na haki ya kusimamisha majojiano haya wakati wowote bila tatizo lolote.

ATHARI:

Mahojiano haya hayatarajiwi kukusababishia athari yoyote lakini iwapo utasikia ugumu kujibu maswali yoyote unaweza kuamua kutojibu maswali hayo; na bado utaweza kuendelea na mahojiano.

FAIDA:

Hakuna faida ya kibinafsi kwako kutokana na utafiti huu, lakini matokeo ya utafiti huu huenda yakasaidia serikali ya Kenya na mashirika mengine kuboresha huduma za afya katika jamii hii na jamii zingine.

Machifu na wanajamii watajulishwa kuhusu matokeo ya utafiti huu utakapokamilika.

USIRI:

Majibu yako yatakuwa ya binafsi na ya siri. Hayatatolewa kwa watu wengine wowote ambao hawahusiki na utafiti huu.

MAWASILIANO:

Utafiti huu umechunguzwa na kuidhinishwa na kamati ya kupeana idhini la shirika la Kenya Medical Research Institute (KEMRI).

Kama una maswali kuhusu haki zako kama mshiriki wa utafiti, unaweza kuwasiliana na
Katibu wa kikundi cha wataalamu wa kuchunguza utafiti ili kuchunga haki zako (KEMRI ERC)
SLP 54840-00200 Nairobi

Barua pepe: erc@kemri.org

Simu: 020-2722541, 020-2726781, 0722 205 901 or 0733 400 003
au waweza kuwasiliana na

The Principal,
College of Health Sciences (CoHES), Jomo Kenyatta University of Agriculture and Technology,
SLP 62000, 00200 Nairobi, Kenya.

Simu: 254-67-52711/52181-4.

Barua pepe: director@itromid.jkuat.ac.ke

USEMI WAKO WA KUKUBALI KUSHIRIKI NA SAHIHI

Kama umesoma fomu ya idhini, ama umesomewa na ukaelewa vyema na umekubali kwa hiari yako kushiriki katika utafiti huu, tafadhali soma kwa makini sentensi zinazofuta na ufikirie kuhusu uchaguzi wako kabla ya kuandika jina lako ama kuweka alama ya kitambulisho hapa chini. Uamuzi wowote utakaofanya hautabadili kitu chochote katika uhusiano wetu:

Nimepewa nafasi ya kuuliza maswali yoyote niliyokua nayo na nimeridhika na majibu yote

Najua rekodi zangu zitawekwa kwa njia ya siri na naweza acha utafiti huu wakati wowote

Nimepewa Jina, nambari ya simu na anwani ya mtu wa kuwasiliana naye kunapotokea hali ya dharura, na habari hiyo pia nimepewa kwa maandishi

Nimekubali habari zangu za awali zitumiwe katika utafiti huu

Nimekubali kushiriki katika utafiti huu kwa hiari, na nitapewa nakala hii ya idhini ya kushiriki

Sahihi au alama ya kidole ya Mshiriki	*Sahihi ya Shahidi kwa utaratibu wa idhini*
Sahihi ya Mtafiti	*Tarehe*

Appendix III: Study Data Collection Tool – English

3.0	**BREASTFEEDING**		
	Now I would like to ask you a few questions about (NAME)'s feeding patterns		
3.1	Has (NAME) ever been breastfed/ Was (NAME) ever breastfed?	Yes…… 1 No …… 2 Don't Know…… 8	→ 4.1
3.2	Is (NAME) still breastfeeding?	Yes…… 1 No …… 2 Don't Know…… 8	→ 4.1 → 4.1
3.3	For how long did (NAME) breastfeed? IF NEVER BREASTFED RECORD 00 IN DAYS, IF LESS THAN A WEEK, RECORD IN DAYS; IF LESS THAN A MONTH, RECORD IN WEEKS OTHERWISE RECORD IN MONTHS. IF DON'T KNOW, CIRCLE '98'	Days…… ☐☐ Weeks…… ☐☐ Months…… ☐☐ Don't Know…… 98	
4.0	**VACCINATION HISTORY**		
	Now I would like to ask you about (NAME)'s vaccination		
4.1	Does/ Did (NAME) have a vaccination card that looks like this? **FW: SHOW A COPY OF A VACCINATION CARD** IF YES: May I see it please?	Yes, card/ book seen…… 1 Yes, card not seen…… 2 No card/Never had a card…… 3 Don't Know…… 4	→ 4.3 → 4.4
4.2	Please tell me the main reason why (NAME) has no vaccination card	Mother too weak to visit HF…… 1 Costs…… 2 No cards/supplies at clinic …… 3 Card lost…… 4 Don't Know…… 98 Other …… 96 Specify_____	4.4
4.3	**FW:** FOR QUESTION 4.3 COPY VACCINATION DATE FOR EACH VACCINE FROM THE CARD.		

		D D	M M	Y Y Y Y
BCG	BCG			
Pentavalent 1	Pentav1			
Pentavalent 2	Pentav2			
Pentavalent 3	Pentav3			
Oral Polio Birth Dose	OPV0			
Oral Polio 1st Dose	OPV1			
Oral Polio 2nd Dose	OPV2			
Oral Polio 3rd Dose	OPV3			
Pneumococcal Dose 1	PCV1			
Pneumococcal Dose 2	PCV2			
Pneumococcal Dose 3	PCV3			
Measles	Measles			

4.4	FW: CHECK 2.1; IF CHILD IS DEAD, CIRCLE "3" ELSE CHECK IF CHILD HAS BEEN GIVEN BCG ASK:		
	Would you mind if I check (NAME) to see if there is an immunization scar? INSPECT THE CHILD'S LEFT ARM FOR BCG SCAR:	Scar Present…… 1 Scar absent …… 2 Child is dead…… 3 Child not examined…… 4	

5.0	**CHILD MORBIDITY**					
GLISH	Now I am going to ask you about a few illnesses that (NAME) may have now or has had in the last 2 weeks.					
5.1	Has (NAME) been ill with any of the following illness at any time in the last two weeks? FW: RECORD FOR 1 =YES; 2 = NO; 8 = DON'T KNOW, IN THE BOXES **FW: IF CHILD HAD COUGH, ASK IF IT WAS ACCOMPANIED BY RAPID BREATH**	a Fever	b Diarrhea	c Cough	d Cough + Rapid Breath	e Convulsions
5.2	For how many days has (NAME) been ill/ was ill with (NAME OF ILLNESS)?	a Fever b Diarrhoea c Cough d Cough + Rapid Breath e Convulsions				
5.3	Apart from the illness I have talked about, does/did (NAME) have any other illness in the last 2 weeks? CIRCLE 1 =YES, 2 = NO, 8 = DON'T KNOW IF "1" RECORD THE ILLNESS IN THE BOX. IF MORE THAN ONE ILLNESS, PROBE AND RECORD THE THREE MOST SERIOUS ILLNESS.	YES..... 1 NO..... 2 DON'T KNOW..... 8 1 _____ 2 _____ 3 _____				
5.0	**CHILD HOSPITALISATION**					
5.4	Was NAME hospitalized (Stayed overnight at a health facility) since birth? RECORD 1 IF HOSPITALIZED AND 2 IF NOT HOSPITALIZED IN THE FIRST CELL, IF MORE THAN 1 HOSPITALIZATION OCCURRED RECORD THE HOSPITALIZATION DETAILS SEPARATELY	1st	2nd	3rd	4th	
	IF THE CHILD HAS NOT HAD ANY THE HOSPITALIZATION SKIP TO Q6.1					
5.5	When did the hospitalisation take place dd/mm/yyyy IF MORE THAN 1 HOSPITALIZATION, RECORD THE DATES SEPARATELY	DD MM YY				
5.6	FW: FOR EACH HOSPITALIZATION ASK: What illness was (NAME) hospitalized for?					
5.7	For how many days was NAME hospitalized?					
6.0	**ANTHROPOMETRIC MEASUREMENTS**					
	Now I would like to take anthropometric measurements of you and your baby.					
6.1	ENTER THE MEASURED **LENGTH** OF THE CHILD (TO THE NEAREST 0.1CM)					
	WEIGHT OF THE CHILD WILL BE DERIVED BY SUBTRACTING THE WEIGHT OF THE MOTHER/CARER FROM THE COMBINED WEIGHT OF THE MOTHER/CARER AND CHILD PAIR.					
6.2	ENTER THE **WEIGHT OF THE MOTHER/CARER** IN KG					
6.3	ENTER THE **COMBINED WEIGHT OF THE MOTHER/CARER AND THE CHILD** IN KG					
6.4	ENTER THE **WEIGHT OF THE CHILD** IN KG					
6.5	**RECORD ANY GENERAL COMMENTS**					

Appendix IV: Study Data Collection Tool – Swahili

Childhood Vaccination Delays: Prevalence, Determinants and Association with Childhood Morbidity and Growth in Korogocho and Viwandani Informal Settlements, Nairobi, Kenya			
Swahili questionairre			
1.0	**TAARIFA ZA MSINGI**		
1.1	MUDA WA KUANZA		
1.2	NAMBA YA MHOJI		
1.3	TAREHE YA MAHOJIANO		
1.4	KITAMBULISHO CHA NYUMBA		
1.5	KITAMBULISHO CHA MAMA		
1.6	KITAMBULISHO CHA MTOTO		
1.7	TAREHE YA KUZALIWA YA MTOTO		
1.8	JINSIA YA MTOTO (1=KIUME; 2=KIKE)		
1.9	JINA FUPI YA MHOJIWA		
1.10	UHUSIANO WA MHOJIWA NA MKUU WA NYUMBA		
1.11	Je, wewe ndiye mama wa (JINA LA MTOTO)? **(1=NDIO; 2=LA)**		
	TAARIFA YA AFYA, UNYONYAJI NA CHANJO YA MTOTO		
2.0	**TAARIFA MUHIMU ZA AFYA KUHUSU MTOTO**		
	Ningependa kukuuliza maswali kuhusu wewe na afya ya mtoto wako.		
2.1	Je, (JINA LA MTOTO) yuko wapi?	Mtoto yuko nyumbani ..... 1 Mtoto hayuko nyumbani lakini yuko hai 2 Mtoto aliaga..... 3	} 3.1
2.2	FW: KAMA MTOTO KAAGA DUNIA PEANA RAMBIRAMBI HALAFU ULIZA: (JINA LA MTOTO) alifariki/ aga dunia lini?		
2.3	Je, (JINA LA MTOTO) alikuwa mgonjwa kabla ya kufariki?	Ndio..... 1 La 2	
2.4	Kwa maoni yako, ni nini kilisababisha kifo cha (JINA LA MTOTO)?	Nimonia..... 01 Kuhara na kutapika..... 02 Shida ya kifua..... 03 Malaria..... 04 Homa..... 05 Siju..... 98 Nyingine_____ 96	

5.0	**TAARIFA KUHUSU MAGONJWA YA WATOTO**						
	Sasa ningependa nikuulize maswali kuhusu magonjwa ambayo (JINA LA MTOTO) huenda alikuwa nayo kwa muda wa wiki mbili zilizopita ama bado anazo.						
5.1	(JINA LA MTOTO) amewahi pata magonjwa yafuatayo kwa muda wa wiki mbili zilizopita? FW: ANDIKA 1 =NDIO; 2 = LA; 8 =SIJUI, KWENYE KIJISANDUKU **FW: KAMA MTOTO ALIKOHOA, ULIZA KAMA KILIFUATNA NA KUPUMUA KWA HARAKA**	a Homa	b Kuhara	c Kukohoa	d Kukohoa +Kupumua	e Degedege	
5.2	(JINA LA MTOTO) amekuwa/alikuwa mgonjwa kwa siku ngapi?	a Homa b Kuhara c Kukohoa d Kukohoa +Kupumua e Degedege					
5.3	Mbali na magonjwa niliyokutajia; je (JINA LA MTOTO) ameugua magonjwa mengine wiki mbili zilizopita? ANDIKA 1 =NDIO, 2 = LA, 8 = SIJUI KAMA NDIO, ANDIKA JINA LA UGONJWA, KAMA ZAIDI YA MOJA ANDIKA MAGONJWA MATATU MAKUBWA YA KWANZA	NDIO..... 1 LA..... 2 SIJUI..... 8 1 _____ 2 _____ 3 _____					
	KULAZWA HOSPITALINI						
5.4	Je, (JINA LA MTOTO) aliwahi kulazwa hospitalini (kulazwa hospitali usiku mzima) tangu azaliwe?	1st	2nd	3rd	4th		
5.5	Alilazwa lini? dd/mm/yyyy	DD MM YY					
5.6	Je, (JINA LA MTOTO) alilazwa kwa ugonjwa gani?	Fafanua _____					
5.7	(JINA LA MTOTO) alilazwa siku ngapi?						
6.0	**UPIMAJI WA UZANI NA UREFU WA MTOTO**						
	Sasa umefika wakati wa kuchukua vipimo vya mama pamoja na mtoto. Nitampima mtoto wako uzani kisha nitakuomba unisaidie tuweze kumpima urefu wake.						
6.1	ANDIKA UREFU WA MTOTO ULIOPIMA HAPA UZANI WA MTOTO UTAPATIKANA KWA KUONDOA UZANI WA MAMA/MLINZI WA MTOTO KUTOKA UZANI WA MAMA NA MTOTO KWA PAMOJA.				.		
6.2	ANDIKA UZANI WA MAMA/MLINZI WA MTOTO KWA KG				.		
6.3	ANDIKA UZANI WA MAMA PAMOJA NA MTOTO KWA KG				.		
6.4	ANDIKA UZANI WA MTOTO KWA KG				.		
	MWISHO						
6.5	**ANDIKA MAONI YA JUMLA KUHUSU MAHOJIANO HAYA**						

Appendix V: Scientific Steering Committee (SSC) Approval

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/SSC/103524 9th February, 2015

Martin Mutua

Thro'
Director, CPHR
NAIROBI

Forwarded 13/02/2015

REF:SSC No. 2974 (Revised) – Childhood Vaccination Delays: Prevalence, Determinants and association with Childhood Morbidity and Growth in Korogocho and Viwandani Informal Settlements, Nairobi, Kenya

I am pleased to inform you that the above mentioned proposal, in which you are the PI, was discussed by the KEMRI Scientific Steering Committee (SSC), during its 223rd meeting held on 4th February, 2015 and has since been approved for implementation by the SSC.

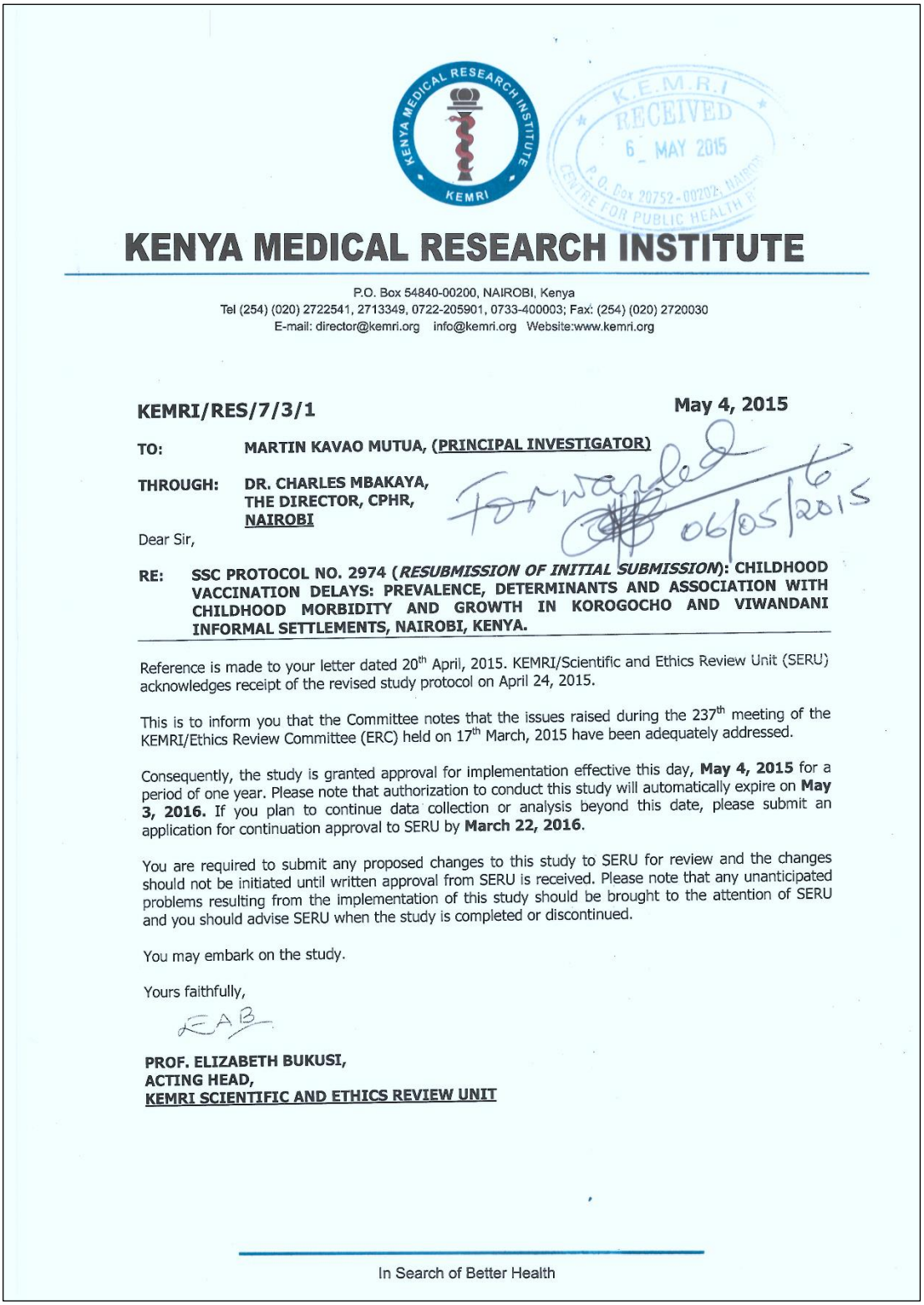
Kindly submit 4 copies of the revised protocol to SSC within 2 weeks from the date of this letter, i.e, 23rd February, 2015 for onward transmission to the ERC.

We advise that work on this project can only start when ERC approval is received.

Sammy Njenga, PhD
SECRETARY, SSC

12

Appendix VI: Scientific and Ethical Review Committee (SERU) Approval



KENYA MEDICAL RESEARCH INSTITUTE

K.E.M.R.I RECEIVED 6 MAY 2015 P.O. Box 20752-00202, NAIROBI CENTRE FOR PUBLIC HEALTH R

P.O. Box 54840-00200, NAIROBI, Kenya
Tel (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 **May 4, 2015**

TO: **MARTIN KAVAO MUTUA, (PRINCIPAL INVESTIGATOR)**

THROUGH: **DR. CHARLES MBAKAYA, THE DIRECTOR, CPHR, NAIROBI**

Forwarded 06/05/2015

Dear Sir,

RE: **SSC PROTOCOL NO. 2974 (*RESUBMISSION OF INITIAL SUBMISSION*): CHILDHOOD VACCINATION DELAYS: PREVALENCE, DETERMINANTS AND ASSOCIATION WITH CHILDHOOD MORBIDITY AND GROWTH IN KOROGOCHO AND VIWANDANI INFORMAL SETTLEMENTS, NAIROBI, KENYA.**

Reference is made to your letter dated 20th April, 2015. KEMRI/Scientific and Ethics Review Unit (SERU) acknowledges receipt of the revised study protocol on April 24, 2015.

This is to inform you that the Committee notes that the issues raised during the 237th meeting of the KEMRI/Ethics Review Committee (ERC) held on 17th March, 2015 have been adequately addressed.

Consequently, the study is granted approval for implementation effective this day, **May 4, 2015** for a period of one year. Please note that authorization to conduct this study will automatically expire on **May 3, 2016.** If you plan to continue data collection or analysis beyond this date, please submit an application for continuation approval to SERU by **March 22, 2016**.

You are required to submit any proposed changes to this study to SERU for review and the changes should not be initiated until written approval from SERU is received. Please note that any unanticipated problems resulting from the implementation of this study should be brought to the attention of SERU and you should advise SERU when the study is completed or discontinued.

You may embark on the study.

Yours faithfully,

EAB

PROF. ELIZABETH BUKUSI,
ACTING HEAD,
KEMRI SCIENTIFIC AND ETHICS REVIEW UNIT

In Search of Better Health

Appendix VII Scientific publication journal of Biomed Central Pediatrics, 2015

Mutua *et al. BMC Pediatrics* (2015) 15:45
DOI 10.1186/s12887-015-0360-5

BMC Pediatrics

RESEARCH ARTICLE Open Access

Effects of low birth weight on time to BCG vaccination in an urban poor settlement in Nairobi, Kenya: an observational cohort study

Martin Kavao Mutua[1,4*], Rhoune Ochako[6], Remare Ettarh[5], Henrik Ravn[2,7,8], Elizabeth Echoka[3] and Peter Mwaniki[4]

Abstract

Background: The World Health Organization recommends Bacillus Calmette-Guérin (BCG) vaccination against tuberculosis be given at birth. However, in many developing countries, pre-term and low birth weight infants get vaccinated only after they gain the desired weight. In Kenya, the ministry of health recommends pre-term and low birth weight infants to be immunized at the time of discharge from hospital irrespective of their weight. This paper seeks to understand the effects of birth weight on timing of BCG vaccine.

Methods: The study was conducted in two Nairobi urban informal settlements, Korogocho and Viwandani which hosts the Nairobi Urban Health and Demographic Surveillance system. All infants born in the study area since September 2006 were included in the study. Data on immunization history and birth weight of the infant were recorded from child's clinic card. Follow up visits were done every four months to update immunization status of the child. A total of 3,602 infants were included in this analysis. Log normal accelerated failure time parametric model was used to assess the association between low birth weight infants and time to BCG immunization.

Results: In total, 229 (6.4%) infants were low birth weight. About 16.6% of the low birth weight infants weighed less than 2000 grams and 83.4% weighed between 2000 and 2490 grams. Results showed that, 60% of the low birth weight infants received BCG vaccine after more than five weeks of life. Private health facilities were less likely to administer a BCG vaccine on time compared to public health facilities. The effects of low birth weight on females was 0.60 and 0.97-times that of males for infants weighing 2000–2499 grams and for infants weighing <2000 grams respectively. The effect of low birth weight among infants born in public health facilities was 1.52 and 3.94-times that of infants delivered in private health facilities for infants weighing 2000–2499 grams and those weighing < 2000 grams respectively.

Conclusion: Low birth weight infants received BCG immunization late compared to normal birth weight infants. Low birth weight infants delivered in public health facilities were more likely to be immunized much later compared to private health facilities.

Keywords: Bacillus Calmette-Guérin, Low birth weight, Immunization

Background

The World Health Organization (WHO) recommends Bacillus Calmette-Guérin (BCG) immunization against tuberculosis (TB) at birth or at first clinical contact to all infants [1] with the exception of HIV-infected infants in whom the BCG vaccine is associated with significant safety concerns [2]. Approximately nine million new cases of TB were diagnosed in 2013, with 1.5 million deaths reported. Most of these cases and deaths occurred in low and middle income countries [3], Kenya is among the 22 high burden TB countries with an estimated incident rate of 268 cases per 100,000 [3]. In Kenya, the Ministry of Health through the Division of Vaccines and Immunization recommends that the BCG vaccine be given at birth or at first clinical contact, except for pre-term and low birth weight (LBW) infants

* Correspondence: mkavao@aphrc.org
[1]African Population and Health Research Center, Manga Close, Nairobi, Kenya
[4]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya
Full list of author information is available at the end of the article

(birth weight less than 2000 grams) who should be vaccinated at the time of discharge from hospital irrespective of the weight [4]. Overall, BCG coverage in Kenya is high (96%) [5], but little is known about how soon the vaccines should be given after birth. BCG immunization delays have been reported in other studies [6,7] even in settings where the coverage is high [8].

When immunization is delayed, there is an increased risk or severity of infections during infancy due to the shortening of the duration of the protective effect of the vaccines [8]. Studies in West Africa have shown BCG immunization to have beneficial non-specific effects (NSE)–effects other than protecting the child from tuberculosis infections [9,10]. The earlier BCG immunization is given to an infant the higher the chances of survival [11-14]. While many studies have looked at timeliness of selected vaccines, few have focused on timeliness of vaccine administration in African settings. Moreover limited literature on timing of BCG among LBW infants is available. This paper, seeks to document the effects of LBW on timeliness of BCG immunization in two urban informal settlements in Nairobi, Kenya where healthcare access through the public sector is limited.

Methods

Study setting

The study was carried out in two informal settlements of Nairobi (Viwandani and Korogocho) where the African Population and Health Research Center (APHRC) runs the Nairobi Urban Health and Demographic Surveillance System (NUHDSS). The NUHDSS has been in operation since 2002 and had about 81,129 registered inhabitants in nearly 31,977 households as of December 2012. These two densely populated communities have high unemployment, poverty, crime, poor sanitation and generally poorer health indicators when compared to Nairobi as a whole [15,16]. The two communities however have notable differences: Viwandani is bordered by an industrial area and attracts migrant workers with relatively higher education levels, while the population in Korogocho is more stable and shows more co-residence of spouses. In addition, Korogocho has less disparity with regard to gender and age distribution of the population compared to Viwandani.

Study population

This study used maternal and child health data collected at the NUHDSS from two periods of survey: The first period 2007–2010 under "Urbanization, Poverty and Health Dynamics" (UPHD) project funded by Wellcome Trust that recruited all infants born from September 2006 and the second period 2011–2013 funded by Danish Development Agency (DANIDA) through INDEPTH Network and recruited infants born from January 2010. In addition to following up infants from the first period. During both periods, mother-child pairs were recruited and followed up with visits every four months as applicable. The same questionnaire was administered during each visit by trained interviewers. Information on place of delivery, child's weight at birth was collected during the first visit, while the children's immunization history including BCG vaccine given at birth collected during the first three visits. A total of 8,756 infants were recruited with 34,969 visits in total during the period of the study. Not all infants were seen during follow up visits due variety of reasons which included deaths, out migration, temporary exits among others. A breakdown of the selected sample for analysis is given in Figure 1. For this study, 3,602 infants (1668 and 1934 from first and second period) for whom an immunization card with a valid BCG vaccine date was seen at least once after 90 days of age and a birth weight recorded during the first visit were included. Only infants who had a BCG immunization and survived more than 90 days were included in the study because they had at least two additional opportunities where the child could have received BCG immunization at 6 and 10 weeks old during the child's visit for the first and second doses of Polio and Pentavalent immunizations.

Variables

Our outcome variable of interest is age at BCG immunization. The weight at birth of the child (recorded from a health card) was used as the primary exposure variable. We defined low birth weight (LBW) and normal birth weight (NBW) as a infants weighing less than 2500 grams and more or equal to 2500 grams respectively [17,18]. For purposes of this analysis, we sub-classified low birth weight to those weighing below 2000 grams and those weighing 2000–2499 grams. Other variables such as; Mother educational level (incomplete/no education, completed primary education or secondary school or above), Place of Delivery (Public or Private), Ethnicity (Kikuyu, Luhya, Luo, Kamba or Others), Settlement area (Korogocho or Viwandani), Child's Gender (Male or Female) and Pregnancy Intention of the index child (Wanted the child at that time, Wanted the child later or did not want the child at all) were used as control variables.

Data analysis

Descriptive statistics, frequencies, proportions and median of all dependent and independent variables of interest were obtained to summarize the data. The main objective was to assess the age when a child is vaccinated with BCG, and compare LBW infants with the normal birth weight infants. Approximately 1% of the infants in the study received their BCG after 90 days; these were censored at 90 days of age. Thus, Survival analysis techniques were used to assess the time to BCG immunization before 90 days. Kaplan-Meier curves were

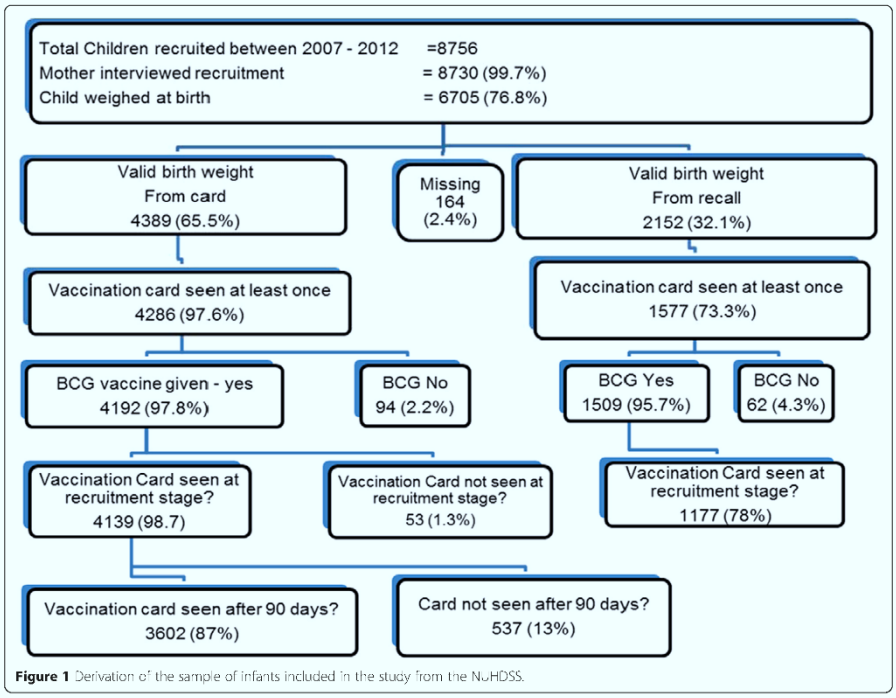


Figure 1 Derivation of the sample of infants included in the study from the NUHDSS.

used to describe the age distribution of getting BCG for the three birth weights group. Cox regression was later used to estimate the impact of low birth weight on the timing of the BCG immunization and identify risk factors of delay to BCG immunization; Cox models assumes proportionality of the hazard function over time. The proportionality assumption did not hold for our data, this was deduced using the Kaplan-Meier curves (Figure 2) and tested statistically using Schoenfeld residuals. Therefore we fitted parametric regression model methods that allow for the baseline hazards to vary for different categories for an independent variable and the hazard function does not need to be proportional. Different distributions for the baseline hazards were considered (exponential, Weibull, Gompertz, Lognormal, Log logistics and gamma). Akaikes information criterion (AIC) was used to pick the best distribution (model) which fits our data well. The AIC suggested a log normal accelerated failure time (AFT) model. Log normal parametric model was thus used to assess the association between LBW and time to BCG immunization.

Unadjusted (*Model 1*) and adjusted (*Model 2*) time ratios (TR) were used to assess the association between birth weight and BCG timing. Time ratio compares the change in the survival time associated with a change in the values of a given covariate. In an AFT model, every subject has the same "baseline" survival curve, the covariates effects serve to accelerate the passage of time.

Interaction models (*Model 3 and 4*) were fitted to see how the birth weight interacts with child's gender and place of delivery (Public or Private Health facility) respectively.

Ethical considerations

The study was approved by Kenya Medical Research Institute (KEMRI) ethical review committee with annual renewals during the second phase of the study. The research assistants were trained on research ethics and obtained written and verbal informed consent from all the study respondents. The NUHDSS, on which the study was nested, also received ethical approval from KEMRI's Ethical Review Board.

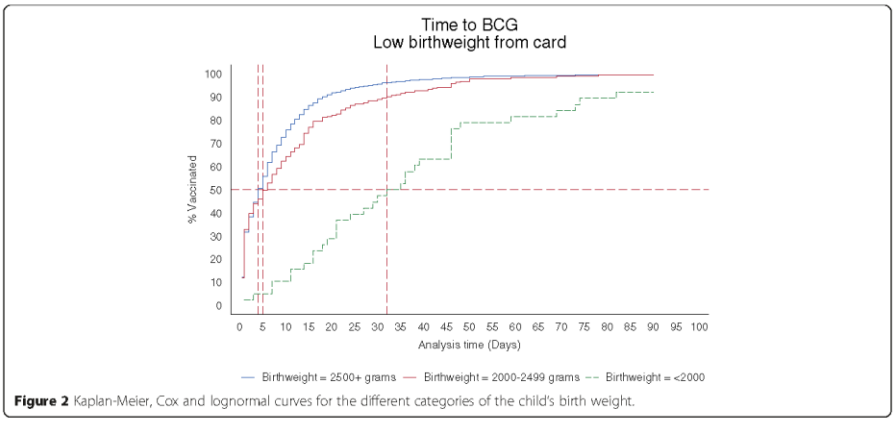


Figure 2 Kaplan-Meier, Cox and lognormal curves for the different categories of the child's birth weight.

Results

Descriptive statistics

A total of 229 out of 3602 infants (6.4%) included in the analysis were LBW (see Table 1). Of these, 38 (16.6%) infants weighed below 2000 grams with a median age at BCG immunization of 34 days interquartile range [IQR] 18–46, 191 (83.4%) weighed between 2000–2499 grams with a median immunization age of 6 days IQR 1–15. The remaining 93.6% had normal birth weight with median age of 4 days IQR 1–10. Infants from Korogocho (52% of the sample) on average were receiving the BCG a day later (median 5 days IQR 1–11) than those from Viwandani (median 4 days IQR 1–10). In terms of mother's education level, the less educated (incomplete or no education) received the BCG vaccine a day later as compared to those who completed primary or higher (median 5 days IQR 1–12 compared to 4 days IQR 1–10) education. In general, infants delivered in a health facility received their BCG earlier (median 4 days IQR 1–10), as expected, compared to infants delivered at home or by a traditional birth attendant (median days IQR 5–16). Additionally, infants delivered at a public health facility had a median age of 1 day IQR 1–7 compared to those delivered at a private health facility (median 6 days IQR 2–11). Males received BCG immunization a day later (median 5 days IQR 1–11) as compared to females (median 4 days IQR 1–10). About 72 infants (2%) of all infants in the study received BCG vaccine together with the first dose of the pentavalent vaccine. Infants who received BCG with the first dose of pentavalent were more likely to weigh less than 2000 grams (21%) compared to normal birth weight infants (2%) and infants weighing 2000–2499 grams (3%). Among infants excluded from the analysis due to lack of BCG information from their immunization cards, 93% had normal birth weight, 4% weighed 2000–2499 grams and 3% weighed below 2000 grams.

Regression analysis

The unadjusted TR shows infants with LBW tended to receive the BCG vaccine much later compared to the NBW infants (Table 2). Infants weighing less than 2000 grams and those weighing between 2000–2499 grams received BCG vaccine later, TR = 7.73 [5.52, 10.82] and TR = 1.22 [0.98, 1.51] respectively when compared to normal birth weight infants. Adjusting for the settlement area, ethnicity, mother's educational level, gender of the child, place of delivery and whether the child was planned, the TR estimates for infants weighing less than 2000 grams and those weighing between 2000–2499 grams became higher, 8.97 [6.01, 13.39] and 1.44 [1.15, 1.82] respectively. The effect of ethnic group of the mother and place of delivery were also statistically significant. Infants from other ethnic groups tend to receive BCG vaccine much later compared to the Kikuyu. Infants delivered at a public health facility received BCG vaccine much earlier (TR = 0.48 [0.44, 0.53]) compared to those delivered at a private health facility. Other variables included in the model did not attain the required level of significance.

Model 3 and 4 shows significant interactions of birth weight with gender and place of delivery respectively. From Table 3, the effect of low birth weight (those weighing between 2000–2499 grams) among female was 1.17 [0.89, 1.54] which is 0.6-times that of males 1.95 [1.31, 2.90]. The effect of low birth weight (those weighing <2000 grams) on female was estimated at 8.82 [4.95, 15.71] which was 0.97-times that of boys. Model 3 shows significant birth weight and place of delivery interaction. The effect of low birth weight (those weighing between 2000–2499 grams) among infants delivered in a public health facility was estimated as 1.79 [1.27, 2.54] which is 1.52-times that of infants born in a private health facility (1.18 [0.88, 1.59]). The effect of low birth weight (those weighing <2000 grams) among infants delivered in a

Table 1 Sample summary statistics

	N	%	Median age (IQR) of BCG vaccination
Child's birth weight (grams)			
<2000	38	1.1	34 (18–46)
2000_2499	191	5.3	6 (1–15)
> = 2500	3,373	93.6	4 (1–10)
Settlement area			
Korogocho	1,881	52.2	5 (1–11)
Viwandani	1,721	47.8	4 (1–10)
Mothers level of education			
Incomplete primary/no education	910	26.4	5 (1–12)
Completed primary	1,564	45.2	4 (1–10)
Secondary+	983	28.4	4 (1–10)
Place of delivery			
Non health facility	136	3.8	9 (5–16)
Health facility	3,466	96.2	4 (1–10)
Type of Health Facility			
Private	2,318	67.1	6 (2–11)
Public	1,139	32.9	1 (1–7)
Child's gender			
Male	1,843	51.2	5 (1–11)
Female	1,759	48.8	4 (1–10)
Pregnancy intention for the current child			
Wanted at that time	1,896	54.4	4 (1–10)
Wanted later	1,220	35	5 (1–11)
Not at all	368	10.5	5 (1–13)
Ethnic group			
Kikuyu	1,094	31.6	3 (1–8)
Luhya	583	16.8	5 (1–12)
Luo	563	16.2	6 (1–12)
Kamba	712	20.6	4 (1–11)
Other	513	14.8	5 (1–12)

public health facility was estimated as 14.41[10.06, 20.64], 3.94-times that of low birth weight (those weighing <2000 grams) infants delivered in a private health facility (3.66[1.78, 7.50]).

Discussion

The importance of BCG immunization in sub-Saharan Africa remains well accepted as it is a proven and cost-effective method of conferring immunity against tuberculosis and reducing the risk of outbreak of the disease. The coverage and timeliness of immunizations are the two key indicators of the population level protection against specific diseases. In this study, although coverage with BCG was above 95%, timeliness varied significantly among specific sub-groups. We found that infants born with low birth weight received the BCG vaccine much later than the normal birth weight infants. In particular, the low birth weight (those weighing <2000 grams) infants received the vaccine eight times later than the normal birth weight infants. Although there have been concerns about administering BCG in pre-term and low birth weight babies [19], evidence indicates a normal immune response to vaccine in low birth weight infants [20,21]. The World Health Organization recommends that pre-term infants should be vaccinated at 40 weeks, and this policy may underlie the delay in BCG administration to low birth weight infants even when delivered at full-term [22]. In Kenya, it is common practice in health facilities to delay immunization of the low birth weight infants, but this delay, if in excess, could have negative health consequences especially if the infant is exposed to tuberculosis before getting the BCG vaccine [22]. Studies have shown that BCG also has beneficial non-specific effects [14]. Low birth weight infants would not benefit from these during the early part of their life, if BCG immunization is delayed.

The tendency for late immunization among infants from the non-Kikuyu ethnic groups in Kenya has been reported previously and is consistent with the lower utilization of health services among non-kikuyu ethnic groups as observed in other studies [5,23]. Early receipt of the BCG vaccine by infants born in public health facilities is also consistent with reports from other parts of Sub Saharan Africa [24], which may be due to better vaccine supply in these facilities compared to the private health facilities in the underserved urban areas [25]. In addition, adherence to immunization schedules is required at public health facilities and may account for the early administration of BCG compared.

We assessed the effect of gender of the child in association with birth weight and BCG timing; and found a non- significant interaction, but results showed more delays in males as compared to female. The reasons for the gender difference in the timing of BCG immunization among low birth weight infants are not clear. Further studies are required to determine if this delay is related to parent or caregiver choices associated with low birth weight infants. This is important as studies in West Africa have shown beneficial effects of BCG to be more pronounced in female than male infants [26-28].

The interaction between birth weight and place of delivery where low birth weight infant delivered in public health facilities were immunized much later compared to their counterparts delivered from private health facilities. This is in contrast to the normal birth weight infants delivered from the public health facilities who get immunized earlier. This may be due to the better trained health workers in public health facilities intentionally delaying BCG immunization to low birth weight infants

Table 2 Unadjusted and adjusted lognormal models estimating the effects of child birth weight on timing of the BCG vaccination

	Model 1 Unadjusted			Model 2 Adjusted		
	Time ratio	**95% CI**	**Overall P-value**	**Time ratio**	**95% CI**	**Overall P-value**
Child's birth weight (ref: NBW (weight > =2500 grams))						
2000-2499 grams	1.22	[0.98,1.51]	<0.0001	**1.44**	**[1.15,1.82]**	**<0.0001**
<2000 grams	**7.73**	**[5.52,10.82]**		**8.97**	**[6.01,13.39]**	
Settlement area (ref: Korogocho)						
Viwandani				0.91	[0.82,1.01]	0.079
Ethnic group (ref: Kikuyu)						
Luhya				**1.16**	**[1.02,1.32]**	**<0.0001**
Luo				**1.22**	**[1.07,1.40]**	
Kamba				**1.27**	**[1.11,1.44]**	
Others				**1.31**	**[1.14,1.51]**	
Mother's level of education (incomplete primary)						
Completed primary				0.91	[0.81,1.02]	0.1773
Secondary+				0.90	[0.80,1.02]	
Pregnancy wanted ness (ref: wanted now)						
Wanted later				1.05	[0.95,1.16]	0.1492
Not at all				1.16	[0.99,1.35]	
Child's gender (ref: male)						
Female				0.95	[0.87,1.03]	0.221
Type of facility (ref: private HF)						
Public HF				**0.48**	**[0.44,0.53]**	**<0.0001**
N	3602			3185		

Estimates of a significance p < 0.05 are in bold writing.

as a precaution, but which staff of private health facilities in the slum may not do.

This study was conducted in two urban slums in the Nairobi and may therefore be indicative of the BCG status of low birth weight infants in similar settlements in Kenya. One limitation of the study is the large number of infants who had to be excluded due to the absence of documented birth weight or immunization status. The exclusion eliminated the effects of recall bias in cases where there is no documentation on birth weight or

Table 3 Interactions lognormal models estimating the effects of child birth weight on timing of the BCG vaccination

	Model 3 HF interaction			Model 4 Sex interaction		
	Time ratio	**95% CI**	**Overall P-value**	**Time ratio**	**95% CI**	**Overall P-value**
Male effect on LBW(2000–2499)				**1.95**	**[1.31,2.90]**	0.1144
Female effect on LBW(2000–2499)				1.17	[0.89,1.54]	
Male effect on LBW(<2000)				**9.10**	**[5.28,15.68]**	
Female effect on LBW(<2000)				**8.82**	**[4.95,15.71]**	
Effect of private health facility on LBW (2000–2499)	1.18	[0.88,1.59]	0.0009			
Effect of public health facility on LBW (2000–2499)	**1.79**	**[1.27,2.54]**				
Effect of private health facility on LBW (<2000)	**3.66**	**[1.78,7.50]**				
Effect of public health facility on LBW (<2000)	**14.41**	**[10.06,20.64]**				
N	3185			3185		

Estimates of a significance p < 0.05 are in bold writing.

BCG immunization date. About 32% of the infants and a further 2% were omitted from the analysis due to lack of documentation of birth weight and/or BCG date respectively. The exclusions is supplemented by the large sample size for the analysis due to the longitudinal nature of the study. In addition, the absence of information from caregivers regarding the reasons for delays in BCG immunization would have clarified the extent of service-related delays.

Conclusions

This study shows that low birth weight infants in Nairobi urban informal settlements receive BCG immunization much later than normal birth weight infants with place of delivery as the main factor of influence. This study contributes to addressing the gap in evidence on timeliness of immunization in urban informal settlements in Kenya as well as other similar settings in low and middle income countries. Additional research should be conducted to further evaluate the timing of the other routine childhood immunizations in similar settings as well as rural and formal urban settlements. These studies should evaluate the effects of immunization delays on overall child health.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MKM: Participated in the overall conceptualization and inception of the idea of this manuscript, with lead roles in conducting literature review, data analysis, writing the results and discussion sections. RO: assisted in conceptualization and writing the background section. RE: assisted in the conceptualization and writing the discussion section. HR: assisted in conceptualization and writing the methods section. EE: assisted in conceptualization the paper. PM: assisted in conceptualization the paper. All the authors read and approved the final manuscript.

Authors' information

MKM is statistician, APHRC and a PhD Epidemiology student at JKUAT.
HR is Chief Statistician, Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project and Statens Serum Institut, Denmark and an Associate Professor, University of Southern Denmark.
RO is a Demographer and Senior Manager, Research, at Population Services Kenya (PS Kenya).
RE is a Research and Evaluation Specialist, Faculty of Medicine, University of British Columbia.
EE is a Senior Researcher, Center for Public Health Research (CPHR), Kenya Medical Research Institute (KEMRI).
PM is a Senior Lecturer, Jomo Kenyatta University of Agriculture and Technology.

Acknowledgements

Projects which contributed data: Urbanization, Poverty, and Health Dynamics (UPHD) research project funded by the Wellcome Trust (Grant Number GR 07830 M) and Monitoring and assessing the impact of immunization and other childhood interventions for both boys and girls, an INDEPTH Network collaboration project funded by the Danish Development Agency (DANIDA) (DFC Project no 09-09-105SSI). This research was also made possible through the generous core funding for the NUHDSS by the Bill and Melinda Gates Foundation (Grant# OPP1021893) and core funding for APHRC by The William and Flora Hewlett Foundation (Grant# 2009--40510), and the Swedish International Cooperation Agency (SIDA) (Grant# 2011--001578). The authors acknowledge the contribution of Alex Ezeh, Peter Aaby and Christine Benn in the design of the two studies. The authors are also highly indebted to the data collection team led by Peterrock Muriuki and the study participants.

Author details

[1]African Population and Health Research Center, Manga Close, Nairobi, Kenya. [2]Research Center for Vitamins and Vaccines, 5 Artillerivej, Copenhagen, Denmark. [3]Center for Public Health Research, Kenya Medical Research Institute, Nairobi, Kenya. [4]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya. [5]Faculty of Medicine, University of British Columbia, Vancouver, Canada. [6]Population Services Kenya, Jumuia Place, Lenana road, Nairobi, Kenya. [7]Bandim Health Project, Statens Serum Institut, 5 Artillerivej, Copenhagen, Denmark. [8]OPEN, University of Southern Denmark/Odense University Hospital, Odense, Denmark.

Received: 21 October 2014 Accepted: 1 April 2015
Published online: 18 April 2015

References

1. World Health Organization. WHO Position Papers. 2014.
2. Nuttall J, Eley B. BCG Vaccination in HIV-Infected Children. Tuberculosis Res Treat. 2011;2011:712736.
3. World Health Organization. Global Tuberculosis Report 2014. Geneva: World Health Organization; 2014.
4. Kenya Ministry of Health: National Policy Guidelines on Immunization 2013. Kenya.
5. (KNBS) KNBoS, Macro I. Kenya Demographic and Health Survey 2008--09. Stud Fam Plann. 2008;42(2):131–6.
6. Roth A, Jensen H, Garly M-L, Djana Q, Martins CL, Sodemann M, et al. Low birth weight infants and Calmette-Guerin bacillus vaccination at birth: community study from Guinea-Bissau. Pediatr Infect Dis J. 2004;23(6):544–50.
7. Olusanya B. Pattern and determinants of BCG immunisation delays in a sub-Saharan African community. Health Res Pol Syst. 2010;8:1.
8. Yadav K, Srivastave R, Kumar R, Chinnakal P, Rai S, Krishnan A. Significant Vaccination Delay can Occur Even in a Community with Very High Vaccination Coverage: Evidence from Ballabgarh, India. J Trop Pediatr. 2012;58(2):133–8.
9. Roth A, Garly M, Jensen H, Nielsen J, Aaby P. Bacillus Calmette-Guerin vaccination and infant mortality. Expet Rev Vaccine. 2006;5(2):277–93.
10. Roth A, Gustafson P, Nhaga A, Djana Q, Poulsen A, Garly M, et al. BCG vaccination scar associated with better childhood survival in Guinea-Bissau. Int J Epidemiol. 2005;34(3):540–7.
11. Fadnes L, Jackson D, Engebretsen I, Zembe W, Sanders D, Sommerfelt H, et al. Vaccination coverage and timeliness in three South African areas: a prospective study. BMC Public Health. 2011;11(1):1–12.
12. Shann F. The Nonspecific Effects of Vaccines and the Expanded Program on Immunization. J Infect Dis. 2011;204:182–4.
13. Biering-Sorensen S, Aaby P, Napirna BM, Roth A, Ravn H, Rodrigues A, et al. Small randomized trial among low-birth-weight children receiving bacillus Calmette-Guerin vaccination at first health center contact. Pediatr Infect Dis J. 2012;31(3):306–8.
14. Aaby P, Roth A, Ravn H, Napirna B, Rodrigues A, Lisse I, et al. Randomized trial of BCG vaccination at birth to low-birth-weight children: beneficial nonspecific effects in the neonatal period? J Infect Dis. 2011;204(2):245–52.
15. Emina J, Beguy D, Zulu E, Ezeh A, Muindi K, Elung'ata P, et al. Monitoring of health and demographic outcomes in poor urban settlements: evidence from the Nairobi Urban Health and Demographic Surveillance System. J Urban Health. 2011;88 Suppl 2:S200–18.
16. Mberu BU, Ciera JM, Elungata P, Ezeh AC. Patterns and Determinants of Poverty Transitions among Poor Urban Households in Nairobi, Kenya. Afr Dev Rev. 2014;26(1):172–85.
17. World Health Organization. Global targets 2025: To improve maternal, infant and young child nutrition. 2014.
18. World Health Organization. Global nutrition targets 2025: low birth weight policy brief. 2014.
19. Barreto M, Pereira S, Ferreira A. BCG vaccine: efficacy and indications for vaccination and revaccination. J Pediatr (Rio J). 2006;82(3 Suppl):S45–54.
20. Kaur S, Faridi M, Agarwal K. BCG vaccination reaction in low birth weight infants. Indian J Med Res. 2002;116:64–9.
21. Jensen KJ, Larsen N, Biering-Sørensen S, Andersen A, Eriksen HB, Monteiro I, et al. Heterologous immunological effects of early BCG vaccination in low-birth weight infants in Guinea-Bissau: a randomized-controlled trial. J Infect Dis. 2015;211(6):956–67.

22. WHO. BCG vaccine. WHO position paper. Releve epidemiologique hebdomadaire/Section d'hygiene du Secretariat de la Societe des Nations = Weekly epidemiological record/Health Section of the Secretariat. 2004;79(4):27–38.
23. Ettarh R, Mutua MK, Kyobutungi C. Ethnicity and delay in measles vaccination in a nairobi slum. Trop Med Health. 2012;40(2):59–62.
24. Babirye J, Engebretsen I, Makumbi F, Fadnes L, Wamani H, Tylleskar T, et al. Timeliness of childhood vaccinations in Kampala Uganda: a community-based cross-sectional study. Plos One. 2012;7(4):e35432.
25. Cutts F. Strategies to improve immunization services in urban Africa. Bull World Health Organ. 1991;69(4):407–14.
26. Aaby P, Jensen H. Routine vaccinations and child survival: effect of gender. BMJ. 2002;321(7274):1435.
27. Aaby P, Jensen H, Rodrigues A, Garly ML, Benn CS, Lisse IM, et al. Divergent female–male mortality ratios associated with different routine vaccinations among female–male twin pairs. Int J Epidemiol. 2004;33(2):367–73.
28. Stensballe L, Nante E, Jensen I, Kofoed P, Poulsen A, Jensen H, et al. Acute lower respiratory tract infections and respiratory syncytial virus in infants in Guinea-Bissau: a beneficial effect of BCG vaccination for girls - Community based case–control study. Vaccine. 2005;23(10):1251–7.

Appendix VIII Scientific publication, Journal of Tropical Medicine and Health, 2016

Mutua *et al. Tropical Medicine and Health* (2016) 44:13
DOI 10.1186/s41182-016-0013-x

Tropical Medicine and Health

RESEARCH Open Access

Fully immunized child: coverage, timing and sequencing of routine immunization in an urban poor settlement in Nairobi, Kenya

Martin Kavao Mutua[1,4*], Elizabeth Kimani-Murage[1,7], Nicholas Ngomi[1], Henrik Ravn[2,5,6], Peter Mwaniki[4] and Elizabeth Echoka[1,3]

Abstract

Background: More efforts have been put in place to increase full immunization coverage rates in the last decade. Little is known about the levels and consequences of delaying or vaccinating children in different schedules. Vaccine effectiveness depends on the timing of its administration, and it is not optimal if given early, delayed or not given as recommended. Evidence of non-specific effects of vaccines is well documented and could be linked to timing and sequencing of immunization. This paper documents the levels of coverage, timing and sequencing of routine childhood vaccines.

Methods: The study was conducted between 2007 and 2014 in two informal urban settlements in Nairobi. A total of 3856 children, aged 12–23 months and having a vaccination card seen were included in analysis. Vaccination dates recorded from the cards seen were used to define full immunization coverage, timeliness and sequencing. Proportions, medians and Kaplan-Meier curves were used to assess and describe the levels of full immunization coverage, vaccination delays and sequencing.

Results: The findings indicate that 67 % of the children were fully immunized by 12 months of age. Missing measles and third doses of polio and pentavalent vaccine were the main reason for not being fully immunized. Delays were highest for third doses of polio and pentavalent and measles. About 22 % of fully immunized children had vaccines in an out-of-sequence manner with 18 % not receiving pentavalent together with polio vaccine as recommended.

Conclusions: Results show higher levels of missed opportunities and low coverage of routine childhood vaccinations given at later ages. New strategies are needed to enable health care providers and parents/guardians to work together to increase the levels of completion of all required vaccinations. In particular, more focus is needed on vaccines given in multiple doses (polio, pentavalent and pneumococcal conjugate vaccines).

Keywords: Fully immunized child, Coverage, Vaccination delay, Vaccination sequence

Background

Inadequate immunization is recognized as a major public health concern as it accounted for about 17 % of all deaths globally in children under five in 2008, preventable with immunization [1]. Achieving universal vaccination coverage for all is one of the global sustainable development targets aimed at reducing childhood mortality from preventable deaths [2]. Full vaccination coverage has been the cornerstone of immunization programmes in many countries, and it is estimated to avert an estimated two to three million deaths every year in all age groups from diphtheria, tetanus, pertussis and measles [3]. Immunization programmes have been very successful in protecting children against specific infections. Poliomyelitis infections are on the verge of complete eradication with infection cases being reported in four countries: Afghanistan, Pakistan, Nigeria and Somalia [4].

* Correspondence: mkavao@aphrc.org; martin.mutuah@gmail.com
[1]African Population and Health Research Center, Manga Close, Nairobi, Kenya
[4]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya
Full list of author information is available at the end of the article

Basic immunization covers all vaccines given at any time within the first year of life and has been the focal point in evaluating immunization programmes [1, 3]. According to the World Health Organization (WHO) guidelines [5], a child is fully immunized with all basic vaccinations if the child has received Bacillus Calmette-Guerin (BCG) vaccine against tuberculosis at birth; three doses each of polio and pentavalent (diphtheria-tetanus-pertussis-hepatitis B (Hep), Haemophilus influenza type B (Hib)) vaccines at 6, 10 and 14 weeks of age; and a vaccination against measles at 9 months of age. Pneumococcal conjugate vaccine (PCV) given in three doses (6, 10 and 14 weeks) was introduced in Kenya in February 2011 and included in the routine immunization schedule [6].

Globally, full immunization coverage for children aged 12–23 months increased to 83 % [1, 7] in 2011. In Kenya, full immunization coverage for children aged 12–23 months currently stands at 79 and 75 %, respectively, when PCV is considered [8]. Only 2 % of the children aged 12–23 months had not received any vaccines [8] in 2014. However, it is also important to note that this figure can hide the variability in vaccine coverage [1, 8, 9] within Kenya and especially in urban informal settlements where the full vaccination coverage was only 44 % [10] in 2002, 58 % [11] in 2010 and 68.5 % in 2012 [12] compared to coverage in Nairobi of 73 % [13] in 2009 and 79 % in 2013 [8]. Full immunization coverage in Nairobi informal settlements depended on background characteristics of the child, mother and the household [8, 10, 12, 14]. Given the inadequate health care services in Nairobi informal settlements [15, 16] where 60–70 % of the Nairobi population resides [10, 12], identification of areas with low immunization coverage and achieving high immunization coverage in these areas become paramount for health intervention [17, 18].

The timing of vaccine is important for effectiveness and safety of the vaccine. Timely administration of vaccines has implications for the success of childhood immunization programmes, and a timely start of immunization is important in the first year of life as the transplacental immunity declines rapidly [19]. In practice, although a few children might be vaccinated early, many will be vaccinated late [20] which reduces the impact of vaccine programmes on disease burden especially in high-risk groups [21]. Vaccines given before 6 weeks of age (excluding BCG and polio at birth) have shown poor response and in some cases could be detrimental to infants as they reduce the immune response of subsequent doses [22]. Similarly, there is need to observe the minimum recommended age for different vaccines which are normally based on the youngest age group at risk for the specific infections where vaccine safety and efficacy have been demonstrated. Therefore, giving doses earlier than scheduled or given closer to each other may lead to a less optimal immune response [22]. On the other hand, when a child's vaccine is delayed, the interval between doses/vaccines is increased and the optimal vaccine protection may not be attained [22]. Simultaneous vaccination (pentavalent, polio and PCV doses) increases the chance that a child will be fully vaccinated on time and hence improving age-specific vaccine coverage [23, 24]. Therefore, the out-of-sequencing, early or delays of vaccines may affect child survival. Several studies have documented various reasons causing delays in the administration of vaccines and their impact. A recent paper from a study in Nairobi informal settlements reveals that low birth weight infants receive BCG immunization later than normal birth weight infants [25]. Measles and BCG vaccines are known to have beneficial *non-specific effects* (NSE) when given on time while the DPT containing vaccines does not seem to [26–31].

Few studies have documented timeliness and sequencing of routine vaccinations in sub-Saharan Africa. In a study done in Ghana in 2010, 44 % of children aged 12–23 months had their measles vaccine delayed [32]. In Burkina Faso, approximately 40 % of children aged 12–23 months had their polio and pentavalent doses delayed [33]. In an earlier study in the same study area as the current study, delays in measles vaccine (MV) were estimated at 20 % among boys and 24 % among girls [34]. Immunization timeliness have been documented in several studies [25, 34–38], but almost none have looked at the levels of out-of-sequence. This gap forms the basis of this paper, which documents the levels of full immunization coverage both overall and by different factors of interest. The study also aims to document the levels of early and delayed immunization. Overall levels of out-of-sequencing of the routine vaccinations in two informal settlements in Nairobi, Kenya, are documented as well as by different factors of interest. A key strength of this study over others is the use of a longitudinal study design particularly to study timing and out-of-sequencing of routine vaccinations in urban poor settings.

Methods

Study setting

The study was carried out in two informal settlements of Nairobi (Viwandani and Korogocho) between 2007 and 2014 in the Nairobi Urban Health and Demographic Surveillance System (NUHDSS) ran by the African Population and Health Research Center (APHRC). The NUHDSS has been in operation since 2002 and had about 81,129 registered inhabitants in approximately 31,977 households as of December 2012. The two

informal settlements are densely populated with high unemployment, crime, poor sanitation and poorer health indicators generally as compared to the whole of Nairobi. There are notable differences between the two settlements: Korogocho is more stable with less disparity in terms of gender and age distribution as compared to Viwandani which borders an industrial area and attracts migrant workers with relatively high education levels. The two communities are mainly served by private health facilities and two public health facilities located outside the area. Details of the study areas and operations of the NUHDSS have been published elsewhere [15, 16, 39].

Study population

This study used data from a longitudinal maternal and child health project implemented in Korogocho and Viwandani whose details have been published elsewhere [25]. The study included all children born in the study area from September 2006 to December 2013. For purpose of this study, we used data for children aged 12–23 months. All children without a vaccination card were excluded from the analysis. Figure 1 gives a diagrammatic description of how the final sample was derived.

Study design

The study involved a longitudinal observational study design to study the outcomes. The mother-child pairs in the study were followed up every 4 months collecting information on the immunization status of the child at each visit using structured questionnaires administered by trained research assistants. We use vaccination data collected from the time of recruitment for children aged 12–23 months.

Variables

This study assessed the levels and patterns of the routine vaccination uptake in the study area. The primary outcome variable of interest was fully immunized children (FIC) coverage. The secondary outcomes of interest were vaccination sequencing and timing of immunization (early or delayed). FIC was defined as a child who has received all the recommended basic vaccines by 12 months of age, i.e. BCG at birth, polio doses at 6 (42), 10 (70) and 14 (98) weeks (days) of age; pentavalent doses at 6 (42), 10 (70) and 14 (98) weeks (days) of age; and measles dose at 9 (274) months (days) of age. Early vaccination was defined as any vaccine given more than 4 days before recommended age for each vaccine/dose [40, 41]. In addition, for the measles vaccine, we assessed doses given more than 2 weeks before the recommended age. A vaccine is delayed if it is given more than 2 weeks after the recommended age for BCG, polio, pentavalent and PCV doses and more than a month for measles [42, 43]. Out-of-sequence (OS) was defined as either receiving (i) BCG after or with any of the other routine vaccines, (ii) any pentavalent vaccine dose with or after the MV or (iii) receiving respective pentavalent and polio doses at different days [44, 45]. A fully immunized child in out-of-sequence (FIC-OS) was defined as a child who is FIC and had at least one vaccine given in out-of-sequence.

Maternal education (none, primary and secondary or higher), ethnicity (Kikuyu, Luhya, Luo, Kamba or other), sex of child and delivery place (health facility or not), wealth status calculated using principal component analysis (lower, middle or upper) and study location (Korogocho or Viwandani) were included in the analysis. FIC coverage was also assessed by year of visit with

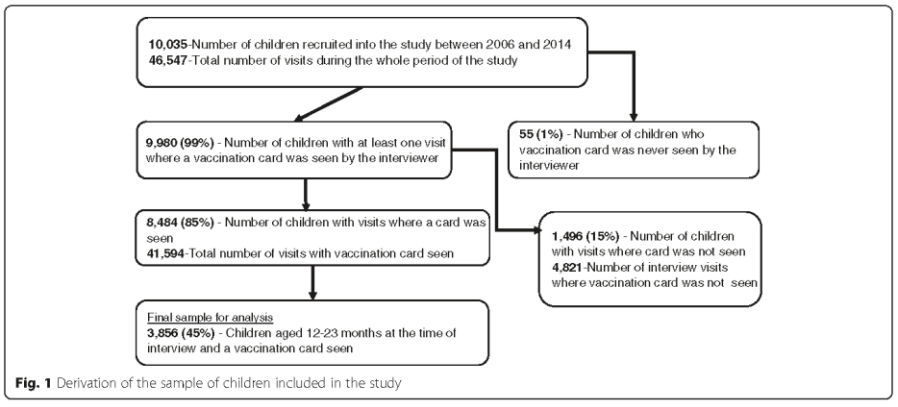


Fig. 1 Derivation of the sample of children included in the study

coverage in a given year reflecting vaccines given between 1 and 2 years earlier.

Data analysis

All children aged 12–23 months of age and a vaccination card seen were included in the analysis. For children with more than one interview visit, the earliest visit was picked for the analysis. Proportions were used to assess the levels of FIC coverage, out-of-sequence, early and delayed vaccination. The Kaplan-Meier method was used to calculate vaccination coverage curves, and the log rank test was used to compare vaccination coverage curves by FIC status. Median age at vaccination was used to assess the levels of vaccination delays. Chi-square test of independence was used to test independence between FIC coverage and levels of out-of-sequence by the different background characteristics while median test was used to test equality of medians. All tests were conducted at a 5 % level of significance. Stata software version 13.1 was used for all data management and analysis.

Ethics, consent and permissions

The study was approved by the Kenya Medical Research Institute (KEMRI) ethical review committee. The research assistants were trained on research ethics and obtained both written and verbal informed consent from all the study respondents. The NUHDSS, on which the study was nested, also received ethical approval.

Results

Descriptive

The descriptive results are summarized in Table 1. A total of 3856 out of 10,035 (38 %) children met the inclusion criteria and were included in the study. Sixty-two percent of the children were excluded due to lack of an interview visit where a vaccination card was seen between 12 and 23 months of age. The sample had slightly more males (50.5 %) compared to females (49.5 %). Most of the children were delivered in a health facility (83.4 %), with majority of the mothers aged below 25 years (56.2 %) and having primary level of education (70 %). Majority of the mother-child pairs attended postnatal care (92.4 %). The last column in Table 1 summarizes FIC coverage by different background factors for children aged 12–23 months. There was no significant difference in FIC coverage between a male and female child. Significantly higher FIC coverage was observed among mothers from Viwandani area (74.1 %) compared to Korogocho (58.1 %) and among mothers who attended postnatal care (67.7 %) compared to mothers who did not attend postnatal care (53.3 %). FIC coverage varied significantly by maternal education level, parity and household wealth status.

Vaccination coverage

Table 2 summarizes coverage for each antigen and overall FIC coverage by year of visit. Overall FIC coverage was estimated at 66.6 % in the study area. FIC coverage was estimated at 66, 69, 72, 70, 68, 61 and 55 % for the years 2008, 2009, 2010, 2011, 2012, 2013 and 2014, respectively. BCG, oral polio vaccine (OPV) 1 and 2 and pentavalent 1 and 2 coverage were estimated at 97.1, 99.1, 96.6, 99 and 96.6 %, respectively. Lower coverages were observed for OPV 3 (82–88 %), pentavalent 3 (85–89 %) and measles (68–87 %). The coverage of PCV doses were low in 2011, the year PCV was rolled out in Kenya. Vaccination coverage of each antigen by different background characteristics are given in Additional file 1: Table S1.

Median age of vaccination

The median age and interquartile range (IQR) of each antigen are summarized for non-FIC children (Additional file 2: Table S2a) and FIC children (Additional file 2: Table S2b) by background characteristics. The median age for BCG was estimated at 6 days (IQR 1–14) for FIC and 8 days (IQR 2–17) for non-FIC children. Median age for BCG varied significantly by postnatal care attendance, delivery place, parity and ethnicity among FIC children and delivery place and ethnicity among non-FIC children. Median age for the third dose of pentavalent was estimated at 107 (102–114) and 110 (103–126) days for non-FIC and FIC children, respectively. The median age for the third dose of polio was estimated at 111 (104–129) days for non-FIC and 107 (102–116) days for FIC children with significant differences observed by maternal level of education, delivery place, parity, ethnicity, wealth status and location for both FIC and non-FIC children. Median age for the MV was estimated at 282 (275–294) days among FIC children and 290 (277–323) days for non-FIC children with significant differences observed by child's gender for FIC children and by postnatal care, mother's age, parity, ethnicity, wealth status and location for non-FIC children.

The coverage curves are shown in Fig. 2 for the whole period and for each year's visit in the additional file (Additional file 3: Figure S1a and S1b). The curves for each vaccine by definition end at 100 % for FIC children. Vaccination timing among FIC are remarkable especially for the polio and pentavalent doses which are almost upright apart from a few children who received them a bit later. The MV and BCG coverage curves appear less upright. The FIC coverage curves for the OPV doses improved over the years. The coverage curves among the non-FIC children do not reach 100 % and are less upright compared to FIC children which shows that more

Table 1 Sample characteristics and FIC coverage at 12 months of age among children aged 12–23 months

		No.	Percent	% FIC	Overall *P* value
Childs gender	Male	1925	50.5	66.0	0.391
	Female	1889	49.5	67.3	
Postnatal care	No	289	7.6	*53.3*	<0.001
	Yes	3511	92.4	*67.7*	
Mother's age group	11–20	907	24.6	64.5	0.254
	21–24	1166	31.6	67.9	
	25–29	928	25.2	68.4	
	30–55	688	18.7	66.1	
Mother's education level	<Primary	94	2.6	*57.4*	<0.001
	Primary	2539	70	*64.9*	
	Secondary+	995	27.4	*72.7*	
Place of delivery	Health facility	3172	83.4	*67.5*	0.017
	Not health facility	630	16.6	*62.5*	
Parity	One	1231	32.4	*71.9*	<0.001
	Two	1171	30.8	*66.4*	
	Three and above	1399	36.8	*62.2*	
Ethnicity	Kikuyu	952	25.8	*70.6*	<0.001
	Luhya	696	18.9	*62.9*	
	Luo	603	16.3	*58.4*	
	Kamba	829	22.5	*73.9*	
	Other	611	16.6	*63.5*	
Wealth status	Lower	1224	33.4	*61.1*	<0.001
	Middle	1216	33.2	*70.2*	
	Upper	1221	33.4	*69.6*	
Study site	Korogocho	1779	46.6	*58.1*	<0.001
	Viwandani	2035	53.4	*74.1*	
Year of visit	2008	921	24.1	*65.6*	<0.001
	2009	303	7.9	*68.6*	
	2010	413	10.8	*72.4*	
	2011	603	15.8	*69.5*	
	2012	941	24.7	*67.7*	
	2013	440	11.5	*60.7*	
	2014	193	5.1	*55.4*	
N		3814			

Proportions significantly different at 5 % level of significance are highlighted in italics

non-FIC children have their vaccines delayed compared to FIC. Results from log rank tests showed significant differences in Kaplan-Meier curves between third doses of polio and pentavalent (*P* value 0.004) and non-significant differences between the first doses (*P* values = 0.242) and second doses (*P* value = 0.054) of polio and pentavalent vaccines in all children, respectively. Significant differences (*P* value <0.001) in Kaplan-Meier curves of each antigen by FIC status were observed from log rank tests. Additional file 4: Table S3 shows children are receiving their vaccines earlier than recommended ages: more than 4 days for OPV 1 (3.3 %) and pentavalent 1 (2.7 %) and MV (8.4 %). Five percent of the children received MV more than 14 days before the appropriate age. The proportion of early immunization is high among the non-FIC compared to FIC children for pentavalent doses (*P* values, 0.005, 0.029 and 0.001 for first, second and third doses, respectively) and the first polio dose (*P* value = 0.010).

Table 2 Immunization coverage at 12 months of age among children aged 12–23 months by year of visit

	Year of visit							
	2008	2009	2010	2011	2012	2013	2014	2008–2014
	% (#)	% (#)	% (#)	% (#)	% (#)	% (#)	% (#)	% (#)
BCG	98.4 (906)	97.7 (296)	96.9 (400)	96.8 (584)	96.3 (906)	96.6 (425)	97.4 (188)	97.1 (3705)
OPV 0	77.0 (709)	83.8 (254)	83.5 (345)	81.1 (489)	84.6 (796)	81.4 (358)	25.9 (050)	78.7 (3001)
OPV 1	99.3 (915)	99.0 (300)	100 (413)	98.3 (593)	99.0 (932)	99.5 (438)	96.9 (187)	99.1 (3778)
OPV 2	97.4 (897)	97.0 (294)	97.1 (401)	95.0 (573)	96.5 (908)	96.8 (426)	95.9 (185)	96.6 (3684)
OPV 3	82.5 (760)	86.1 (261)	87.9 (363)	84.1 (507)	88.1 (829)	88.4 (389)	84.5 (163)	85.8 (3272)
Penta 1	99.3 (915)	98.7 (299)	100 (413)	98.7 (595)	99.0 (932)	99.3 (437)	96.4 (186)	99.0 (3777)
Penta 2	97.1 (894)	96.7 (293)	97.6 (403)	96.5 (582)	96.2 (905)	96.1 (423)	94.8 (183)	96.6 (3683)
Penta 3	86.6 (798)	87.5 (265)	88.9 (367)	88.6 (534)	86.0 (809)	88.2 (388)	85.5 (165)	87.2 (3326)
PCV 1				61.4 (248)	90.6 (853)	97.7 (430)	93.3 (180)	86.5 (1711)
PCV 2				45.3 (183)	83.2 (783)	94.1 (414)	91.2 (176)	78.7 (1556)
PCV 3				31.4 (127)	70.1 (660)	80.0 (352)	79.3 (153)	65.3 (1292)
Measles	81.2 (748)	82.8 (251)	86.7 (358)	85.7 (517)	81.6 (768)	73.0 (321)	68.4 (132)	81.1 (3095)
FIC 8	65.6 (604)	68.6 (208)	72.4 (299)	69.5 (419)	67.7 (637)	60.7 (267)	55.4 (107)	66.6 (2541)
N	921	303	413	603	941	440	193	3814

Vaccine sequence

Table 3 summarizes levels of FIC-OS. Overall, 21.7 % of FIC children were FIC-OS. The levels of FIC-OS were significantly higher among mothers not attending postnatal care (29.2 %), those that did not deliver at a health facility (31.0 %) and those from the Korogocho settlement area (30.5 %) and also differed significantly by ethnicity group and household wealth status. The main cause of being FIC-OS was not receiving pentavalent and polio doses together (18.2 %).

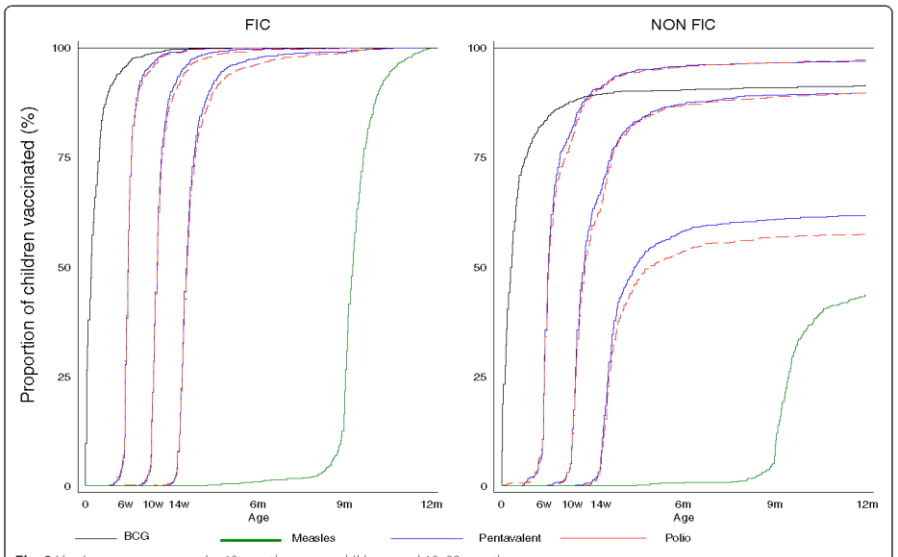


Fig. 2 Vaccine coverage curves by 12 months among children aged 12–23 months

Table 3 Proportion of children receiving vaccination in out-of-sequence (FIC-OS) by 12 months of age among children aged 12–23 months by different background factors

	Late BCG (%)	Pentas<>OPVs (%)	Penta>=MV (%)	FIC-OS (%)	N	Overall *P* value
Overall	4.0	18.2	0.8	21.7	2541	–
Sex						
Male	4.5	17.5	0.9	21.3	1270	0.646
Female	3.5	18.9	0.8	22.1	1271	
Postnatal						
No PN	6.5	*24.0*	0.6	*29.2*	154	0.021
PN	3.9	*17.7*	0.8	*21.2*	2378	
Mother's age group						
11–20	4.3	20.2	0.9	24.1	585	0.185
21–24	4.3	16.5	0.8	20.3	792	
25–29	3.0	17.5	0.8	20.0	635	
30–55	4.0	19.3	0.7	22.6	455	
Education						
<Primary	1.9	*25.9*	0.0	25.9	54	0.080
Primary	4.0	*18.7*	0.9	22.2	1647	
Secondary+	3.6	*15.2*	0.4	18.5	723	
Delivery place						
Health facility	*2.5*	17.7	*0.6*	*20.0*	2140	
Non-HF	*12.2*	20.3	*2.0*	*31.0*	394	<0.001
Parity						
Parity1	4.1	18.0	*0.2*	21.5	885	0.543
Parity2	3.9	17.2	*1.2*	20.6	778	
Parity3+	4.1	19.1	*1.1*	22.9	870	
Ethnicity						
Kikuyu	*2.7*	*20.1*	*0.0*	*22.2*	672	0.001
Luhya	5.0	*20.3*	*1.4*	*25.1*	438	
Luo	5.4	*22.2*	*1.4*	*26.7*	352	
Kamba	3.8	*14.4*	*0.7*	*17.9*	613	
Other	3.6	*14.7*	*1.0*	*17.5*	388	
Wealth status						
Lower	4.3	*25.4*	1.2	*29.0*	748	<0.001
Middle	3.5	*17.7*	0.5	*20.5*	854	
Upper	4.2	*12.6*	0.8	*16.7*	850	
Study site						
Korogocho	4.4	*26.9*	1.1	*30.5*	1033	
Viwandani	3.8	*12.2*	0.7	*15.7*	1508	<0.001

Proportions significantly different at 5 % level of significance are highlighted in italics
Late BCG BCG given together or after any pentavalent or measles, *Pentas<>OPVs* corresponding pentavalent and polio not given together, *Penta>=MV* pentavalent given together or after measles, *FIC-OS* fully immunized child by 12 months with either late BCG, Pentas<>OPVs or Penta>=MV

Table 4 summarizes reasons for a child not being FIC in the study area. Approximately 60 and 17 % of children who were not FIC were missing only one or two vaccines, respectively. The main vaccines missing were OPV 3 (42 %), MV (47 %) and pentavalent 3 (38 %). The above-mentioned reasons are consistently observed in all years where data was available (see Additional file 2: Figure S1a and S1b)

Discussion

This study looks at the levels of coverage of fully immunized children (FIC) by 12 months, timing of

Table 4 Proportion of non-FIC children with missing vaccines by number and type of vaccines among children aged 12–23 months

	2008	2009	2010	2011	2012	2013	2014	Total
	%	%	%	%	%	%	%	%
Number of vaccine missing								
0 (FIC after 12 months)	6.9	6.3	6.1	7.6	7.2	3.5	5.8	6.4
1	58.4	62.1	59.6	55.4	56.9	71.1	70.9	60.6
2	18.0	16.8	19.3	18.5	19.7	11.6	9.3	17.0
3	9.8	4.2	7.9	8.7	6.9	4.6	4.7	7.3
4	4.1	4.2	3.5	3.8	4.3	5.2	2.3	4.1
5	1.9	4.2	2.6	3.3	3.3	2.9	2.3	2.8
6	0.6	0.0	0.9	0.5	0.7	0.0	0.0	0.5
7	0.3	2.1	0.0	2.2	0.7	0.6	4.7	1.1
8	0.0	0.0	0.0	0.0	0.3	0.6	0.0	0.2
Vaccine missing by type								
BCG	4.4	6.3	11.4	9.2	10.9	8.7	2.3	7.9
OPV 1	1.6	2.1	0.0	4.3	1.6	1.2	4.7	2.0
OPV 2	7.3	8.4	10.5	15.2	9.5	8.1	5.8	9.3
OPV 3	50.5	43.2	43.9	51.1	35.5	29.5	32.6	41.8
Penta 1	1.9	4.2	0.0	3.8	3.0	1.7	8.1	2.8
Penta 2	8.5	10.5	8.8	10.9	11.8	9.8	11.6	10.2
Penta 3	38.8	40.0	40.4	37.0	43.4	30.1	32.6	38.3
MV	42.6	46.3	39.5	37.0	46.1	63.0	59.3	46.5
N	317	95	114	184	304	173	86	1273

vaccinations (early and delays) and sequencing of the routine childhood vaccination in children aged 12–23 months in urban informal settlement in Nairobi, Kenya. FIC coverage was estimated at 66.6 %. Individual antigen coverage were above 90 % apart from MV, OPV 3 and pentavalent 3. Overall FIC coverage was shown to depend on postnatal care attendance, education, parity, ethnicity, household wealth status and location. The median age of the different vaccines revealed significant delay in immunization among the non-FIC children compared to FIC children. Proportion of fully immunized children in out-of-sequence (FIC-OS) was estimated at 22 %. FIC-OS differed significantly by postnatal care attendance, delivery place, ethnicity, household wealth status and location. The study highlights main reasons for not being FIC and identifies levels and sources of FIC-OS.

The overall FIC coverage in this study was higher compared to 44 % in a previous study conducted in approximately all informal settlements in Nairobi [10] in 2002. The estimates are similar to (68 %) results obtained from a cross-sectional study targeting approximately all informal settlements in Nairobi [14] conducted in 2012. The FIC coverage in this study still lags behind Nairobi (81 %) and national estimates (79 %) [46]. The increase in FIC coverage (57–68 %) in the study area may be attributed to efforts made by the ministry of health and other stakeholders to improve the uptake of health services and awareness from interventions conducted in the study area, even though more needs to be done to reduce the gap existing between informal settlements and other parts of Nairobi. Increases in immunization coverage have been reported in other low- and middle-income countries over the years [7, 47]. Our results show FIC coverage differed by different background characteristics. FIC coverage was high among mothers who attended postnatal care, and this is expected as their children have more chances of getting the vaccines than those who do not make any follow-up contact with a health centre after delivery. FIC coverage was higher among children of mothers with high education level, resonating with other studies [11, 13, 14, 48]. Mothers with lower parity had higher coverage compared to mothers with higher parity, which has been found in other studies [11, 49]. The more children a mother has the more constraints on the little resources available especially in informal settlements where levels of poverty are high and affect health care utilization [20]. Ethnicity also played a role in determining FIC coverage. FIC coverage was higher among Kamba and Kikuyu ethnic groups compared to other ethnic groups. Similar results were found in other studies done in

Kenya, and this has been linked to cultural differences in addition to education and income disparities among the different ethnicities [11, 14, 34]. FIC coverage was higher among children from households with higher wealth status. This has been documented in other studies done in Kenya [8, 11, 13, 14] and India [48] where health outcomes are better off among the wealthier in the community compared to the less wealthy households. FIC coverage was found to be higher in Viwandani compared to Korogocho study area in line with earlier studies [11]. Viwandani area is next to an industrial area, and residents here are better off than Korogocho residents.

This study showed higher coverage for vaccines given during an infant's early part of life and lower for vaccines given later in life specifically OPV 3, pentavalent 3, PCV 3 and MV. This resonates well with previous findings in the study area [11, 13] and other studies conducted in Burkina Faso, Nigeria and South Africa [33, 36, 37]. The issue of not completing recommended doses of a vaccine is a concern. A child is protected optimally from specific infections if the child received all the three doses. When a dose is skipped, delayed or missed altogether, the child becomes vulnerable from the specific infection and also 'herd' immunity is compromised [50]. The low coverage of MV poses similar concerns. Studies have shown MV and BCG vaccines to be having non-specific beneficial effects on child survival [26–28, 31, 51–58]. The high number of infants missing out on MV vaccines could be missing out on these benefits.

The study showed an initial increase of FIC coverage between 2008 and 2010 followed by a decrease between 2011 and 2014. Further investigation is needed in the study area to understand this scenario. In general, there has been an increase in FIC coverage from the study area compared to similar studies conducted in the current area [10, 11]. Another cross-sectional study conducted in approximately all informal settlements in Nairobi in 2012 showed equivalent FIC coverage [14]. Though this study provides evidence of increase in FIC coverage over the last decade [10], the coverage is still lower in poor urban settlements as compared to estimates from other urban areas and Nairobi in particular [8, 13]. Children missing MV, OPV 3 and pentavalent 3 vaccines were identified by the study as the main reasons of not being fully immunized. Similar observations were made by other studies conducted in other settings [36, 59].

A substantial number of children started their routine immunization much earlier than the recommended age. Similar result has been reported elsewhere in Nigeria, Mozambique and Guinea [37, 60]. Studies have shown that vaccines given more than 4 days earlier than the recommended age may not be optimally effective [24] and one may need to re-vaccinate.

The study established substantial levels of delays in BCG, OPV 3, pentavalent 3 and measles vaccine coverage. This is consistent with other studies in sub-Saharan Africa [37]. The study showed most of the specific vaccines delays were associated with postnatal attendance, ethnicity, education level and delivery place, social economic status and location of the household. These same factors were identified as being associated with being FIC by 12 months of age. Similar results have been found in other studies as determinants of vaccine delays [32, 33, 45, 61, 62].

This study provides evidence of children receiving vaccines in a different sequence than recommended. The main contributor of being FIC-OS was identified as not receiving the pentavalent and corresponding polio dose together. This highlights levels of missed opportunities in immunization programmes as the child had contact with a health care person and was only given one vaccine instead of two. This may be occasioned by vaccine stock-outs.

Overall, the study underscores the importance of a child being fully immunized and getting the vaccines on time and in the correct sequence. The existence of disparities even among the underprivileged in these population have implications that policymakers need to be aware of. The results highlight the simple measures which can be taken to improve on coverage, timing and sequencing of the vaccines. This means that the lower immunization coverage and age-specific vaccination coverage can easily be improved by targeting the disadvantaged groups. Special focus is needed on the uptake of all the three doses for polio, pentavalent and PCV vaccines, at the same time making sure a child is given all the doses that are supposed to be given at the same day when there is contact with a health centre. Ensuring that parents/guardian know the importance of the children receiving all the three doses of the key vaccination will improve not only coverage but also making sure the child has received the vaccine at the right time.

This study was conducted in an urban informal settlement, and therefore, the estimated coverages, levels of delays and out of sequence may only represent similar populations. A major limitation of this study was that we did not see a vaccination card for a large number (62 %) of those recruited during the visits between 12 and 23 months of age and hence they were excluded from the analysis. However, on the positive side, the exclusion eliminated the possibility of introducing recall and survival bias in the analysis. Despite the exclusion, the analysis still included a reasonable sample size. However, excluding children without an observed vaccination card may impact the internal validity of the results within the target population as vaccine coverage among these children may differ in substantial ways from

children with an observed vaccination card. The major strength of the study was the longitudinal nature of the study which gives an opportunity of visiting the respondent several times. This helps in getting better estimate and trend data compared to cross-sectional studies which only give a snapshot of vaccination coverage at a given time.

Conclusions

The study reveals high levels of missed opportunities in the administration of routine childhood vaccinations. A substantial number of children were not fully immunized by the end of their first year of life; even when they are fully immunized, a sizeable number received their vaccines inappropriately, either early, delayed or in a different sequence from the recommended schedule. New strategies are needed to enable health care providers and parents/guardians to work together to increase the levels of completion of all required vaccines. In particular, more focus is needed on measles and vaccines given in multiple doses (polio, pentavalent and pneumococcal conjugate vaccine) to make sure children receive all the three doses. This study contributes to the documentation of patterns of routine immunization uptake in urban poor settlements in Kenya and similar settings.

Additional files

Additional file 1: Table S1. Proportion of fully immunized children by 12 months of age by different background factors. The file lists the vaccination coverage of each antigen by different background characteristics for children aged 12-23 months. (XLSX 14 kb)

Additional file 2: Median age of vaccination. Table S2a: Median age of vaccination (days) among non-FIC children aged 12–23 months. Table S2b: Median age of vaccination (days) among FIC children aged 12–23 months. (XLSX 17 kb)

Additional file 3: Vaccine coverage curves. Figure S1a: Vaccine coverage curves by 12 months among children aged 12–23 months by year of visit and FIC status (2008–2011). Figure S1b: Vaccine coverage curves by 12 months among children aged 12–23 months by year of visit and FIC status (2012–2014). (PDF 117 kb)

Additional file 4: Table S3. Proportion of children aged 12–23 months given vaccines more than 4 (14 for MV) days before the recommended age. The file shows children are receiving their vaccines earlier than recommended ages. (XLSX 10 kb)

Abbreviations

APHRC: African Population and Health Research Center; BCG: Bacillus Calmette-Guerin; FIC: fully immunized child; FIC-OS: fully immunized child in out-of-sequence; KEMRI: Kenya Medical Research Institute; MV: measles vaccine; NSE: non-specific effects; NUHDSS: Nairobi Urban Health Demographic Surveillance System; OPV: oral polio vaccine; PCV: pneumococcal conjugate vaccine.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MKM participated in the overall conceptualization and inception of the idea of this manuscript, with lead roles in conducting literature review, data analysis and writing the results and discussion sections. NN assisted in writing the background section. EK assisted in writing the discussion section. HR assisted in the conceptualization and writing the methods section. EE and PM assisted in the conceptualization of the paper. All the authors read and approved the final manuscript.

Authors' information

MKM is a statistician at African Population and Health Research Center and a PhD Epidemiology student at Jomo Kenyatta University of Agriculture and Technology.
HR is Chief Statistician, Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project and Statens Serum Institut, Denmark, and an Associate Professor, University of Southern Denmark.
NN is a Research Officer at African Population and Health Research Center.
EK is a Research Scientist at African Population and Health Research Center.
EE is a Senior Researcher, Centre for Public Health Research (CPHR), KEMRI.
PM is a Senior Lecturer at Jomo Kenyatta University of Agriculture and Technology.

Acknowledgements

Projects which contributed data: Urbanization, Poverty, and Health Dynamics (UPHD) research project funded by the Wellcome Trust (Grant Number GR 07830 M) and monitoring and assessing the impact of immunization and other childhood interventions for both boys and girls, an INDEPTH Network collaboration project funded by the Danish Development Agency (DANIDA) (DFC Project no 09-09-105SSI). This research was also made possible through the generous core funding for the NUHDSS by the Bill and Melinda Gates Foundation (Grant# OPP1021893) and core funding for APHRC by The William and Flora Hewlett Foundation (Grant# 2009–40510) and the Swedish International Cooperation Agency (SIDA) (Grant# 2011–001578). The authors are also highly indebted to the data collection team led by Peterrock Muriuki and the study participants.

Author details

[1]African Population and Health Research Center, Manga Close, Nairobi, Kenya. [2]Research Center for Vitamins and Vaccines, 5 Artillerivej, Copenhagen, Denmark. [3]Centre for Public Health Research, Kenya Medical Research Institute, Nairobi, Kenya. [4]Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya. [5]Bandim Health Project, Statens Serum Institut, 5 Artillerivej, Copenhagen, Denmark. [6]OPEN, University of Southern Denmark/Odense University Hospital, Odense, Denmark. [7]International Health Institute, Brown University, Providence, RI, USA.

Received: 19 November 2015 Accepted: 15 April 2016
Published online: 16 May 2016

References

1. World Health Organization. United Nations Children's Fund (UNICEF). 2008. Global Immunization Data.
2. United Nations. Sustainable Development Goals. 2015.
3. World Health Organization. Global immunization data. 2014.
4. Global Polio Eradication Initiative. Polio eradication and endgame strategic plan (2013–2018). Geneva: World Health Organization, Global Polio Eradication Initiative; 2013. p. 2013.
5. World Health Organization. WHO Recommendations for Routine Immunization. 2013.
6. Moszynski P. A pneumococcal vaccine is launched in Africa to cut child deaths. BMJ. 2011;342.
7. World Health Organization. Global vaccine action plan 2011–2020. 2011.
8. Kenya National Bureau of Statistics, Ministry of Health, National AIDS Control Council, Kenya Medical Research Institute and National Council for Population and Development. Kenya demographic and health survey 2014. 2014. Key Indicators Report.
9. Pande RP, Yazbeck AS. What's in a country average? Wealth, gender, and regional inequalities in immunization in India. Soc Sci Med. 2003;57:2075–88.
10. African Population and Health Research Center. Population and health dynamics in Nairobi's informal settlements: report of the Nairobi Cross-

sectional Slums Survey (NCSS) 2000. Nairobi, Kenya: African Population and Health Research Center, 2002
11. Mutua MK, Kimani-Murage E, Ettarh R. Childhood vaccination in informal urban settlements in Nairobi, Kenya: who gets vaccinated? BMC Public Health. 2011;11:6.
12. African Population and Health Research Center (APHRC). Population and health dynamics in Nairobi's informal settlements report of the Nairobi Cross-sectional Slums Survey (NCSS) 2012. Nairobi: African Population and Health Research Center; 2014.
13. Kenya National Bureau of Statistics, ICF Macro. Kenya demographic and health survey 2008–09. 2010.
14. Egondi T, Oyolola M, Mutua MK, Elung'ata P. Determinants of immunization inequality among urban poor children: evidence from Nairobi's informal settlements. International J Equity in Health. 2015;14:24.
15. Mberu BU, Ciera JM, Elungata P, Ezeh AC. Patterns and determinants of poverty transitions among poor urban households in Nairobi, Kenya. African Development Review. 2014;26:172–85.
16. Emina J, Beguy D, Zulu E, et al. Monitoring of health and demographic outcomes in poor urban settlements: evidence from the Nairobi Urban Health and Demographic Surveillance System. J Urban Health. 2011;88 Suppl 2:S200–18.
17. Rosenthal J, Rodewald L, McCauley M, et al. Immunization coverage levels among 19- to 35-month-Old children in 4 diverse, medically underserved areas of the United States. Pediatrics. 2004;113:e296–302.
18. Santoli JM, Setia S, Rodewald LE, O'Mara D, Gallo B, Brink E. Immunization pockets of need: science and practice. Am J Prev Med. 2000;19:89–98.
19. Heininger U, Stehr K, Cherry J. Serious pertussis overlooked in infants. Eur J Pediatr. 1992;151:342–3.
20. Ndiritu M, Cowgill KD, Ismail A, et al. Immunization coverage and risk factors for failure to immunize within the Expanded Programme on Immunization in Kenya after introduction of new Haemophilus influenzae type b and hepatitis b virus antigens. BMC Public Health. 2006;6:132.
21. Heininger U, Zuberbühler M. Immunization rates and timely administration in pre-school and school-aged children. Eur J Pediatr. 2006;165:124–9.
22. European Centre for Disease Prevention and Control (ECDC). Scientific panel on childhood immunisation schedule: Diphtheria-tetanus-pertussis (DTP) vaccination, ECDC Guidance, Stockholm, Sweden, 2009 [cited 12 November, 2015]. Available from http://ecdc.europa.eu/en/publications/Publications/0911_GUI_Scientific_Panel_on_Childhood_Immunisation_DTP.pdf.
23. National Vaccine Advisory Committee. Standards for child and adolescent immunization practices. Pediatrics. 2003;112:958–63.
24. Kroger A, Sumaya C, Pickering L, Atkinson W, Centers of Disease Control and Prevention. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recommendations Report. 2012;60:3–60.2011.
25. Mutua MK, Ochako R, Ettarh R, Ravn H, Echoka E, Mwaniki P. Effects of low birth weight on time to BCG vaccination in an urban poor settlement in Nairobi, Kenya: an observational cohort study. BMC Pediatr. 2015;15:45.
26. Kabir Z, Aaby P. Non-specific effect of measles vaccination on all-cause child mortality: revisited. Indian Pediatr. 2005;42:541–4.
27. Roth A, Gustafson P, Nhaga A, et al. BCG vaccination scar associated with better childhood survival in Guinea-Bissau. Int J Epidemiol. 2005;34:540–7.
28. Veirum J, Sodemann M, Biai S, et al. Diphtheria-tetanus-pertussis and measles vaccinations associated with divergent effects on female and male mortality at the paediatric ward in Bissau, Guinea-Bissau. Vaccine. 2005;23:1197–204.
29. Aaby P, Ibrahim SA, Libman MD, Jensen H. The sequence of vaccinations and increased female mortality after high-titre measles vaccine: trials from rural Sudan and Kinshasa. Vaccine. 2006;24:2764–71.
30. Benn CS, Aaby P. Diphtheria-tetanus-pertussis vaccination administered after measles vaccine: increased female mortality? Pediatr Infect Dis J. 2012;31:1095–7.
31. Welaga P, Nielsen J, Adjuik M, et al. Non-specific effects of diphtheria-tetanus-pertussis and measles vaccinations? An analysis of surveillance data from Navrongo, Ghana. Trop Med Int Health. 2012;17:1492–505.
32. Gram L, Soremekun S, ten Asbroek A, et al. Socio-economic determinants and inequities in coverage and timeliness of early childhood immunisation in rural Ghana. Trop Med Int Health. 2014;19:802–11.
33. Schoeps A, Ouedraogo N, Kagone M, Sié A, Müller O, Becher H. Socio-demographic determinants of timely adherence to BCG, penta3, measles, and complete vaccination schedule in Burkina Faso. Vaccine. 2013;32:96–102.
34. Ettarh R, Mutua MK, Kyobutungi C. Ethnicity and delay in measles vaccination in a Nairobi slum. Tropical Med Health. 2012;40:59–62.
35. Laryea DO, Parbie EA, Frimpong E. Timeliness of childhood vaccine uptake among children attending a tertiary health service facility-based immunisation clinic in Ghana. BMC Public Health. 2014;14:90.
36. Fadnes LT, Jackson D, Engebretsen IM, et al. Vaccination coverage and timeliness in three South African areas: a prospective study. BMC Public Health. 2011;11:404.
37. Sadoh AE, Eregie CO. Timeliness and completion rate of immunization among Nigerian children attending a clinic-based immunization service. J Health Popul Nutr. 2009;27:391–5.
38. Clark A, Sanderson C. Timing of children's vaccinations in 45 low-income and middle-income countries: an analysis of survey data. Lancet. 2009;373:1543–9.
39. Beguy D, Elung'ata P, Mberu B, et al. Health & Demographic Surveillance System Profile: The Nairobi Urban Health and Demographic Surveillance System (NUHDSS). Int J Epidemiol. 2015;44:462–71.
40. Kroger AT, Atkinson WL, Marcuse EK, Pickering LK. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep Recomm Rep. 2006;55:1–47.
41. Manning S, Rupprecht C, Fishbein D, et al. Advisory Committee on Immunization Practices Centers for Disease Control and Prevention (CDC). Human rabies prevention—United States, 2008: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2008;57:1–28
42. Hull BP, McIntyre PB. Timeliness of childhood immunisation in Australia. Vaccine. 2006;24:4403–8.
43. Akmatov MK, Mikolajczyk RT. Timeliness of childhood vaccinations in 31 low and middle-income countries. J Epidemiol Community Health. 2012;66:e14–4.
44. Hornshøj L, Benn CS, Fernandes M, Rodrigues A, Aaby P, Fisker AB. Vaccination coverage and out-of-sequence vaccinations in rural Guinea-Bissau: an observational cohort study. BMJ open. 2012;2:e001509.
45. Ouédraogo N, Kagoné M, Sié A, Becher H, Müller O. Timeliness and out-of-sequence vaccination among young children in Burkina Faso--analysis of health and Demographic Surveillance System (HDSS) data. 2013.
46. Kenya National Bureau of Statistics, ICF Macro. Kenya demographic and health survey 2014. 2015.
47. World Health Organization, United Nations Children's Fund, Expanding Immunization Coverage. 2011 [cited 10 November, 2015]. Available from http://www.unicef.org/immunization/index_coverage.html.
48. Lauridsen J, Pradhan J. Socio-economic inequality of immunization coverage in India. Health Econ Rev. 2011;1:11.
49. Rahman M, Obaida-Nasrin S. Factors affecting acceptance of complete immunization coverage of children under five years in rural Bangladesh. Salud Publica Mex. 2010;52:134–40.
50. Fine PE. Herd immunity: history, theory, practice. Epidemiol Rev. 1993;15:265–302.
51. Benn CS, Fisker AB, Rodrigues A, et al. Sex-differential effect on infant mortality of oral polio vaccine administered with BCG at birth in Guinea-Bissau. A natural experiment. PLoS One. 2008;3:e4056.
52. Shann F, Nohynek H, Scott JA, Hesseling A, Flanagan KL and Working Group on Nonspecific Effects of V. Randomized trials to study the nonspecific effects of vaccines in children in low-income countries. Pediatr Infect Dis J. 2010;29:457–61.
53. Roth AE, Benn CS, Ravn H, et al. Effect of revaccination with BCG in early childhood on mortality: randomised trial in Guinea-Bissau. Br Med J. 2010;340:c671.
54. Moulton LH, Rahmathullah L, Halsey NA, Thulasiraj R, Katz J, Tielsch JM. Evaluation of non-specific effects of infant immunizations on early infant mortality in a southern Indian population. Trop Med Int Health. 2005;10:947–55.
55. Lehmann D, Vail J, Firth MJ, de Klerk NH, Alpers MP. Benefits of routine immunizations on childhood survival in Tari, Southern Highlands Province, Papua New Guinea. Int J Epidemiol. 2005;34:138–48.
56. Kristensen I, Aaby P, Jensen H. Routine vaccinations and child survival: follow up study in Guinea-Bissau, West Africa. Br Med J. 2000;321:1435–8.
57. Holt EA, Moulton LH, Siberry GK, Halsey NA. Differential mortality by measles vaccine titer and sex. J Infect Dis. 1993;168:1087–96.
58. Sankoh O, Welaga P, Debpuur C, et al. The non-specific effects of vaccines and other childhood interventions: the contribution of INDEPTH Health and Demographic Surveillance Systems. Int J Epidemiol 2014;43:645-53

59. Fadnes LT, Nankabirwa V, Sommerfelt H, et al. Is vaccination coverage a good indicator of age-appropriate vaccination? A prospective study from Uganda. Vaccine. 2011;29:3564–70.
60. Cutts F, Zell E, Soares A, Diallo S. Obstacles to achieving immunization for all 2000: missed immunization opportunities and inappropriately timed immunization. J Trop Pediatr. 1991;37:153–8.
61. Canavan ME, Sipsma HL, Kassie GM, Bradley EH. Correlates of complete childhood vaccination in East African countries. PLoS One. 2014;9:e95709.
62. Calhoun LM, van Eijk AM, Lindblade KA, et al. Determinants and coverage of vaccination in children in western Kenya from a 2003 cross-sectional survey. Am J Trop Med Hyg. 2014;90:234–41.