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Factors associated with pneumococcal conjugate and rotavirus vaccines uptake among infants: Evidence from the Africa Centre Demographic Surveillance Site, South Africa, 2008-2011

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University of Witwatersrand,

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of

Master of Science

in

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Declaration

I, ***Georgina Badu-Gyan***, declare that this is my own work. It is being submitted for the degree of Master of Science in Epidemiology in the field of Population-Based Field Epidemiology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

Signature: 

Full Name: Georgina Badu-Gyan

Date: 03 Day of July, 2013

Dedication

I dedicate this work to my lovely family, Badu-Gyan family, for their prayers and support throughout my stay away from home; especially to my lovely mom Vida Donkor for her encouragement throughout my university education till now.

I also dedicate this work to my uncle Dr. Seth Owusu-Adjei for his support and for instilling a sense of confidence in me.

Lastly, I dedicate my MSc to my lovely fiancé Philip Amankwah for his support and words of encouragement during my stay at Wits.

Abstract

Introduction: Despite advances in prevention and treatment of vaccine-preventable diseases, diarrhoeal and pneumococcal diseases remain a major source of morbidity and mortality among children worldwide. The introduction of vaccines has led to dramatic reductions in the burden of infectious diseases and mortality among children. South Africa was the first country in Africa to introduce rotavirus vaccine (RV) and pneumococcal conjugate vaccine (PCV) in 2008 as part of its national immunisation programme. Performance of immunization programmes is commonly measured by the coverage and uptake of vaccines, hence ensuring that every child is immunized at the earliest or appropriate age is an important public health goal. We therefore assessed proportions and factors associated with uptake of RV and PCV among infants who were followed during the routine demographic surveillance system of the Africa Centre Demographic Surveillance Area (DSA) in a rural South Africa setting.

Methods: An open cohort of children resident in the DSA aged 12 months or below was prospectively followed between January 2008 and December 2011. Trained interviewers visited households and administered a standardised questionnaire. Mothers and caregivers were asked to show the interviewers the South African Road-To-Health (RTH) card for all children aged 12-23 months at the time of the visit or through maternal recall for children whose RTH card was not available. The RTH card includes dates of all routine vaccinations a child has received. Rotavirus vaccine doses are given at 6 and 14 weeks of age and PCV doses at 6 and 14 weeks and 9 months. Complete uptake was defined as “complete” if a child received all recommended doses of either RV or PCV and incomplete if a child did not receive any dose or received one dose of RV or PCV. Logistic regression

models were used to assess factors associated with uptake of RV and PCV separately.

Results: A total of 6,263 children were included in the analysis, of which 3,082 (49%) were females. At birth, 3,823 (61%) children were living in rural areas and about one-sixth of the children were living in households located far from a health facility (≥5km). The overall uptake of RV and PCV vaccines among children aged 12 months or below was 50% and 37% respectively. Infants who ever migrated outside the DSA had reduced odds of complete RV and PCV vaccination compared to infants who did not out migrate (adjusted OR=0.49, 95% CI 0.41-0.57) and (adjusted OR=0.52, 95% CI 0.43-0.63) respectively. Complete uptake of RV was associated with the increase in education levels of mothers compared secondary education (adjusted OR=1.70, 95 % CI 1.02-2.34) or tertiary education (adjusted OR=1.80, 95 % CI 0.97-2.44). Infants whose mothers were employed were less likely than infants whose mothers were not employed to have complete vaccination for RV or PCV (adjusted OR=0.71, 95 % CI 0.60-0.84) and (adjusted OR=0.81, 95% CI 0.68-0.96) respectively. Similarly, infants whose mothers were resident in the DSA were more likely than infants whose mothers were not resident to have complete vaccination for RV or PCV (adjusted OR=1.97, 95 % CI 1.49-2.60) and (adjusted OR=1.55, 95% CI 1.16-2.08) respectively.

Conclusion and recommendation: The uptake of complete RV and PCV were generally low among children in rural South Africa within our study period. Child outmigration, maternal employment, maternal education and maternal residency in the DSA at child birth were associated with complete uptake of RV and PCV vaccines. Programmes targeting mothers of lower socio-economic status are required. Such programmes may include vaccine awareness and immunization

campaigns at the community level to improve vaccine uptake and more targeted interventions in areas with low RV and PCV uptake.

Keywords: infant; rotavirus, pneumococcal conjugate, vaccine uptake, South Africa

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Definition of terminologies

Cohort: A group of people sharing a common temporal demographic experience who are observed through time.

Demographic Surveillance System (DSS): A set of field and computing operations to handle the longitudinal follow-up of well-defined entities or primary subjects (individuals, households, and residential units) and all related demographic and health outcomes within a clearly circumscribed geographic area.

Demographic Surveillance Area (DSA): The catchment area of a Health and Demographic Surveillance System.

Household: A social group of one or more individual members eating from the same pot. They are usually but not always related biologically or by blood.

Vaccine: A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters (WHO definition).

Vaccination uptake: Number of routine doses of a vaccine administered to a child. In this study, the vaccines considered are Rotavirus and Pneumococcal conjugate vaccine.

Risk factor: An aspect of personal behaviour or lifestyle, environmental exposure, or inborn or inherited characteristic which, on the basis of epidemiologic evidence, is known to be associated with a health-related condition considered important to

prevent (WHO definition). In this study, the risk factors considered are the socio-economic and demographic characteristics of infants and their mothers.

Socioeconomic status (SES): A classification of the social group of an individual based on his/her assets, type of residence and utilities.

Verbal Autopsy: A systematic process of soliciting information from a close relative, friend or caretaker who was present either during the illness that led to death or the circumstances that led to the death of the person to be able to assign cause of death where medical certification of cause of death is not available

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List of Abbreviations and Acronyms

ACDIS	Africa Centre Demographic Information System
ART	Antiretroviral Therapy
ARTmis	ART Evaluation and Monitoring System
CHF	Child Health Form
DSA	Demographic Surveillance Area
EPI	Expanded Programme on Immunization
EPI-SA	Expanded Programme on Immunization-South Africa
GAVI	Global Alliance for Vaccines and Immunisation
IPD	Invasive Pneumococcal Disease
PCV	Pneumococcal Conjugate vaccine
RV	Rotavirus vaccine
RTH	Road-to-health
UNICEF	United Nations International Children's Emergency Fund
WHO	World Health Organisation

Chapter 1: Introduction

1.1 Background

The advent of vaccines has led to dramatic reductions in the burden of infectious diseases and mortality among children worldwide (1). Recently**,** vaccination has been shown to be one of the most cost-effective health interventions worldwide, through which a number of serious childhood diseases have been successfully prevented or eradicated (2). No other undertaking, not even the development of antibiotics, has had as much impact in lowering mortality among children globally (3). These achievements have been accomplished mainly with vaccines delivered through a global system, the Expanded Programme on Immunization (EPI), which has received sustained support for more than 30 years from national governments, donor organisations, and international agencies such as the United Nations International Children's Emergency Fund (UNICEF) and World Health Organisation (WHO) (4). The EPI was introduced by the WHO and UNICEF in 1974 with the aim of vaccinating all children below the age of one year against the six killer diseases namely diphtheria, polio, tetanus, tuberculosis, measles and whooping cough (5). After the introduction of the EPI, new vaccines against other severe diseases have been developed. However, diseases such as *Streptococcus pneumonia*, diarrhoea, meningitis, and measles, which are currently preventable by vaccination, still account for about 25% of child deaths in low-income countries (4).

The Expanded Programme on Immunisation South Africa (EPI-SA) was Introduced in 1995 and initially covered only the six diseases (6). The mission of

the EPI-SA is to reach and protect all targeted children in South Africa with safe high-quality vaccines that are delivered to the recipient with recent technology whilst promoting and developing local capacity and skills (7). Specifically the programme aimed at reaching a full immunisation coverage of 90% for children under one year of age in 90% of the districts by the end of 2009 (7). The EPI-SA has made significant progress in the control of vaccine-preventable diseases. South Africa has been declared free of wild poliovirus (8). The number of measles cases per year dropped from an average of 22,000 to 38 cases between 1992 and 2012 (9). Haemophilus influenzae type b (Hib) cases have been markedly reduced and maternal and neonatal tetanus has been eliminated (7). Review of coverage data indicates a progressive increase in the routine coverage from 2000 to 2006, with 84% fully immunised coverage recorded at national level in 2006 (7). Currently, efforts of the immunisation programme are directed at maintaining a high routine coverage and improving the quality of routine data.

With an increasing global burden of rotavirus and pneumococcal diseases, vaccine introduction has been a high priority for several international agencies, including the WHO and the GAVI Alliance. *Streptococcus pneumonia* and diarrhoeal are the leading causes of mortality and morbidity among infants and young children in the developing countries (10). The availability of RV and PCV has attracted great attention because of their potential to have significant impact on diarrhoea and *Streptococcus pneumonia* morbidity and mortality respectively. South Africa introduced RV and PCV in its EPI in 2008 which was a significant step towards achieving the MDG4 (11). South Africa was in the fortunate position

to be able to include many of these new options into its national EPI and adjust the EPI schedule according to the disease epidemiology of the country. By 2009, under EPI RV and PCV were provided free of charge at public health facilities in South Africa.

Rotavirus vaccine is a vaccine which protects infants and young children against severe diarrhoeal diseases and PCV is a pneumococcal vaccine used to protect infants and young children against *Streptococcus pneumonia* caused by the bacterium *Streptococcus pneumonia* Rotavirus vaccine doses are given at 6 and 14 weeks of age and PCV doses at 6 and 14 weeks and at 9 months. *Streptococcus pneumonia* is an important pathogen causing invasive diseases such as sepsis, meningitis, and pneumonia. The burden of disease is highest in the youngest and oldest group of people in both more or less developed countries. According to the WHO data published in April 2011, influenza and *Streptococcus pneumonia* deaths reached 52,985 and diarrhoeal diseases deaths reached 35,567 of total deaths in South Africa.

The WHO strongly recommends all infants and children receive routine immunizations at the scheduled time. Performance of immunization programmes is commonly measured by the coverage and uptake of vaccines. Thus ensuring that every child is immunized at the earliest or appropriate age is an important public health goal (12). The South African Department of Health provides free RV and PCV to all infants and children up to nine months from time of birth thereby providing infants and children with additional protection from *Streptococcus pneumonia* and diarrhoeal disease. Despite these efforts, many children do not

receive their vaccinations. Even in areas with high vaccination coverage there are groups of children, who are either not immunised or not completely immunised and therefore these children are at a high risk of pneumococcal and diarrhoeal diseases. The South African Department of Health reported low coverage and vaccine shortages in many health facilities after the introduction of RV and PCV (13). With the introduction of new vaccines in developing countries, assessing vaccine uptake and coverage will become an increasingly critical component of public health. Therefore the introduction of RV and PCV into the immunisation programme of industrialising countries such as South Africa, require robust surveillance to evaluate the uptake of the vaccines in such settings like the DSA which have a routine longitudinal data on child immunisations.

1.2 Problem Statement

Streptococcus pneumonia and diarrheal diseases are the causes of childhood illness and deaths globally. Introduction of RV and PCV have had a significant impact in reducing the incidence of pneumococcal and diarrheal diseases, as well as a reduction in hospitalizations and mortality among children. Monitoring the uptake of these vaccines remains one of the key public health challenges. Clinical studies have demonstrated efficacy and safety of RV and PCV (14, 15) in Africa, but there is inadequate data on the uptake of RV and PCV in resource-poor settings since their introduction. To date, there is no study conducted using a longitudinal demographic data to assess the uptake of RV and PCV in an African setting. The availability of Africa Centre demographic surveillance data will provide an opportunity to adequately assess the uptake and coverage of RV

and PCV in this setting and also share best practices leant in the implementation of the programme.

1.3 Justification of the study

Child vaccinations are the most cost-effective public health interventions. Nonetheless, uptake of vaccines in developing countries is still low compared to developed countries, leading to deaths among children which could otherwise be prevented. Vaccine uptake has been shown to be mainly hindered by difficulty in assessing primary care, transport requirements and by user characteristics, such as parental education, birth order, household structure and socioeconomic status. Assessing RV and PCV uptake would allow closer follow-up and more targeted interventions in areas with low vaccine uptake and coverage, thus improving infant health outcomes. Furthermore, the results from this study may offer additional findings to develop a strong base for policy framework and implementation of comprehensive vaccination activities in EPI-SA.

1.4 Literature Review

Child vaccination has been shown to be one of the most important public health interventions to date (16). Nevertheless, child vaccination coverage and uptake is still far from universal, especially in developing countries, leading to preventable deaths among infants and children. Between 2000 and 2007, child deaths from measles reduced by an estimated 74% globally and 89% in Africa, polio which is a major cause of disability and mortality among children is now close to eradication (17). This success is attributed to the EPI which has seen rapid scale up of routine immunizations.

The leading causes of childhood illness and deaths globally are *Streptococcus pneumonia* and diarrheal diseases (18). *Streptococcus pneumonia* and rotavirus are two of the most important vaccine-preventable pathogens which together are responsible for over 2 million annual deaths among children less than 5 years of age globally (19-21).

Despite the fact that studies on vaccination coverage are well documented, uptake and coverage of the newly introduced vaccines remain unclear. The objective of this chapter therefore is to review relevant literature with the aim of identifying and critiquing the most important issues involved in RV and PCV uptake among infants.

1.4.1 Pneumococcal conjugate vaccine uptake

PCV has had a significant impact in reducing the incidence of pneumococcal disease as well as the associated morbidity and mortality. *Streptococcus pneumonia* represents the single most significant cause of deaths in children under the age of 5 years globally, accounting for about 2 million childhood deaths annually (22). Due to the high burden of childhood pneumococcal diseases in developing countries, there have been global efforts to expand access to pneumococcal vaccines in these countries. According to a study conducted in the United States between 2001 and 2004, the percent of children who received PCV increased with time however, less than half of the children received their immunizations according to the recommended schedule (23). Similarly, one prevalence study conducted in Spain in 2005 reported PCV vaccine uptake among children aged less than five years was only 33% (24). The authors concluded that there were dramatic reductions in Invasive Pneumococcal

Disease (IPD) from direct and indirect vaccine effects due to the few children who had received the recommended complete vaccine schedule.

Streptococcus pneumonia remains a leading cause of childhood death in South Africa, aggravated by the HIV/AIDS epidemic (25). In 2010, the South Africa Department of Health, estimated that the national coverage for the third dose of PCV was 61% with only four provinces having a coverage of 70% and above (13). In the same report, Gauteng province was the only province which had 86% coverage of PCV third dose and this was however still low compared to the national target of 90% coverage.

Studies conducted in the developed countries showed that uptake of PCV vaccines were high soon after their introduction. In United States of America and Canada, the uptake of PCV was more than 80% less than one year after newly introducing them (26, 27). However, studies conducted in the developing countries, have shown the uptake of PCV is still low. Previous studies conducted in Asia and Pacific countries showed that PCV uptake in Korea and Singapore which are both regarded as developed countries were 65% and 60% respectively in 2010. However, in the same study, the rate of PCV uptake in Taiwan was around 30% and less than 10% in other countries (28). One possible explanation for the low uptake of PCV in the developing countries could be due to low levels of funding assigned to these vaccines and the type of health services in these settings compared to developed countries. The low levels of PCV uptake in the developing countries leave the majority of the infants and children at risk of invasive pneumococcal disease (IPD).

A meta-analysis review conducted in developing countries across Asia and Africa supported the effectiveness of PCV in reducing *Streptococcus pneumonia* mortality by 36% among infants and children (29) in high mortality countries. An evaluation based on large efficacy trials in the USA after the introduction of PCV, showed that the vaccine reduced pneumococcal disease among unvaccinated members in the community in addition to the direct effect of PCV upon invasive pneumococcal disease in vaccinated children (30-32). In Gambia, a recent result from a clinical trial of 17,437 children aged 6-51 weeks showed that children immunized with the 9-valent vaccine of PCV had 37 percent fewer cases of *Streptococcus pneumonia*, 15 percent fewer hospitalizations and a 16 percent reduction in overall mortality. The study further concluded that PCV is efficacious against IPD (33). These findings were similar to other findings from the USA (14, 34) and South Africa (35).

In addition to preventing a greater than expected burden of invasive disease, the vaccine has also been associated with marked reduction in pneumococcal disease among unvaccinated members of the population (36).

1.4.2 Rotavirus vaccine uptake

Rotavirus is the most important cause of severe diarrhoeal diseases and dehydration among children worldwide and continues to have a major global impact on childhood morbidity and mortality (37). In 2009, WHO estimated that globally 527,000 deaths occurred among children and the majority (>85%) in developing countries of Asia and Africa. Close to a quarter million deaths due to rotavirus infection occurred in sub-Saharan Africa in 2009 (38-40).

Previous studies have shown that approximately six children die a day from severe rotavirus gastroenteritis in South Africa (41, 42). Diarrhoeal diseases are ranked the third major cause of childhood mortality in children <5 years and the majority of these deaths are among black African children in South Africa (43).
Since the introduction of RV in EPI-SA, RV coverage has increased rapidly. Currently, the RV uptake varies from province to province. In 2010, 67% of the children aged less than one year had received a complete 2-dose series of RV and 80% received at least one dose (44) which is still low compared to the national target of 90% coverage.

A study conducted in the United States between 2007 and 2008 estimated that the uptake of RV among infants, children aged one year and children aged 2 and 4 years were 57%,17% and 0% respectively (45). One possible explanation for the differences in rotavirus uptake among these children in the US regions suggested by the authors was due to the direct protection of the youngest vaccinated children compared to the older children.

In Germany, a previous study showed that the uptake of RV was slightly above 50% in children aged between 6 and 23 months in five eastern federal states and it was slightly above 20% in the 11 western states (46). Similarly, in Brazil a study showed that the administrative coverage with the two-dose series of RV ranged from 80 to 84% compared to the six recommended infant immunizations which were around 95 to 99% (47). The authors reported that RV coverage was steadily increasing but remained lower than coverage levels of other routine infant immunizations.

Previous studies conducted in Asia and Pacific countries indicated that the uptake for RV were approximately 50% in Singapore, 30% in Korea and Taiwan, and lower than 10% in other countries in 2010 (28). Generally, uptake of newly developed vaccines such as RV and PCV are low in developing countries and it is estimated that more than half of the children hospitalized in these areas for diarrhoea are infected with rotavirus (48).

1.4.3 Factors associated with uptake of vaccinations

To improve vaccine uptake and implement appropriate interventions, factors influencing the immunization status of children should be identified and addressed.

In general, vaccination uptake is not uniform across populations, but varies among different sociodemographic, political, ethnic and cultural groups. Previous studies which have assessed the risk factors associated with uptake of different vaccines have shown different results (49-54). Some of the factors include maternal age, maternal education, distance to health facility, migrations, maternal HIV status and other demographic factors.

Maternal HIV Status

A previous study conducted in the rural South Africa in 2009 showed that positive maternal HIV status independently reduced children's probability to receive child vaccinations (50). Similarly, a cross-sectional study conducted among pregnant women in Rakai, Uganda, showed that children born to HIV-infected mothers were significantly less likely to be vaccinated (55). The study further concluded

that maternal HIV-infection was associated with childhood under-immunisation and this was mediated by a mother's knowledge of her HIV status.

Maternal Education

Maternal education remains statistically significant for children's immunization status in most countries even after individual-level and community-level controls are introduced (56). It has been shown that improving female education can improve vaccination uptake. A study conducted in Nigeria showed that children aged between 12 and 24 months whose mothers had at least secondary education were more likely to complete immunization (57). The authors of the study concluded that improving female education in rural locations can improve immunization uptake. This result is in consistency with another study conducted in both rural and urban Ethiopia which also found similar findings (58). Yadlapalli et al in their study also concluded that the likelihood of a child receiving full immunization rose with maternal educational attainment and the frequency of her use of health care (59).

Distance to health care facility

Improving access to childhood vaccines in low-income countries has been a major goal of public health services both at international and national levels (60). A key factor in the reduction of child mortality and the promotion of child health is universal accessibility of health-care services which is determined by many different factors including travel distance (61). Studies conducted in rural western Kenya and Papua New Guinea have showed that long distance to health facilities significantly reduced the use of health services by the population (62-64). Findings from a study conducted in 2006 in East Harlem and the Bronx in

New York City, showed that participants who were isolated from the health care service were less likely to have been vaccinated in the past (65). In a cross-sectional study conducted in 2012 among children aged between 12 and 59 months, travel time to vaccine providers in health posts appeared to be a barrier to the delivery of infant vaccines in a remote Ethiopian community (66).

Migration

Migration has been shown as one of the behavioural processes affecting immunization uptake and had been shown as an important determinant of child immunization uptake (63). The main barriers of immunisation identified among children of migrant workers from Myanmar living in Tak province, Thailand in the year 2009 included the continued migration among mothers (67). The findings of previous research in rural and urban Gambia among mothers conducted in 2004 identified mothers whose children did not complete their vaccination schedules as recent immigrant mothers (68).

Similarly, another study conducted in Delhi, India among rural–urban migrant mothers with a child aged up to 2 years found immunization coverage rates were lower among migrant children and even lower among recent migrants. The authors concluded that migrant status favoured low immunization uptake (59).

Demographic factors

A study conducted in India showed inequality in immunization among child sex within-household, which indicated that immunization scores of girls were significantly lower than that of boys (69). Similar findings have been reported in other studies, which showed that boys had higher immunization rates compared to girls although the extent of this difference varied by state (70).

Maternal age has been found to play an important role in predicting child health in both developed and developing countries (71). In the United States, maternal age was an important factor in explaining variations in up-to-date vaccinations coverage among children aged between 19 and 35 months of age. The study showed children with a mother aged 17 and 24 years had 69% coverage compared with 79% coverage among children whose mothers were 25 years or older (72).

1.5 Aims and objectives of the study

The main aim of the study was to assess uptake of RV and PCV among infants and to examine factors associated with RV and PCV uptake in the DSA, KwaZulu-Natal South Africa between January 2008 and December 2011.

1.5.1 Specific objectives

1. To describe baseline characteristics of the infants receiving RV and PCV in the DSA, between January 2008 and December 2011.

2. To assess vaccination uptake of RV and PCV among infants in the DSA, between January 2008 and December 2011.

3. To describe geographic variations in the uptake of RV and PCV among infants in the DSA.

4. To assess factors associated with the uptake of RV and PCV vaccines among infants in the DSA.

1.6 Outline of the research report

This report is organized into five chapters. The second chapter is methodology which provides a brief description of the study settings, study design, study population, data collection and statistical analysis. Chapter Three presents the study results. Chapter Four is discussion of the study results. Finally, chapter Five is the conclusion of the results as well as remarks and policy recommendations based on the study findings.

Chapter 2: Methods

2.1 Background

This chapter describes the study design, study setting, study population, study sample size, data collection, and description of study variables and data analysis.

2.2 Study design

This study was a secondary data analysis based on a prospective quantitative cohort study conducted from data longitudinally collected from the Africa Centre household surveillance from January 2008 to December 2011.

2.3 Study Setting

The study was conducted at the Africa Centre Demographic Surveillance Area which is located near the market town of Mtubatuba in the uMkhanyakude District of northern KwaZulu-Natal, South Africa. The area includes a formally urban township, peri-urban areas and rural areas. All homesteads in the study area have been mapped by fieldworkers using differential global positioning system (GPS) and homesteads database is continuously updated (73). In the sub-district, the health service infrastructure comprises a central community hospital, 16 fixed clinics and 31 mobile clinics points. The mobile clinics offer childhood vaccination in addition to family planning advice and antenatal care. The study utilized data collected as part of the DSA household surveillance. The Africa Centre household surveillance involved twice (since 2012 three times)-

yearly visits to all households in the surveillance area and an interview with a senior household member recording vital events including vaccinations (74).

2.4 Study population and study size

The study population comprised children aged 12 months old or below who were residents of the DSA between January 2008 to December 2011. During the study period; there were 6,272 children in the cohort. The study utilized only the relevant records which met the inclusion criteria during the study period.

2.4.1 Inclusion criteria

1. Children aged 6 weeks to 12 months old.
2. Children residents in the DSA during the study period.
3. Children whose mothers or caregivers were registered in the DSA at the time of their birth from January 2008 to December 2011.
4. Children with vaccination information from a RTH card or maternal recall if card were not available.

2.4.2 Exclusion criteria

1. Children with missing vaccination information.
2. Children who died before 6 weeks of birth.

2.5 Measurement of outcome and exposure variables

2.5.1 Outcome variables

The main outcome variables in the study were complete RV and PCV uptake. These variables were defined as described below.

Vaccination uptake was defined as the number of routine doses of either RV or PCV administered to a child within 12 months of birth from January 2008 to December 2011.

Rotavirus vaccine uptake was defined as the number of routine doses of RV administered to a child within 12 months of birth from January 2008 to December 2011. Children were followed up until end December 2012 to allow all children to have one year of follow-up to assess their vaccine uptake. Rotavirus vaccine uptake was described as a dichotomous variable; complete or incomplete RV uptake. Complete RV uptake was defined as 1 if a child received both recommended doses of RV and incomplete was defined as 0 if a child did not receive any dose or received one dose of RV.

Rotavirus vaccine is administered orally with an interval of at least four weeks between the two doses. The recommended vaccination is a two-dose schedule, administered orally at 6 and 14 weeks of age along with other EPI vaccines. The first dose is given at 6 weeks, but not later than 14 weeks and the second dose given at 14 weeks but not later than 24 weeks **(Appendix A1).**

Pneumococcal conjugate vaccine uptake was defined as the number of routine doses of PCV administered to a child within 12 months of birth for all three doses of PCV from January 2008 to December 2011. Children were

followed up until end December 2012 to allow all children to have one year of follow-up to assess their vaccine uptake. Pneumoccocal conjugate vaccine uptake was described as a dichotomous variable; complete or incomplete PCV uptake. Complete PCV uptake was defined as 1 if a child received all three recommended doses of PCV and incomplete PCV uptake defined 0 if a child did not receive any dose or one or two doses of PCV.

Pneumoccocal conjugate vaccine is administered intramuscularly with a minimum interval of four weeks between the first two doses and a minimum interval eight weeks between the second and third doses. The recommended vaccination is a three-dose schedule, administered at 6 weeks, 14 weeks and 9 months of age along with other EPI vaccines.

2.5.2 Exposure variables

The following exposure variables were considered: child sex, child HIV status, maternal age, maternal education, maternal HIV status, child migration, maternal vital status, distance to fixed clinics, place of residence, parity, twin, mother employment and socioeconomic status. These factors were selected based on careful literature review on vaccine coverage. A summary of individual-level variables is presented in **Appendix B1.**

2.6 Data management and Processing

2.6.1 Data sources

Data used in this study were obtained from the ACDIS in rural South Africa. The Centre's demographic surveillance collects data on all resident and non-resident members of the households in the study area and makes a distinction between

membership (self-defined on the basis of links to other household members) and residency (residing at a physical structure within the surveillance area at a particular point in time). Individuals can be members of more than one household at some point in time (e.g. polygamous married men whose wives maintain separate households). During the household data collection cycle, a set of questionnaires are routinely administered every six (now every 4) months to a key informant in each household (74).

Information recorded are key attributes and events regarding physical structures, household and individuals and their relationship to each other. Additional modules administered include; household socio-economic data, individual socio-economic data and child grants. The HIV surveillance is nested within the ACDIS. The surveillance takes place annually to all consenting resident individuals aged 15 years and above who were eligible for HIV testing in the surveillance. Trained field workers visited each eligible individual in his or her household. After written informed consent, the field workers collected blood by finger prick and prepared dried blood spots for HIV testing according to the Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO guidelines (74, 75). Maternal HIV status information was obtained from the annual HIV-surveillance in the DSA and the Africa Centre's ART Evaluation and Monitoring System (ARTmis) database. ARTmis database is an operational database of HIV-infected people on ART in 17 clinics in the DSA and 40% of the patients in the database live in the DSA.

Immunisation data

Data on immunization is collected as part of the household surveillance round Part of the information collected during such visits was on the vaccination status of young children who had passed their first birthday since the last surveillance visit. Mothers, caregivers, or the head of the household (in absence of the mother or caregiver) were asked to show the interviewers the RTH card for all children aged 12-23 months at the time of the surveillance visit. The RTH card records dates of all routine vaccinations a child has received. When the child's RTH card was ,missing, interviewers asked mother to recall whether the child had received each of the vaccinations included in the South African National Immunisation Schedule (76). Immunization data, including the dates of immunization, are available for the following vaccines: Bacillus Calmette Guerin (BCG), Diphtheria-Tetanus-Pertussis (DTP), Oral Polio Vaccine (OPV), Hepatitis B (HepB), measles *Haemophilus influenzae* type B (Hib), rotavirus (RV) and pneumococcal conjugate (PCV)vaccinations.

Vaccination details are collected using a Child Health Form (CHF) to update immunization data at the Africa Centre **(Appendix C1).** The form is only filled in for children who are between 1 year and 4 years of age and are resident in the households within the DSA. This implies that if a child migrates outside the DSA, vaccination information for that child will not be available for updates which could explain why some vaccination information was missing.

Data were collected on all resident children in the DSA using standardised forms. During a second visit to the households, two pieces of information exist, on the case report forms of that particular household, that help to avoid double filling the

CHF forms. These include the last visit date to a household and the age of the children in the household. If the age of a child at the last visit was less that 12 months, then the field worker can find out the date of birth, and if the child is 12 months and above, as of the second visit date, then he/she fills in a CHF.

The data were captured from the household interviews and delivered to the Africa Centre data centre. Quality control checks are applied to all the forms collected for consistency and validity and all incomplete forms are sent back to the field for verification. The Africa Centre Demographic Information System database is built on a Structured Query Language (SQL) platform and was then transferred to STATA 12.0 (STATA Corporation, College Station, Texas, USA) for further cleaning and analysis.

2.6.2 Data processing

The extracted data were cleaned to identify all missing values and to check for internal consistency of the responses. Any irregularities in the data were corrected and the necessary changes were made. Variables that required recoding were recoded using STATA 12. All the variables for this research were extracted from different tables in the database and were merged. All the tables were linked to each other by either the individual permanent ID or the household ID and through these unique identifiers, all the required variables were extracted and stored into one table. During data cleaning, we used the principle that vaccinations were given in sequence. For example; first dose of RV is administered before the second dose. We compared the dates when RV2 was administered to ensure it was after RV1 was given. Where the dates indicated that RV1 was given after RV2, we compared the dates of administration of RV1

with those of PCV1 and RV2 with that of PCV2, since they are administered at the same time, and made the corrections as appropriate. This was done across all the vaccines to ensure accuracy and consistency in the data. , We also checked for the dates that RV1 and PCV1 were given to ensure this was within 6 weeks of their birth or after their birth. This was ensured for accuracy, consistency and completeness of the data before analysis.

2.7 Data Analysis

2.7.1 Descriptive Analysis

The baseline characteristics of children enrolled into the study were assessed using Mean (SD), median (IQR), graphs, thematic maps and pie charts to compare differences in proportions and also to describe the study population. Vaccination uptake of RV and PCV by RTH card verses maternal recall was assessed. Maternal education level was dichotomized as 1-7 (primary school) years and >7 years (secondary school), as per the school life in South Africa. Maternal age was categorised as <25 and >25 years. Child outmigration from DSA was categorised as Never, before 12 months or after 12 months. For the purposes of this analysis, we categorized missing information on some of the exposure variables which includes, maternal education, maternal HIV status and mother employment as an unknown category. We did this in order to maintain the sample size of the study.

2.7.2 Inferential Analysis

The main aim of the study was to assess factors associated with complete RV and PCV doses hence the outcome variable was categorised as complete vs

incomplete. The main outcome measure was complete vaccine uptake for children who were aged 12 months. Complete RV uptake was defined as 1 if a child received both recommended doses of RV and incomplete was defined as 0 if a child did not receive any dose or received one dose of RV. Likewise, complete PCV uptake was defined as 1 if a child received all three recommended doses of PCV and incomplete PCV uptake defined 0 if a child did not receive any dose or one or two doses of PCV. Rotavirus vaccine and PCV were given by the first year of life. Each of these was analysed as separate outcome variables. The age cut-off point corresponding to the first birthday was chosen because WHO recommends that vaccination should be assessed for children after this age and also all doses of RV and PCV are expected to be received before a child turns a year old. This allows a three months period for children to receive all PCV doses and about 9 months more for all RV doses. Logistic regression was used to explore the effect of the exposure variables on vaccine uptake. The association between sex of child, child migrations, place of residence, parity, maternal HIV status, distance to health facility, maternal education level, maternal age, maternal residency and socio-economic status with vaccination uptake were examined in the bivariate analysis. Covariates were entered into a multivariable model if they had p–value of less than 0.25 in univariable analysis, except child sex which was included *a priori* in the multivariable analysis regardless of statistical significance. Forward stepwise regression methods were used for the multivariable logistic regression to assess the association between RV and PCV uptake and covariates of interest. Starting from the most significant variable identified in the univariable analysis, likelihood

ratio test was used to determine whether the inclusion of a new covariate helped improve the fit of the model.

We only included covariates with a two-sided p-value of equal to or less than 0.05 in our final model. Interactions were tested in all the models with interaction terms using likelihood ratio tests. All interaction terms were not significant so were not included in the final models. All estimates were reported with 95% confidence intervals (CI). In all the models used in the analysis, the log-likelihood ratio tests were used to assess contribution of covariates to the models and linear trend for categorical covariates. Pearson Chi-squared goodness-of-fit test was used to assess model adequacy.

Multinomial logistic regression models were also considered to investigate vaccine uptake. This method was used to check if there would be methodological differences in the analysis methods used in the study. Given that we used logistic regression with binary outcome, we wanted to check if using multinomial regression procedure would have significant effect on our results.

2.8 Ethical considerations

The primary project (surveillance) was cleared by the Biomedical Research Ethics Committee at the University of KwaZulu-Natal, with annual re-certification. Permission was obtained from Africa Centre for the use of their dataset. The study was approved by the Research Ethics Committee of the University of Witwatersrand (Human) **Appendix D1**. The data collected for this study did not include any personal identifiers and all study participants were identified by unique identifier. Thus no personal identifiers were available in the dataset and the data was analysed anonymously.

Chapter 3 : Results

3.1 Introduction

This chapter presents results from the analysis of a dataset for all children aged 12 months old or below, born between January 2008 and December 2011 and were followed up until end December 2012 to allow all children to have one year of follow-up and who were residents in the Africa Centre DSA. The analyses are in two parts: the first part describes the cohort, trends of RV and PCV uptake, and geographic variations in RV and PCV uptake. The second part investigates the risk factors associated with RV and PCV uptake separately using logistic regression models.

3.2 Participants of the study

During the study period, 6,272 children were followed in our study cohort. In the analyses, we however could not include all the 6,272 children because data on vaccination information was not available in the Africa Centre Demographic Information System (ACDIS) for all the children. Out of the 6,272 children, 9 died before 6 weeks of their birth hence were excluded. Of the children remaining in the cohort, 5,133 (82%) and 5,209 (83%) had complete information on the uptake of RV and PCV respectively. For RV and PCV analyses, 1,130 and 1,054 respectively were dropped because they had missing information **(Figure 3.1)**.

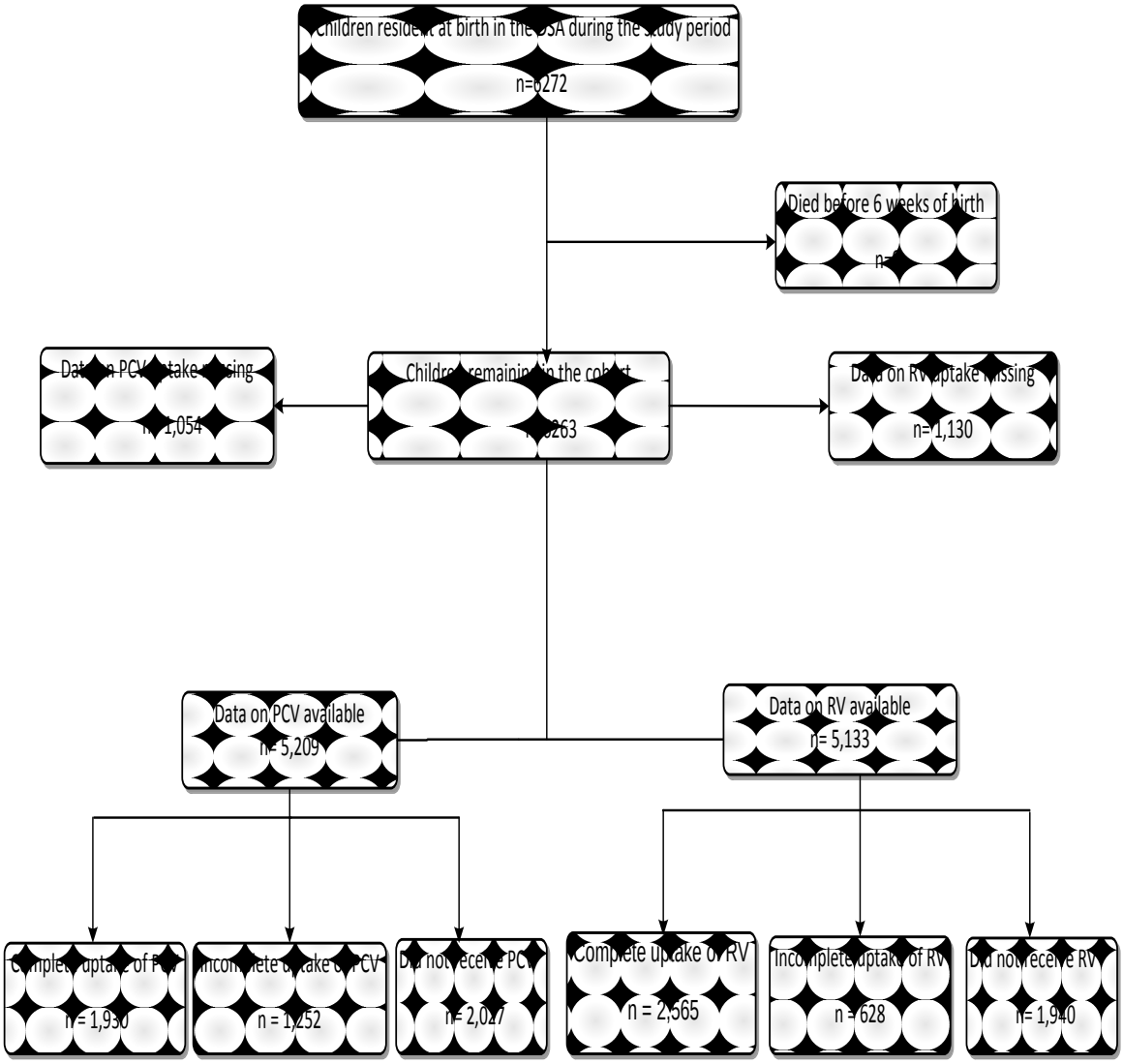


Figure 3.1: A flow chart of children included in the cohort from 2008 to 2011

3.3 Baseline characteristics of the study participants

Child characteristics

A total of 6,263 children were included in the study. Of these, 3,082 (49%) were females. The proportions of children born and eligible for the study in each year from 2008 to 2011 were comparable (around 25%). Out of the total number of children, 5,772 (92%) had RTH cards and only 1,402 (22%) were seen by a

fieldworker at the time of interview. However, 143 (2%) did not have a RTH card and 348 (6%) RTH card information was missing. About 5,350 (85%) children never migrated outside the DSA as of December 2011. At the time of their birth, 3,823 (61%) children were living in rural areas. About one-sixth of the children were living in households located far from a health facility (≥5km). Less than one percent (57) of the children initiated antiretroviral therapy (ART) during the study period. Of the total number of children, 154 (2%) were either twins or triplets. The baseline characteristics of the study participants are shown in **Table 3.1**.

Maternal characteristics

There were 5,539 mothers who contributed 6,263 children in the study. About half of the women (47%) had parity of between 2 and 4 and the median age was 23 years (Interquartile range (IQR) 20-29). A total of 1,044 (17%) mothers had unknown level of education. Of those who had data on education, 3,995 (64%) mothers had secondary school education (up to grade 12). For every 100 mothers, 23 were HIV positive at child delivery. . More than half of the HIV positive mothers on ART (57%) initiated ART after child birth. Five thousand, eight hundred and ninety seven (94%) of the children had their mothers who were residents in the DSA at their birth.

Table 3.1: Characteristics of the sample population in the DSA (n= 6,263)

Characteristic	Number (n)	Proportion (%)
Sex of child		
Female	3,082	49
Male	3,181	51
Year of birth		
2008	1,706	27
2009	1,583	25
2010	1,553	25
2011	1,421	23
Child out migrated from DSA		
Never	5,350	85
Ever	913	15
Child Immigrated to DSA		
Never	5,969	95
Ever	294	5
Place of residence		
Rural	3,823	61
Peri-urban	1,973	32
Urban	467	7
Has Vaccination card		
Yes, card seen	1,402	22
Yes, but card not seen	4,370	70
No	143	2

Missing	348	6
Distance to health facility		
Near (<5km)	5,329	85
Far (≥5km)	934	15
Wealth index		
Lowest	1,218	19
Second	1,169	19
Middle	1,215	19
Fourth	1,157	19
Highest	942	15
Missing	562	9
Maternal age		
<20	1,506	24
20-29	3,336	53
>=30	1,404	23
Missing	17	<1
Maternal vital status		
Alive	6,161	98
Death	102	2
Maternal education		
None	116	2
Primary	690	11
Secondary	3,995	64
Tertiary	418	6
Unknown	1,044	17

Maternal HIV status at child birth		
Positive	1,179	19
Negative	3,604	56
Unknown	1,583	25
Mother out-migrated from DSA		
Never	5,350	85
Before 12 months	315	5
After 12 months	598	10
Mother Immigrated to DSA		
Never	5,969	95
Before 12 months	34	1
After 12 months	260	4
Mother resident in the DSA at child birth		
Yes	5,897	94
No	349	6
Missing	17	<1
Mother Resident in DSA at end of study		
Yes	4,557	73
No	1,689	27
Missing	17	<1

Type of Toilet		
Flush toilet	527	9
Ventilated improved pit	1,025	16
Others	3,536	56
None	872	14
Missing	303	5
Type of Water		
Piped water	3,649	58
Borehole	477	8
Other	1,857	30
Missing	280	4
Type of Electricity		
Yes	4,409	25
No	1,566	70
Missing	288	5

Mortality and underlying causes

During the study period, 148 (2%) children died. However, data on underlying causes of deaths were available for 144 deaths only. There were 38 (26%) deaths due to diarrhoea and gastroenteritis, while 49 (34%) deaths were caused by unspecified *Streptococcus pneumonia* and acute lower respiratory infections, 29 (20%) were due to unspecified reasons related to HIV (**Figure 3.2**). Underlying causes of death were not known for 11 (8%) children. In 4 (3%) children, causes of death were also unknown because their proxy respondents

refused to participate in the interviews while for the remainder, 13 (9%) children died due to other causes.

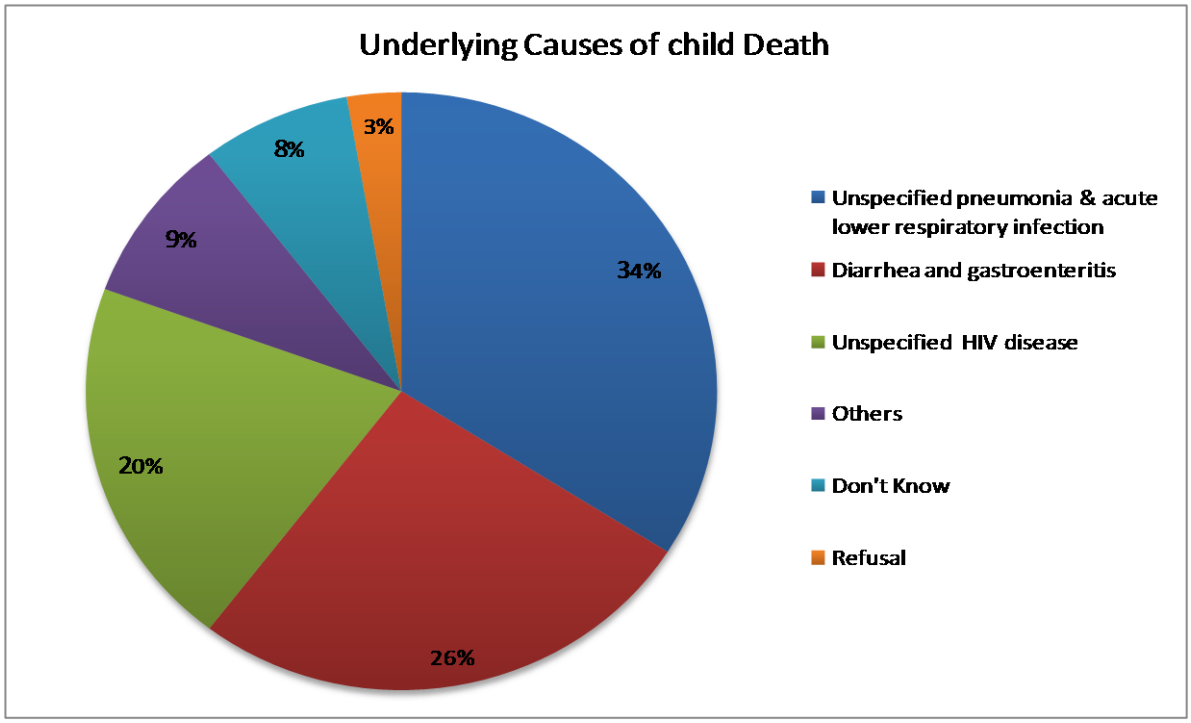


Figure 3.2: Underlying causes of death among 144 children, 2008 to 2011

3.4 Vaccine uptake

Among 6,263 children enrolled, 5,133 children had RV vaccination information available at the end of the study period. Of these, 2,565 (50%) children received the two-dose series of RV and thus had complete RV vaccination. Among children who had incomplete RV uptake, 628 (12%) children had one dose of RV and 1,940 (38%) had no dose of RV at the end of the study period.

Among the 1,130 children who did not have data available on their RV vaccinations, 568 (50%) had never migrated outside the DSA. However, 270 (24%) migrated outside the DSA before 12 months of their birth and 292 (26%) migrated outside the DSA after 12 months of their birth. Children who migrated

outside the DSA before their first birthday were more likely not to have received their RV doses within the DSA, hence may contribute to the missing RV vaccination data. Most of the missing data on RV vaccinations were obtained from children born in 2008 compared to the other years. This was partly due to the fact that the vaccines were newly introduced and many mothers did not know the vaccines.

Table 3.2: RV and PCV uptake from January 2008 to December 2011

Vaccine uptake	N	None n (%)	Incomplete n (%)	Complete n (%)
RV	5,133	1,940 (37.8)	628 (12.2)	2,565 (50.0)
PCV	5,209	2,027 (38.9)	1,252 (24.0)	1,930 (37.1)

Among 6,263 children enrolled, 5,209 children had PCV vaccination information available during the study period. Of these, 1,930 (37%) had received the three-dose series of PCV, thus having complete PCV uptake, 1,252 (24%) had incomplete doses of PCV and 2,027 (39 %) had no dose of PCV at the end of the study period. About 60% of the children born in 2011 received complete doses of PCV while less than 14% of the children born in 2008 got complete doses of PCV. Among the 1,054 children who did not have data available on their PCV vaccinations, 517 (50%) had never migrated outside the DSA and 258 (24%) who had migrated outside the DSA before 12 months of their birth. However, 279 (26%) migrated outside the DSA after 12 months of their birth. Similar to RV, most of the missing data on PCV vaccinations were obtained from children born in 2008 compared to the other years. This again, was partly due to the fact that

the vaccines were newly introduced and many mothers did not know the vaccines.

Table 3.3: PCV uptake by RTH card and Maternal Recall

Source of Vaccine uptake	N	None n (%)	Incomplete n (%)	Complete n (%)
RTH Card	1,362	357 (20.9)	382 (28.6)	623 (31.5)
Maternal Recall	3,653	1,349 (79.1)	952 (71.4)	1,352 (68.5)

Table 3.4: RV uptake by RTH card and Maternal Recall

Source of Vaccine uptake	N	None n (%)	Incomplete n (%)	Complete n (%)
RTH Card	1,351	389 (22.0)	163 (25.7)	799 (31.5)
Maternal Recall	3,588	1,382 (78.0)	471 (74.3)	1,735 (68.5)

Among the children enrolled, 1,351 (27%) and 3,588 (73%) had their RV vaccination uptake information available through the RTH card and Maternal Recall respectively during the study period. Of those whose vaccine uptake information were recorded from the RTH card, 799 (32%) had received all the three-dose series of RV, whiles those whose vaccine uptake was obtained from maternal recall and had also received all the three-dose series of RV were 1,735 (68%). However, 1,362 (27%) and 3,653 (73%) had their PCV vaccination uptake

information available through the RTH card and Maternal Recall respectively. Children who received complete PCV and had their vaccination information recorded from the RTH card were 623 (32%), whiles those who received complete PCV but their vaccination information were obtained through maternal recall were 1,352 (68%). The vaccination uptake by RTH card verses maternal recall of the study participants are shown in **Table 3.3** and **Table 3.4**.

3.4.1 RV uptake proportions from 2008 to 2011 in DSA

Table 3.4 shows RV uptake from 2008 to 2011 in the DSA. The uptake of RV was highest in 2011 and lowest in 2008. More than three-quarters of the children born in the year 2011 received complete doses of RV at the end of the year while less than a quarter of the children born in 2008 received complete doses of RV at the end of the year. There was a linear trend in the uptake of RV across the study period (X^2=36.98, p-value=<0.01). The number of children who received complete RV increased sharply over time from the year 2008 to 2010; however, the year 2010 to 2011 experienced a steady increase in the uptake of RV. Similarly, the number of children who did not receive any dose of RV decreased sharply from the year 2008 to 2010, with a gradual decrease from 2010 to 2011 and the number of children who had incomplete RV slightly increased from 2008 to 2009 and with observed steady decrease from 2009 to 2011. **(Figure3.3**The overall uptake of RV in the study area was 50% between 2008 and 2011(**Table 3.4**) with the uptake of RV increasing across the years **(Appendix E1)**.

Table 3.5: RV uptake proportions from 2008 to 2011 in DSA (n=5,131)

		Rotavirus vaccine uptake, n (%)		
Year	**Number(n)**	**Complete RV**	**Incomplete RV**	**None**
2008	1,331	199 (14.9)	109 (8.2)	1,023 (76.9)
2009	1,332	516 (38.7)	203 (15.2)	613 (46.0)
2010	1,309	917 (70.1)	173 (13.2)	219 (16.7)
2011	1,161	933 (80.4)	143 (12.3)	85 (7.3)
Total	5,133	2,565 (49.9)	623(12.2)	1,940 (37.8)

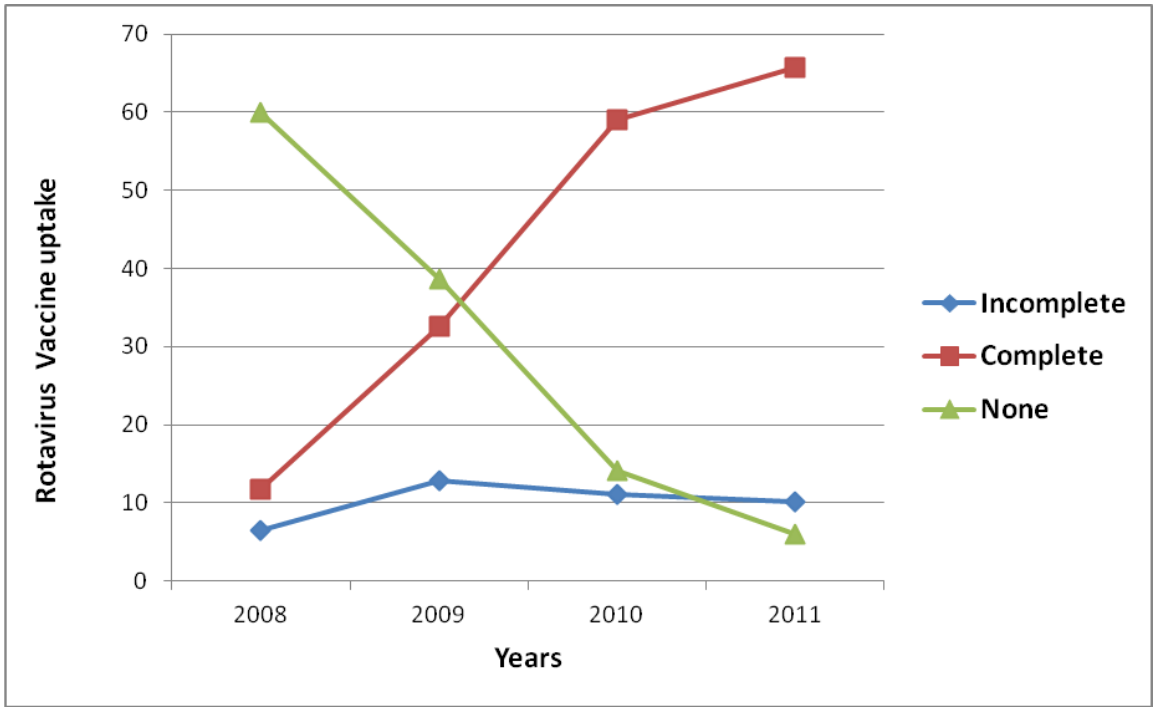


Figure 3.3: RV uptake trends over time among infants, 2008 to 2011

3.4.2 PCV uptake proportions from 2008 to 2011 in DSA

Table 3.6 shows PCV uptake proportions from 2008 to 2011 in the DSA. The uptake of PCV was highest in 2011 and lowest in 2008. More than half (58%) of the children in 2011 received complete doses of RV while in 2008 only less than a 12% of the children received complete doses of RV. There was a linear trend in the uptake of PCV across the study period (X^2=40.56, p-value=<0.01). The number of children who received complete PCV increased sharply over time from the year 2008 to 2010; with a steady decrease from 2010 to 2011. Similarly, the number of children who did not receive any dose of PCV decreased sharply from the year 2008 to 2010, with a gradual decrease from 2010 to 2011.

However, the number of children who had incomplete PCV increased sharply from 2008 to 2009 with an observed steady increase from 2009 to 2011 **(Figure3.4)**. The overall uptake of PCV in the study area was 37% between 2008 and 2011(**Table 3.6**) with the uptake of complete PCV increasing across the years **(Appendix F1)**.

Table 3.6: PCV uptake proportions from 2008 to 2011 in the DSA (N=5,209)

		Pneumococcal conjugate vaccine Uptake, n (%)		
Year	**Number(N)**	**Complete PCV**	**Incomplete PCV**	**None**
2008	1,359	159 (11.7)	149 (10.9)	1,051 (77.3)
2009	1,347	372 (27.6)	361 (26.8)	614 (45.6)
2010	1,326	712 (53.7)	362 (27.3)	252 (19.0)
2011	1,177	687 (58.4)	380 (32.3)	110 (9.4)
Total	5,209	1,930 (37.1)	1,252 (24.0)	2,027 (38.9)

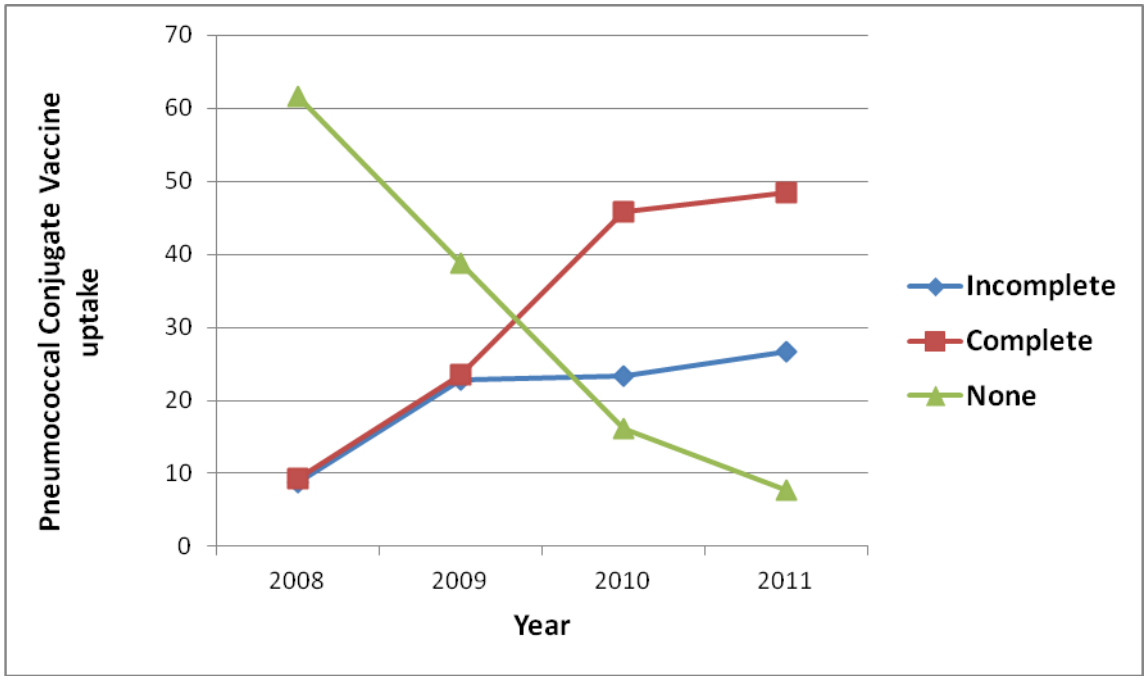
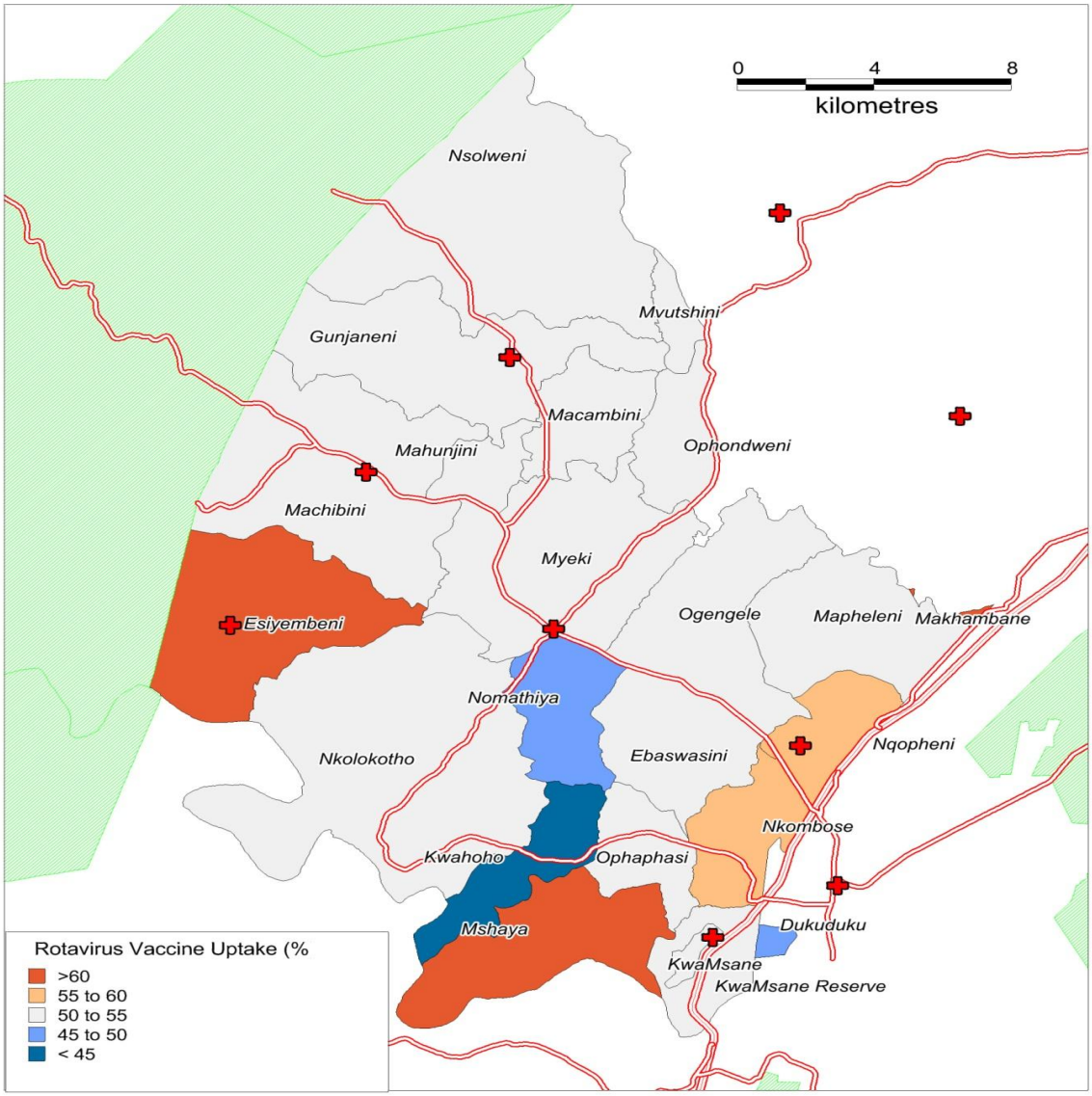


Figure 3.4: PCV uptake trends over time among infants, 2008 to 2011

3.7 Geographic variations of RV and PCV uptake

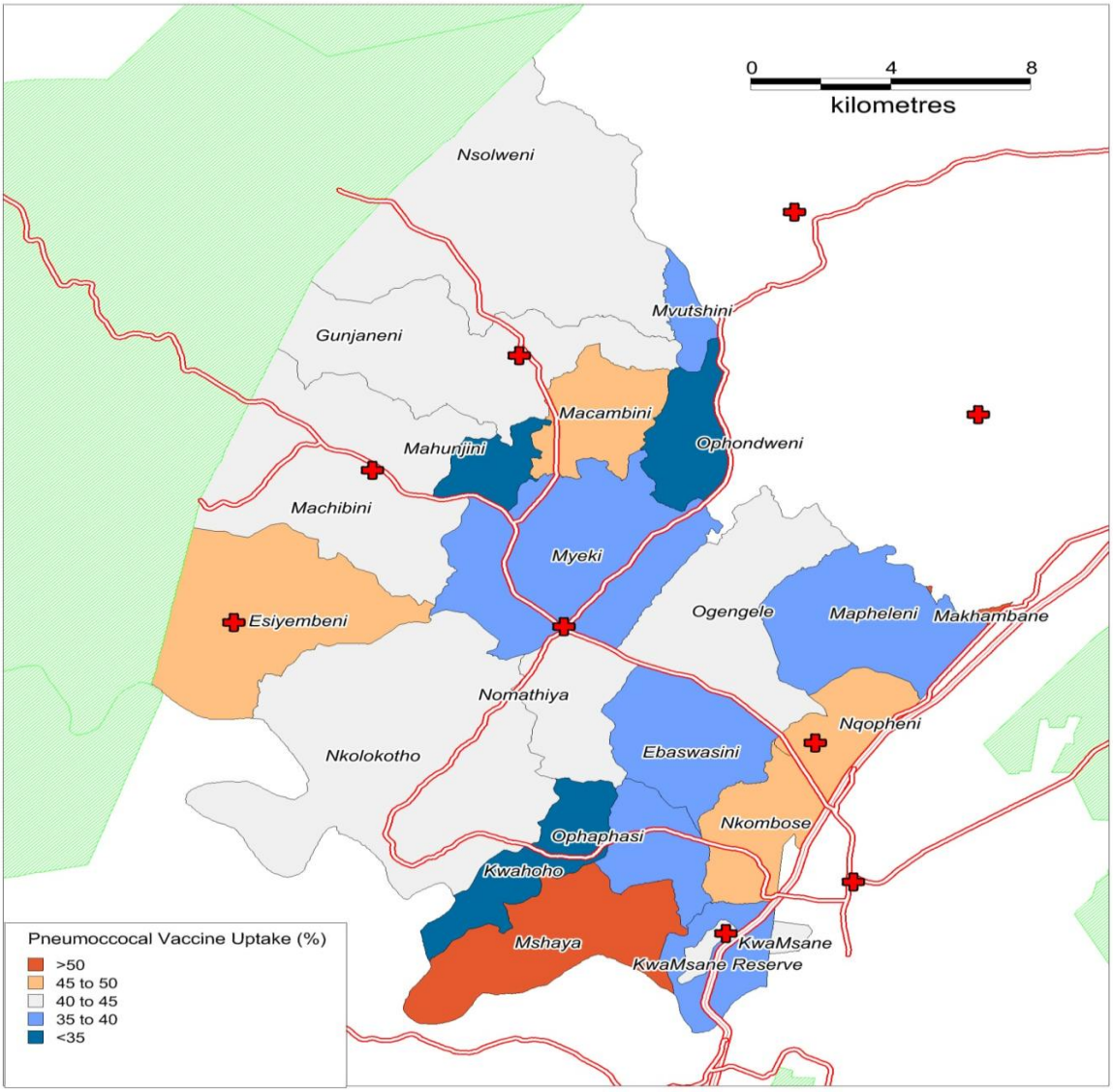
There were geographic variations in the uptake of both RV and PCV in the DSA during the study period. In general, local areas which were close to the fixed clinics had relatively high uptake of both RV and PCV compared to areas which were far from fixed clinics during the study period. Additionally, areas which were close to the main road had high uptake of RV and PCV compared to those who were far from the main road. Some local areas had the greatest proportions of complete RV uptake >60% although they do not have a fixed clinic close by (**Figure 3.5**). Majority of the local areas with gray colour in the map had RV uptake around 50 to 55%, with only one local area coloured deep blue having RV uptake less than 45%.



Note: Red crosses are fixed clinics

Figure 3.5: Areas with complete RV uptake in the DSA, 2008 to 2011

Some of the areas which recorded high levels of RV uptake also recorded the highest proportion for complete PCV uptake (**Figure 3.6**). Majority of the local areas with gray colour in the map had PCV uptake around 40 to 45%, with only one local area coloured deep blue having PCV uptake less than 35%.



(Red crosses = Fixed clinics)

Figure 3.6: Areas with complete PCV uptake in the DSA, 2008 to 2011

3.8 Factors associated with RV uptake in the DSA

The factors associated with uptake of RV were assessed. Complete uptake was defined as the uptake of all recommended doses of RV; and incomplete uptake defined as the uptake of one dose of RV or none. Univariable and multivariable models were fitted using logistic regression.

In the univariable analysis, having out migrated from DSA, maternal status, maternal education, maternal HIV status, mother employed and mother resident in the DSA at child birth was associated with the uptake of RV **(Table 3.7)**. However, associations with being a twin, maternal age, wealth index, child's sex, parity and distance to health facility were not statistically significant.

Table 3.7: Factors associated with complete RV uptake among infants in the DSA, 2008 to 2011 (n=5,133)

RV Characteristic	uOR (95 % CI)	p-value	aOR (95 % CI)	p-value
Sex of child				
Female	1		1	
Male	0.97(0.87-1.08)	0.55	0.97(0.88-1.09)	0.64
Child out migrated from DSA				
Never	1		1	
Ever	0.47(0.39-0.57)	<0.01	0.49(0.41-0.57)	<0.01
Twin				
No	1			
Yes	0.91(0.65-1.29)	0.61		
Place of residence				
Urban	1			
Peri-urban	1.07(0.87-1.32)	0.52		
Rural	1.09(0.88-1.36)	0.43		
Distance to health facility				
<5km	1			
≥5km	0.97 (0.83-1.13)	0.67		
Wealth index				
Lowest	1			
Second	0.95(0.79-1.13)	0.56		
Middle	0.95(0.79-1.13)	0.55		
Fourth	1.07(0.89-1.27)	0.48		
Highest	1.00(0.83-1.21)	0.98		

Maternal age				
≤25	1		1	
>25	1.07(0.96-1.20)	0.21	1.23(1.05-1.43)	0.01
Mother vital status				
Alive	1		1	
Dead	0.61(0.38-0.98)	0.05	0.63(0.38-1.02)	0.06
Maternal education				
None	1		1	
Primary	1.12 (0.70-1.67)	0.59	1.22(0.74-1.78)	0.37
Secondary	1.47 (0.93-2.10)	0.06	1.70(1.02-2.34)	0.01
Tertiary	1.40 (0.89-2.21)	0.15	1.80(0.97-2.44)	0.02
Unknown	1.95 (1.27-2.99)	<0.01	1.89(1.21-2.94)	0.01
Maternal HIV status at child birth				
Negative	1		1	
Positive	1.12(1.08-1.44)	0.09	1.16(0.99-1.34)	0.05
Unknown	1.10(0.98-1.27)	0.18	1.08(0.94-1.25)	0.29
Parity				
Parity 1	1		1	
Parity 2-4	1.12(0.97-1.31)	0.13	1.01(0.86-1.19)	0.89
Parity >5	0.90(0.69-1.18)	0.45	1.21(1.04-1.40)	0.01
Mother Employed				
No	1		1	
Yes	0.74(0.64-0.86)	<0.01	0.71(0.60-0.84)	<0.01
Unknown	1.21(1.06-1.37)	<0.01	1.19(1.01-1.40)	0.04
Mother resident in the DSA at child birth				
No	1.00		1	
Yes	2.08 (1.58-2.72)	<0.01	1.97 (1.49-2.60)	<0.01

uOR**:** unadjusted odds ratio, aOR**:** Adjusted odds ratio, 95% CI: 95% confidence interval

In the multivariable logistic regression analysis, the following variables were significantly associated with RV uptake after adjusting for the variables in the model: child out migrated from DSA, maternal age, maternal education, mother employed, parity, mother resident in the DSA at child birth and maternal HIV

status at child birth. However, maternal vital status was only marginally associated with RV uptake. Children who ever migrated outside the DSA were 51% (adjusted OR=0. 0.49, 95 % CI 0.41-0.57) less likely to receive complete doses of RV compared to those who did migrate. However, there was evidence of a significantly increases odds of complete RV uptake among children whose mothers had secondary (adjusted OR=1.70, 95 % CI 1.02-2.34) or tertiary education (adjusted OR=1.80, 95 % CI 0.97-2.44 compared to those whose mothers no education. The multivariable analysis also demonstrated that maternal age was associated with RV uptake. Children born to older mothers were 23% more likely to receive complete doses of RV than those from young mothers from the DSA (adjusted OR=1.23, 95 % CI 1.05-1.43). Likewise, children whose mothers were employed were 29% less likely to receive RV (adjusted OR=0.71, 95 % CI 0.60-0.84) than those whose mothers were not employed. Children born to HIV positive mothers were more likely to be vaccinated with complete doses of RV (adjusted OR=1.16, 95 % CI 0.99-1.34) than those born to HIV negative mothers, but the association was not statistically significant. Complete RV uptake was also associated with an increase with parity of five or more (adjusted OR=1.21, 95 % CI 1.04-1.40). The odds of complete RV uptake for children whose mothers had parity of 5 or more were 21% higher than those whose mothers had parity of one (adjusted OR=1.21, 95 % CI 1.04-1.40.

Further, children whose mothers were resident in the DSA at their birth were significantly more likely to be vaccinated with RV compared to those whose mothers were resident outside the DSA at their birth (adjusted OR=1.97, 95 % CI 1.49-2.60).

3.9 Factors associated with PCV uptake in the DSA

The uptake of PCV was assessed using logistic regression. Complete uptake was defined as the uptake of all recommended doses of PCV; and incomplete uptake defined as the uptake of either one or two doses of PCV or none. Univariable and multivariable analyses were fitted with these two types of PCV uptake as outcome variables.

In the univariable analysis, child out migrated from DSA, mother vital status, maternal HIV status and mother resident in the DSA at child birth was associated with the uptake of PCV **(Table 3.9).** Child's sex, year of birth, twin, maternal age, wealth index, parity, distance to health facility, place of residence and maternal education were not significant.

Table 3.8: Factors associated with complete PCV uptake among infants in the DSA 2008 to 2011 (n=5,209)

Characteristic	uOR (95 % CI)	p-value	aOR (95 % CI)	p-value
Sex of child				
Female	1		**11**	
Male	1.02(0.91-1.14)	0.78	1.02(0.91-1.14)	0.73
Child out migrated from DSA				
Never	1		1	
Ever	0.51(0.42-0.62)	<0.01	0.52 (0.43-0.63)	<0.01
Place of residence				
Urban	1			
Peri-urban	0.95(0.77-1.18)	0.67		
Rural	0.97(0.77-1.22)	0.79		
Distance to health facility				
<5km	1			
≥5km	1.08(0.92-1.26)	0.35		

Wealth index				
Lowest	1			
Second	0.93(0.78-1.12)	0.45		
Middle	0.95(0.80-1.14)	0.62		
Fourth	0.97(0.81-1.16)	0.72		
Highest	1.06(0.88-1.29)	0.53		
Maternal age				
<=25	1		1	
>25	1.06(0.94-1.19)	0.33	1.07(0.95-1.23)	0.25
Mother vital status				
Alive	1		1	
Dead	0.56(0.33-0.95)	0.03	0.58(0.34-0.98)	0.04
Maternal education				
None	1		1	
Primary	0.89 (0.61-1.52)	0.61	0.90(0.59-1.41)	0.67
Secondary	1.11 (0.69-1.60)	0.62	1.18(0.78-1.82)	0.43
Tertiary	1.18 (0.74-1.89)	0.48	1.38(0.86-2.23)	0.18
Unknown	1.35 (0.87-2.09)	0.18	1.23(0.78-1.93)	0.38
Maternal HIV status at child birth				
Negative	1		1	
Positive	1.11(0.96- 1.27)	0.16	1.15(0.99-1.33)	0.06
Unknown	1.16(1.01-1.34)	0.03	1.17(1.01-1.35)	0.03
Parity				
Parity 1	1			
Parity 2-4	1.08(0.92-1.26)	0.35		
Parity >5	0.98(0.74-1.30)	0.91		
Mother Employed				
No	1		1	
Yes	0.84 (0.71-0.98)	0.03	0.81(0.68-0.96)	0.01
Unknown	1.17 (1.03-1.33)	0.02	1.18(1.01-1.38)	0.04
Mother resident in the DSA at child birth				
No	1		1	
Yes	1.62(1.22-2.16)	<0.01	1.55(1.16-2.08)	<0.01

uOR**:** unadjusted odds ratio, aOR**:** Adjusted odds ratio, 95% CI: 95% confidence interval

In the multivariable logistic regression analysis, the following variables were significantly associated with PCV uptake after adjusting for the other variables in the model: child out migrated from DSA, maternal HIV status, maternal vital status, mother employed and mother resident in the DSA at child birth. Children who ever migrated outside the DSA were 48% (adjusted OR=0.52, 95% CI 0.43-0.63) less likely to receive PCV than those who never migrated. There was evidence of reduced odds of complete PCV uptake among children whose mothers died compared to those whose mothers were alive (adjusted OR=0.58, 95% CI 0.34-0.93). On the other hand, children whose mothers HIV status were unknown were more likely to receive PCV (adjusted OR=1.17, 95% CI 1.01-1.35) compared to those whose mothers were HIV negative. However, children whose mothers were HIV positive were marginally associated with PCV uptake. Likewise, children whose mothers were employed were 19% less likely to receive PCV (adjusted OR=0.81, 95 % CI 0.68-0.96) compared to those who mothers were not employed. Lastly, children whose mothers were residents in the DSA at their birth (adjusted OR=1.55, 95% CI 1.16-2.08) were also significantly more likely to be vaccinated with PCV compared to those whose mothers were resident outside the DSA at their birth.

4.0 Factors associated with both RV and PCV uptake in the DSA

The uptake of both vaccines were assessed as follows; complete RV and PCV uptake was defined as the uptake of all recommended doses of RV and PCV together; and incomplete RV and PCV uptake was defined as the uptake of less than the recommended doses of RV and PCV (less than two doses of RV and

less than three doses of PCV). Univariable and multivariable analyses were fitted with both RV and PCV uptake together as outcome variables.

In the univariable analysis, child out migrated from DSA, maternal vital status, maternal HIV status, mother employed and mother resident in the DSA at child birth was associated with the uptake of both RV and PCV **(Table 3.9).** Maternal age, wealth index, child's sex, twin, parity, distance to health facility and maternal education were not significant.

Table 3.9: Factors associated with complete RV and PCV uptake among infants in the DSA 2008 to 2011 (n= 5,216)

Characteristic	uOR (95 % CI)	p-value	aOR (95 % CI)	p-value
Sex of child				
Female	1		1	
Male	1.01(0.90-1.13)	0.89	1.01(0.90-1.13)	0.84
Child out migrated from DSA				
Never	1		1	
Ever	0.51(0.42-0.63)	0.01	0.52 (0.43-0.63)	<0.01
Twin				
No	1			
Yes	0.99(0.69-1.41)	0.98		
Place of residence				
Urban	1			
Peri-urban	0.96(0.77-1.19)	0.75		
Rural	0.99(0.79-1.24)	0.94		
Distance to health facility				
<5km	1			
≥5km	1.07(0.92-1.26)	0.38		
Wealth index				
Lowest	1			
Second	0.93(0.77-1.12)	0.43		
Middle	0.96(0.80-1.14)	0.62		

Fourth	0.97(0.81-1.16)	0.72		
Highest	1.06(0.87-1.28)	0.56		
Maternal age				
<=25	1		1	
>25	1.05 (0.94-1.18)	0.39	1.08(0.94-1.22)	0.27
Mother vital status				
Alive	1		1	
Dead	0.57(0.34-0.97)	0.04	0.59(0.35-1.01)	0.05
Maternal education				
None	1		1	
Primary	0.87(0.57-1.34)	0.54	0.89(0.57-1.37)	0.59
Secondary	1.10(0.72-1.68)	0.67	1.17(0.77-1.79)	0.46
Tertiary	1.09(0.68-1.75)	0.71	1.28(0.79-2.07)	0.31
Unknown	1.34(0.87-2.08)	0.18	1.22(0.77-1.92)	0.40
Maternal HIV status at child birth				
Negative	1		1	
Positive	1.10(0.96- 1.27)	0.17	1.14(0.98-1.32)	0.07
Unknown	1.17(1.01-1.34)	0.03	1.17(1.02-1.35)	0.03
Parity				
Parity 1	1			
Parity 2-4	1.06(0.91-1.24)	0.46		
Parity >5	0.99(0.75-1.32)	0.97		
Mother Employed				
No	1		1	
Yes	0.82(0 .69-0.96)	0.02	0.80(0.67-0.95)	0.01
Unknown	1.17(1.03-1.33)	0.02	1.18(1.01-1.38)	0.04
Mother resident in the DSA at child birth				
No	1		1	
Yes	1.64(1.23-2.17)	<0.01	1.56(1.17-2.08)	<0.01

uOR**:** unadjusted odds ratio, aOR**:** Adjusted odds ratio, 95% CI: 95% confidence interval

In the multivariable logistic regression analysis, the following variables were significantly associated with both RV and PCV uptake after adjusting for the variables in the model: child out migrated from DSA, maternal vital status mother

status during the study period, maternal HIV status, mother employed and mother resident in the DSA at child birth. Children who ever migrated outside the DSA were 48% (adjusted OR=0.52, 95% CI 0.43-0.63) less likely to receive both RV and PCV. There was evidence of a significant reduced odds of RV and PCV uptake among children whose mothers were not alive (adjusted OR=0.59, 95% CI 0.35-1.01), On the other hand, children whose mothers HIV status were not known were more likely to receive both RV and PCV (adjusted OR=1.17, 95% CI 1.02-1.35) compared to those whose mothers were HIV negative. However, children whose mothers were HIV positive were marginally associated with both RV and PCV uptake in the DSA. Children whose mothers were employed were less likely to receive both RV and PCV (adjusted OR=0.81, 95 % CI 0.68-0.96) compared to those who mothers were not employed. Lastly, children whose mothers were residents in the DSA at their birth (adjusted OR=1.56, 95% CI 1.17-2.08) were also significantly more likely to be vaccinated with both RV and PCV compared to those whose mothers were resident outside the DSA at their birth.

A multinomial logistic regression models were also considered. Multinomial logistic regression model is appropriate as it is applied to categorical outcomes that have more than two categories. These outcome variables were defined as; 0 for “none” if a child did not receive any dose at all, 1 for “incomplete” if a child received one and one or two doses of RV and PCV respectively, and 2 for “complete” if a child received all doses of both RV and PCV.

Appendix G1 shows the multinomial logistic regression tables. In these tables, our reference category was children who received complete doses of both RV and PCV. We therefore compared children who received no vaccinations to

those who received complete doses and similarly compared children who received incomplete doses to those who had complete doses. As seen on the multinomial tables, the logistic and multinomial regression models yielded the same results and we therefore reported the results from the Logistic regression model only.

Chapter 4 : Discussion

Child vaccination is one of the most significant achievements in terms of preventing infectious diseases and promoting child health. We investigated the uptake of RV and PCV among children aged 12 months who were residents in the DSA in rural South Africa between January 2008 and December 2011. Specifically, the study assessed vaccination uptake of RV and PCV; the geographic variations in the uptake of RV and PCV and the factors associated with RV and PCV uptake. This chapter presents discussions of the findings.

4.1 Uptake of complete RV and PCV in the DSA

The uptake of RV and PCV were 50% and 37% respectively. In this study setting, the uptake of RV and PCV remained considerably low compared to other routine infant immunisations administered in EPI-SA. Comparing RV uptake during the study period in the DSA with the national coverage in 2012, the proportion of children fully vaccinated in the present study was lower by 17% and that of PCV was lower by 24%. Beside this, the current findings are lower than the national target of 90% coverage in the country. This difference may be due to the method of data collection used in the absence of a RTH card. Maternal recall was used and considering that these vaccines are new, the likelihood of a mother or caregiver forgetting was high. This could have led to the underestimation of RV and PCV uptake in the DSA. The implication of this result is that infants in this area were not fully protected from rotavirus and pneumococcal diseases. However the study shows that the uptake of RV increases across the years whiles PCV uptake had a steady increase been stable between 2010 and 2011.

Rotavirus vaccine uptake

Our results are consistent with findings from other studies conducted in both developed and developing countries which also assessed uptake of RV. A study conducted to estimate uptake and coverage of RV in seven Asian countries showed that the rate of RV uptake in these countries was less than 50% in 2010 (28). Similarly, according to an epidemiological review of RV conducted in South Africa the uptake of RV among children less than one year was reported to be 67% in 2012 (44).However, other studies show high uptake levels of RV. In Brazil the uptake of the two-series of RV among children ranged from 80 to 84% between 2007 and 2010 (47). Similar findings of a study conducted in Australia reported RV uptake for a full vaccine course ranging from 80 to 85% in 2010 after its introduction into their national immunisation (77). We can only speculate that the differences in uptake levels observed in these areas might be as a result of the differences in funding for these vaccines since different governments fund these vaccines differently. Although WHO recommends that infants worldwide should be routinely vaccinated against rotavirus (78), our study shows that the routine vaccination of RV remains low in this rural area of South Africa compared to the national coverage of 67% and a national target of 90% coverage.

Pneumoccocal conjugate vaccine uptake

The study has shown that PCV uptake in the DSA during the study period was 37%. Generally, this is low compared to the national coverage rate for the third dose of PCV reported in 2010 by the South Africa Department of Health. Pneumoccocal conjugate vaccine coverage was reported to be 61% and four provinces had coverage of more than 70% (13). This confirms the uptake of PCV

is low in the DSA and also compared to other existing vaccines such as BCG, measles and Polio. Similarly, low levels of PCV uptake were also witnessed in countries such as Taiwan, Philippines, Malaysia and Japan in 2010 where uptake was shown to be less than 35% (28). Studies conducted In Europe have shown that PCV uptake is high. A study done among infants and children born between 2007 and 2009 in Denmark in 2012 showed that PCV coverage after three years of PCV introduction in their childhood immunization programme to be above 85% for the all the three doses PCV (79). The authors attributed the high uptake of PCV to immunization catch-up campaigns which were initiated to vaccinate all children in the target age group in multiple cohorts who received supplementary dose of PCV.

Although in the developing countries, the uptake of PCV is high, in the developing countries still remain a challenge.

4.2 Geographic variations of RV and PCV uptake

This study has revealed that there is differential uptake of vaccines between geographical areas in the study area. There were substantial differences in the uptake of complete RV and PCV among the different geographical and administrative local areas. Local areas which were close to the fixed clinics had relatively high uptake of both RV and PCV compared to areas which were far from fixed clinics during the study period. Additionally, areas which were close to the main road had high uptake of RV and PCV compared to those who were far from the main road.

These findings are consistent with results of a study conducted in the same DSA which also showed marked geographic differences in DPT3 vaccination

coverage in 2009 (50). The study however looked at five different vaccines other than PCV and RV. Differences between uptake of RV and PCV within the DSA observed were due to the fact that some areas are strategically positioned because of their closeness to the health facilities and road network where they might easily access the vaccines. These geographic variations in vaccine uptake were also reported from other studies conducted in Sub Saharan Africa (66) (80).

4.3 Factors associated with complete RV and PCV uptake in the DSA

Maternal age, maternal education, child out migration from the DSA, maternal HIV status at child birth, parity, maternal employment and maternal residency in the DSA at child birth were found to be factors associated with uptake of RV among children aged 12 months or below in rural South Africa. However, there was no significant association between complete RV uptake and the following factors, child sex, place of residence, distance to health facility, wealth index and mother status. On the other hand, the factors associated with the uptake of PCV were, child out migration, maternal status, maternal HIV status at child birth, maternal employment and maternal residency in the DSA. Similarly, the study did not identify significant differences in child sex, place of residence, distance to health facility, wealth index, maternal age, and maternal education in the uptake of complete PCV among infants in the DSA.

The findings of this study reveal a strong relationship between mothers' education level and the vaccination status of their infants. Children born to mothers with secondary school education or higher were more likely to receive RV compared to those whose mothers had no education. These results confirm

with findings of previous studies conducted in Nigeria, Ethiopia and India (57-59). This is partly due to the fact that the mothers who have secondary school education or higher are more likely to have knowledge of child vaccinations as opposed to those who had no education. Education is also associated with greater awareness of proper immunization schedules. This knowledge can help them make informed decisions to vaccinate their children hence the higher uptake in this category. However maternal education was not significantly associated with complete PCV uptake. Maternal education is not associated with PCV uptake in this study, however an increasing trend in the uptake of PCV was observed with an increase in the maternal education levels.

We found that migration was significantly associated with vaccine uptake. Children who ever migrated outside the DSA during the study period were less likely to receive RV or PCV. Our study finding is consistent with previous studies that have also showed that there was low uptake of vaccination among migrants compared to non-migrants populations (63, 67). One possible reason for this could be due to the changes associated with the process of migration as some vaccination programs are performed by mobile clinics and campaigns at specific period therefore migrant children are likely to miss some vaccinations compared to non-migrant children. The likelihood that children who migrated outside the DSA with their mothers had no vaccination information in our study is high, given that key informants were less likely to remember all the vaccines a child received.

The study also demonstrated an association between maternal age and RV uptake. Children born to older mothers (>25 years) were more likely to receive complete RV compared to those of younger mothers (≤25 years). This study

finding is consistent with findings from other studies which showed that older women are more likely to vaccinate their children compared to younger mothers (72, 81). The authors of this paper suggest that younger mothers are more likely to have lower incomes compared with older mothers and this is a risk factor for low vaccination. However, we could no assess mother income as a factor for vaccine uptake due to lack of maternal income information. Again, older women are more likely to have knowledge and experiences of vaccination benefits and schedules compared to younger women hence are more likely to vaccinate their children. However, maternal age was not significantly associated with PCV uptake. This study finding is consistent with study findings conducted in the same study area where maternal age was not associated with PCV (50).

Our study also showed that mother residency in the DSA at child birth was associated with the complete uptake of RV or PCV. Children whose mothers were residents in the DSA at child birth were more likely to receive complete doses of RV compared to those whose mothers were not residents at child birth. The scientific significance of this finding is not known. However, there is a report which demonstrated that with the increased rural-urban migration in most sub-Saharan countries including South Africa, migration is a likely factor of low immunization uptake (80). However, little is known about the role of maternal residency in the DSA on child health outcomes such as childhood immunization.

The study demonstrated that maternal HIV positive status was a significant predictor of the uptake of complete RV or PCV. There was a marginally significant association between maternal HIV positive status and complete uptake of RV or PCV. Children whose mothers were HIV positive were more likely to receive complete RV or PCV compared to those children from HIV

negative mothers. This may be due to the fact that HIV positive mothers visit the clinics often for their monthly HIV visits for pre-ART and ART treatment and get the opportunity of being educated on the benefits of vaccination so as to keep their children well and also get to know when vaccinations are due for their children. However, this result does not support findings of a analytical cross-sectional study by Ndirangu *et al* in the same study setting in which children born to HIV-positive mothers were less likely to be vaccinated compared to those born to HIV-negative mothers (50). Our study looked at two new vaccines compared to the study by Ndirangu *et al* who looked at five vaccines. Additionally, certain differences in specific criteria used to define uptake and coverage of vaccines could also contribute to the differences observed between the present study and that of Ndirangu *et al*.

Our study also showed that employment status of mothers was associated with RV or PCV uptake. Children whose mothers were employed were less likely to receive complete doses of RV compared to mothers who were not employed. Studies which have looked at employment status of the mother on child vaccination have shown differing results. Some studies have shown that employment status of the mother is associated with low uptake of vaccination (82) while other studies have shown that children were more likely to be unimmunised if their mother was not employed or was self-employed (83). Mothers who are employed usually do not have time to vaccinate their children compared to mothers who are not working hence mothers who are working are less likely to vaccinate their children.

4.4 Limitations of the study

In considering the findings of this study, it is important to bear in mind the following limitations.

The first limitation of the study was that the data collection was done within the ongoing demographic surveillance of a relatively homogenous population and thus only limited information was collected and therefore other potential factors associated with vaccine uptake identified in other studies such as religion, and place of delivery were not available.

The second limitation of the study included reporting bias. Reporting bias could have occurred in cases where maternal recall was used to ascertain vaccine uptake status for a child. The mother may be reluctant or selective to report on her child's vaccine uptake status because of attitudes, beliefs and perception. Maternal recall however, is considered a valid measure of child vaccination coverage in the absence of vaccination records in developing countries (50, 84). Data is collected once every six (four since 2012) months from a key informant in a household. This may also introduce reporting bias since the key informant may not recall accurately the information concerning all members of the household over a period of the last six months and more especially for migrating mothers and children.

The third limitation is differential loss to follow up. Loss to follow-up bias may have occurred as a result of the differences in retention during the follow-up period or if the children who were lost from the cohort had different outcome distributions from those who remained in the cohort. We could not track all the children in the entire cohort for their vaccine uptake status. Children were lost to

follow-up as a result of death or migration. Among the 1,130 and 1,054 children whose vaccination uptake was unknown for RV and PCV respectively, 50% had never migrated outside the DSA. However, about 24% migrated outside the DSA before 12 months of their birth. Children who migrated outside the DSA before their first birthday were more likely not to have received their RV and PCV doses within the DSA. Differences in loss to follow-up can lead to bias as the children who were lost to follow-up may be more or less likely to have received complete RV or PCV. However, we do not think this biased our findings since the children whose vaccine uptake was not known and also migrated outside the DSA were few.

Finally our findings cannot be generalized to the entire South African children taken into consideration that the cohort included in the study was only children residents in the DSA.

4.5 Strengths of the study

To our knowledge, this is first study conducted in South Africa to specifically assess the uptake of RV and PCV after being introduced in 2008 using a population based longitudinal demographic surveillance data. The majority of the studies conducted on these new vaccines only examined their efficacy, safety and cost effectiveness.

The large population under surveillance in the DSA and the rigorous demographic surveillance system which continuously capture vital population statistics like births, deaths and migration longitudinally provided a platform for a reliable and rich data hence enables calculation of accurate vaccination rates.

The use of a population-based sample limits the issue of selection bias that would otherwise be introduced by hospital based studies and results obtained are consistent and comparable with other scientific findings in other settings hence the validity of the results were not compromised.

Chapter 5: Conclusions and Recommendations

5.1 Conclusions

While major progress has been made in the fight against vaccine-preventable diseases; gaps in vaccination uptake show that strengthening immunization programs remains vital. Our study showed that the uptake of complete RV and PCV were generally low among children in rural South Africa. The study found that the uptake of complete RV was higher among the children compared to the uptake of complete PCV. This may be as a result of the differences in the dose schedules for both vaccines since the last dose of PCV is administered on the 9 month. It is expected that RV coverage should be higher than PCV because of dropout and the long time gap between the second and third doses, in which the mother may not return back for the third dose. The limited uptake of complete RV documented in the study cohort and particularly for complete PCV uptake indicates the need for strategies to address the situation.

This study has identified migration as an important determinant of child vaccination for complete uptake of RV and PCV. The likelihood for complete uptake of both vaccines was higher among non-migrant children compared to children who migrated outside the DSA. These differences may had arise as a result of differentials by socio-economic status, catchment areas where mobile clinics operate, vaccine stock outs in some areas and the availability of health workers within local areas with limited access to health care facilities.

Another reason for the differences observed in RV and PCV uptake in the DSA and that of the national coverage may had arise from the differences in the

sources of data used to estimate uptake. In our study, vaccination information was based primarily on surveillance data, the proportion of vaccination information from maternal recall was high and also when vaccinations are not reported by lower administrative levels or part of the population is excluded from the data collection or reporting system, coverage can be underestimated.

Maternal age, maternal education, child out migration from the DSA, maternal HIV status at child birth, parity, maternal employment and maternal residency in the DSA were found to be factors associated with uptake of RV in rural South Africa. On the other hand, the factors found to be associated with the uptake of PCV were, child out migration, maternal status, maternal HIV status at child birth, maternal employment and maternal residency in the DSA.

5.2 Recommendations and Policy implications

Introduction of RV and PCV in South Africa is one of the greatest public health achievements. To have adequate diarrheal and pneumococcal disease protection, there is the need for continued interventions to improve RV and PCV uptake among children. Hence, the need to better understand the factors associated with the uptake of RV and PCV. Our findings point to a great need for comprehensive approaches to target interventions that aim to increase childhood uptake of complete doses of RV and PCV. Below are some recommendations:

1. Programmes targeting mothers of lower socio-economic status such as those with primary or no education are required. Such programmes may include vaccine awareness and immunization campaigns at the community level to improve vaccine uptake.

2. The rate of out-migrations among mothers especially among children whose mothers migrated within 12 months of their birth suggests the need for community level efforts in rural areas at increasing vaccination uptake, by improving the socio-economic situation of mothers in rural communities.

3. There is also a need to target areas with low uptake of RV and PCV in the DSA for equitable spatial distribution of maternal and child health services such as increasing the number of fixed clinics and mobile clinics for child vaccinations in the various small geographical areas in the DSA. This could improve vaccine uptake and reduce the disparities observed among the different local areas.

4. There should be national policy and strategy for monitoring and assessing the uptake of new vaccines. Efforts should be directed towards providing quality and equitable healthcare infrastructures that will maximize the uptake of vaccines and reduce the risk of diarrhoeal and pneumococcal diseases.

5. Further research is also needed in this area to explore why some children are not vaccinated. For instance there were some local areas which did not have fixed clinics but still had high RV and PCV uptake compared to some areas which had fixed clinics. In addition, there should be qualitative research exploring reasons why mothers do not take their children to be vaccinated.

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Appendices

Appendix A1: Vaccine Schedules for South Africa

health

Department:
Health
REPUBLIC OF SOUTH AFRICA

Expanded Programme on Immunisation – EPI (SA)
Revised Childhood Immunisation Schedule from April 2009

Age of Child	Vaccines needed	How and where is it given?
At Birth	**BCG** Bacilles Calmette Guerin	Right arm
	OPV (0) Oral Polio Vaccine	Drops by mouth
6 Weeks	**OPV (1)** Oral Polio Vaccine	Drops by mouth
	RV (1) Rotavirus Vaccine	Liquid by mouth
	DTaP-IPV//Hib (1) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined	Intramuscular / Left thigh
	Hep B (1) Hepatitis B Vaccine	Intramuscular / Right thigh
	PCV7 (1) Pneumococcal Conjugated Vaccine	Intramuscular / Right thigh
10 Weeks	**DTaP-IPV//Hib (2)** Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined	Intramuscular / Left thigh
	Hep B (2) Hepatitis B Vaccine	Intramuscular / Right thigh
14 Weeks	**RV (2)** Rotavirus Vaccine*	Liquid by mouth
	DTaP-IPV//Hib (3) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined	Intramuscular / Left thigh
	Hep B (3) Hepatitis B Vaccine	Intramuscular / Right thigh
	PCV7 (2) Pneumococcal Conjugated Vaccine	Intramuscular / Right thigh
9 Months	**Measles Vaccine (1)**	Intramuscular / Left thigh
	PCV7 (3) Pneumococcal Conjugated Vaccine	Intramuscular / Right thigh
18 Months	**DTaP-IPV//Hib (4)** Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine and *Haemophilus influenzae* type b Combined	Intramuscular / Left arm
	Measles Vaccine (2)	Intramuscular / Right arm
6 Years (Both boys and girls)	**Td Vaccine** Tetanus and reduced strength of diphtheria Vaccine	Intramuscular / Left arm
12 Years (Both boys and girls)	**Td Vaccine** Tetanus and reduced strength of diphtheria Vaccine	Intramuscular / Left arm

* Rotavirus Vaccine should NOT be administered after 24 weeks.

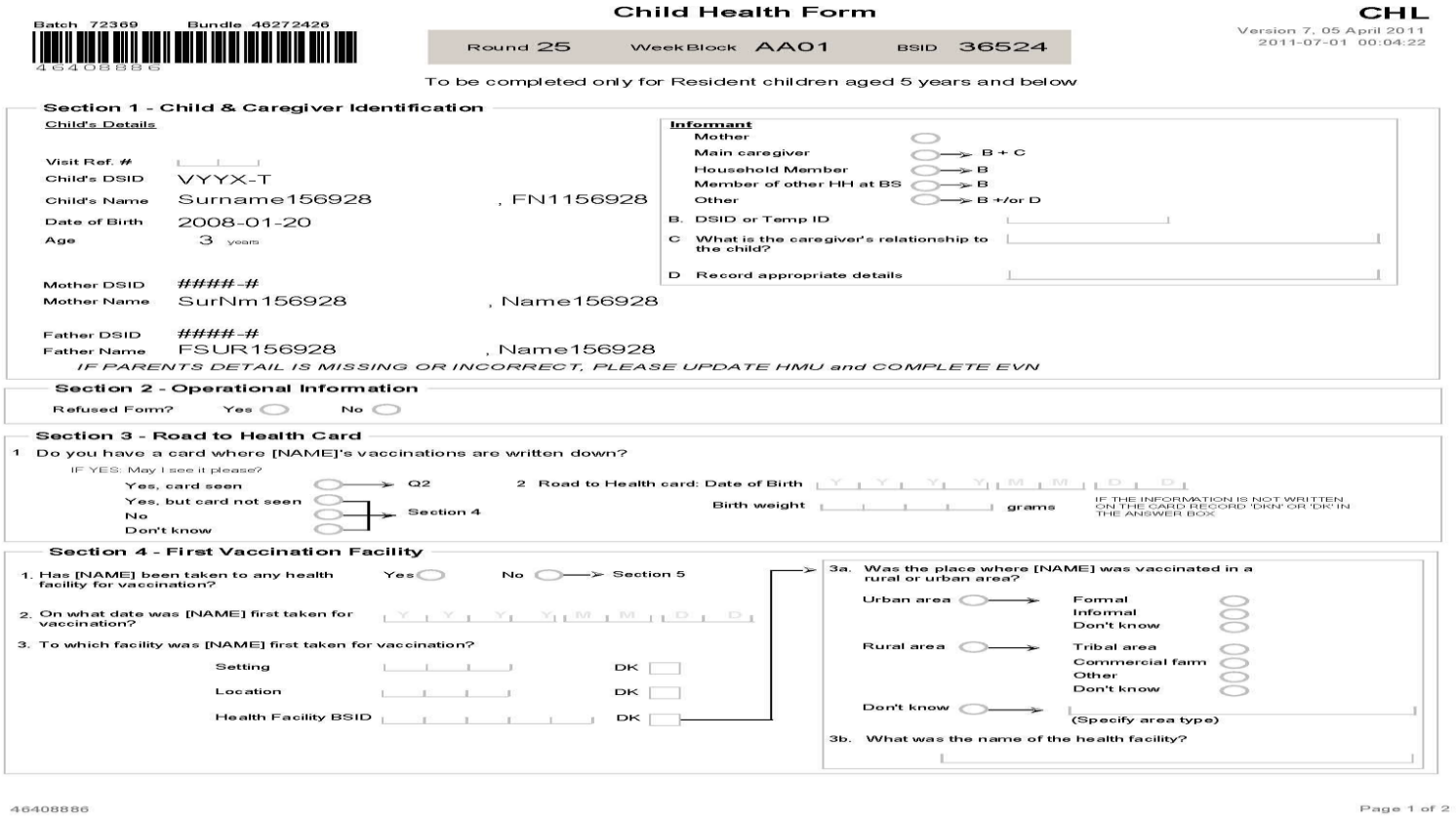
sanofi pasteur
The vaccines division of sanofi-aventis Group

Appendix B1: A summary of variables included in the study

Variable	Definition	Time of data collection	Variable type	Variable coding
Maternal Age	Age of the mother	Every census count	Independent	Dummy variables; categorised as <20; 20-290; >=30
Child gender	Gender of the child	Every census count	independent	Dummy variables: male or female
Child ART status	HIV status of the child	Every census count	independent	Dummy variables: Yes or No 0 = no;1 = yes
Maternal HIV status	Maternal HIV status	Every census count	independent	Dummy variables: positive; negative or unknown
Distance to health facility	Distance to the health facility	Every census count	independent	Categorised as Near (< 5Km) and Far (>= 5 Km)
Socio-economic status	Household socioeconomic status	Every census count	independent	Categorised as Poorest; Very poor Poor; Less poor; Least poor
Mother's vital status	Defined as whether mother as alive or dead	Every census count	independent	Categorised as alive or dead
Migration	Defined as whether a caregiver has moved into the study area or not	Every census count	independent	Categorised as Never; After 12 months; or Before 12 months

Rotavirus Vaccine uptake (RV)	Defined as whether a child had received complete RV or not during the study period.	Every census count	Dependent	Categorised as Complete or None 0 = none; 1 = complete
Pneumococcal conjugate vaccine uptake (PCV)	Defined as whether a child had received complete PCV or not during the study period.	Every census count	Dependent	Categorised as Complete or None 0 = none; 1 = complete

Appendix C1: Data collection form: Child Health Form (CHL)



Batch 72369 Bundle 46272426
46408886

Child Health Form — **CHL**
Version 7, 05 April 2011
2011-07-01 00:04:22

Round 25 Week Block AA01 BSID 36524

To be completed only for Resident children aged 5 years and below

Section 1 - Child & Caregiver Identification

Child's Details

Visit Ref. #
Child's DSID VYYX-T
Child's Name Surname156928 , FN1156928
Date of Birth 2008-01-20
Age 3 years

Mother DSID #####-#
Mother Name SurNm156928 , Name156928

Father DSID #####-#
Father Name FSUR156928 , Name156928

IF PARENTS DETAIL IS MISSING OR INCORRECT, PLEASE UPDATE HMU and COMPLETE EVN

Informant
Mother
Main caregiver → B + C
Household Member → B
Member of other HH at BS → B
Other → B +/or D

B. DSID or Temp ID
C What is the caregiver's relationship to the child?
D Record appropriate details

Section 2 - Operational Information

Refused Form? Yes No

Section 3 - Road to Health Card

1 Do you have a card where [NAME]'s vaccinations are written down?
IF YES: May I see it please?
Yes, card seen → Q2
Yes, but card not seen → Section 4
No → Section 4
Don't know → Section 4

2 Road to Health card: Date of Birth Y Y Y Y M M D D
Birth weight grams
IF THE INFORMATION IS NOT WRITTEN ON THE CARD RECORD 'DKN' OR 'DK' IN THE ANSWER BOX

Section 4 - First Vaccination Facility

1. Has [NAME] been taken to any health facility for vaccination? Yes No → Section 5
2. On what date was [NAME] first taken for vaccination? Y Y Y Y M M D D
3. To which facility was [NAME] first taken for vaccination?
Setting DK
Location DK
Health Facility BSID DK

3a. Was the place where [NAME] was vaccinated in a rural or urban area?
Urban area → Formal / Informal / Don't know
Rural area → Tribal area / Commercial farm / Other / Don't know
Don't know → (Specify area type)

3b. What was the name of the health facility?

46408886 Page 1 of 2

Appendix D1: Human Research Ethics Clearance Certificate for the study

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Georgina B Gyan

CLEARANCE CERTIFICATE	**M120936**
PROJECT	Factors Associated with Pneumococcal Conjugate and Rotavirus Vaccines Uptake among Under-Five Children: Evidence from the Africa Centre Demographic Surveillance Site, South Africa, 2008-2012
INVESTIGATORS	Ms Georgina B Gyan.
DEPARTMENT	School of Public Health
DATE CONSIDERED	28/09/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

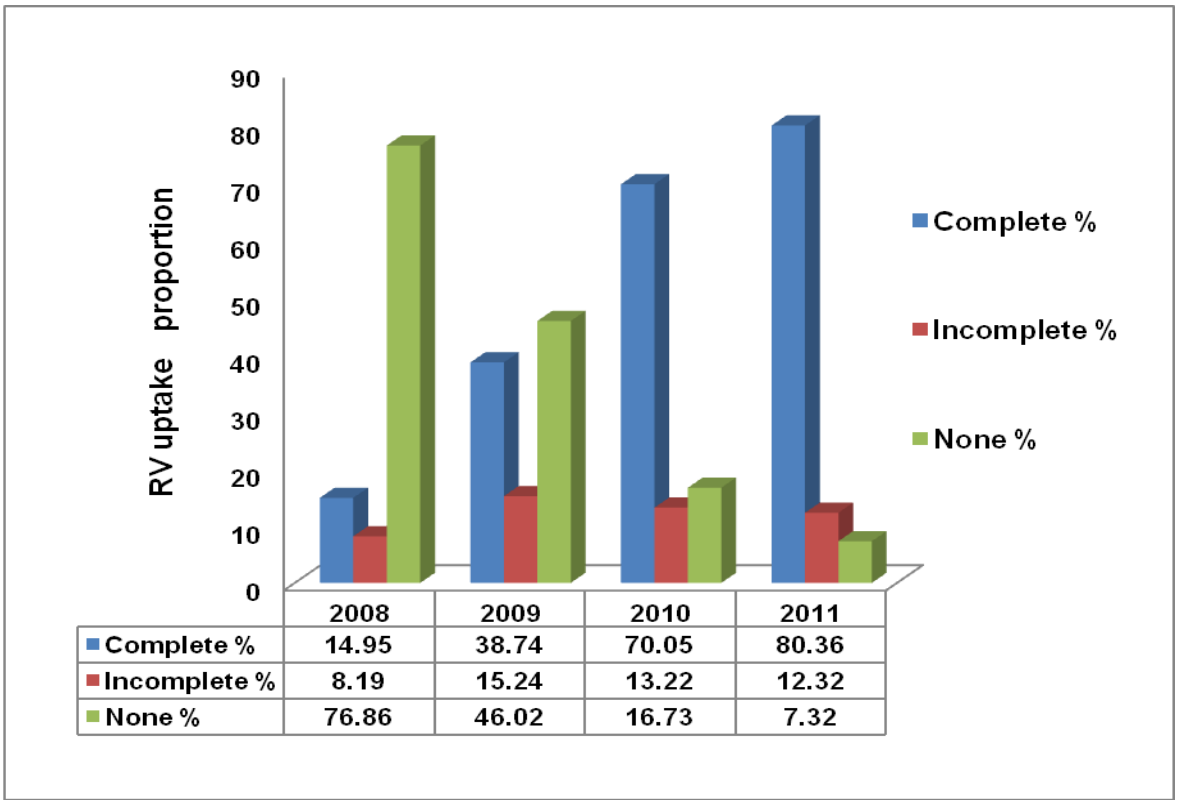
DATE 28/09/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr Charles Chasela

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

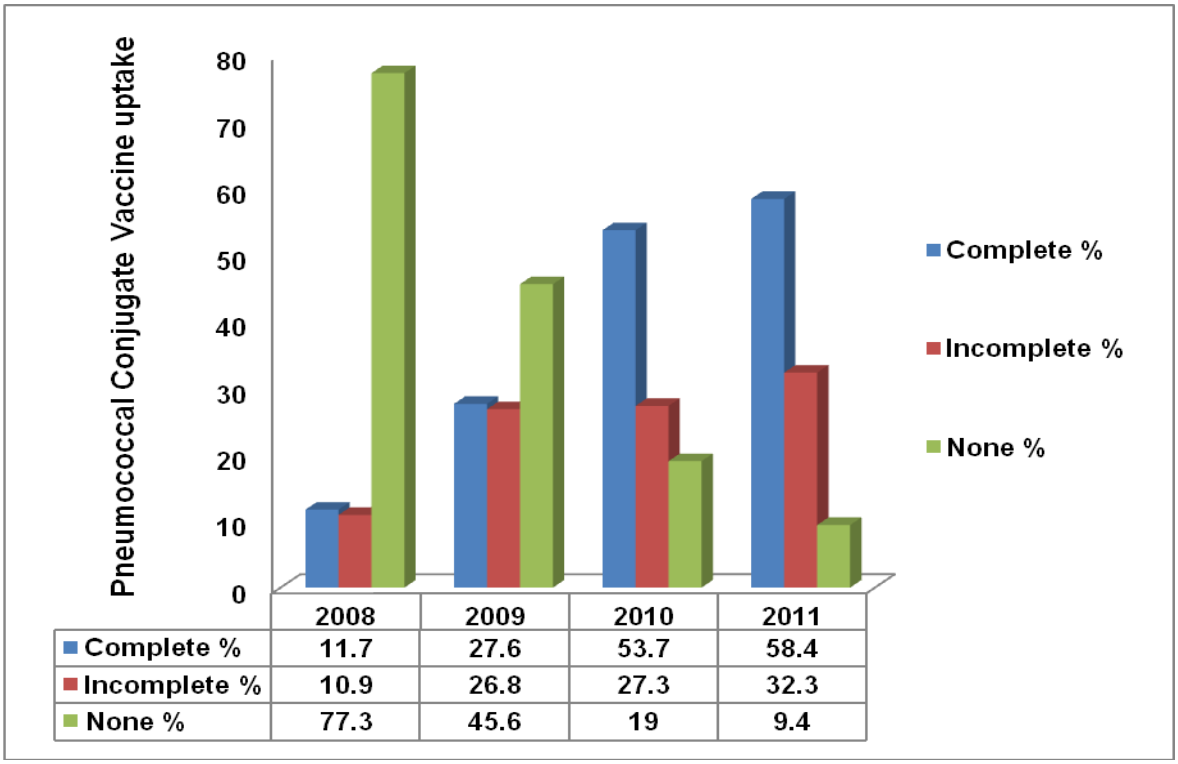
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix E1: Annual RV uptake among infants, 2008 to 2011



	2008	2009	2010	2011
Complete %	14.95	38.74	70.05	80.36
Incomplete %	8.19	15.24	13.22	12.32
None %	76.86	46.02	16.73	7.32

Appendix F1: Annual PCV uptake among infants, 2008 to 2011



	2008	2009	2010	2011
Complete %	11.7	27.6	53.7	58.4
Incomplete %	10.9	26.8	27.3	32.3
None %	77.3	45.6	19	9.4

Appendix G1: Multinomial logistic regression

Table 1: Factors associated with RV uptake among infants in univariable model.

Characteristic	None vs Complete RV		Incomplete vs Complete RV		
	Odds ratio (95% CI)	**p-value**	**Odds ratio (95% CI)**	**p-value**	**P-value (Overall Model)**
Sex of child					
Female	1		1		0.24
Male	0.99(0.87-1.08)	0.98	1.15(0.97-1.37)	0.10	
Child out migrated from DSA					
Never	1		1		<0.01
Ever	2.34(1.94-2.83)	<0.01	1.45(1.09-1.94)	0.01	
Place of residence					
Urban	1		1		0.02
Peri-urban	1.04(0.82-1.31)	0.72	0.68(0.50-0.93)	0.01	
Rural	0.96(0.75-1.23)	0.75	0.81(0.58-1.12)	0.63	
Distance to health facility					
<5km	1		1		0.52
≥5	1.07(0.91-1.26)	0.41	0.92(0.71-1.19)	0.39	
Wealth index					
Lowest	1		1		
Second	0.99(0.82-1.20)	0.94	1.27(0.96-1.69)	0.10	0.54
Middle	1.00(0.83-1.21)	0.97	1.24(0.93-165)	0.13	
Fourth	0.94(0.77-1.13)	0.49	0.95(0.71-1.28)	0.73	
Highest	0.96(0.78-1.17)	0.68	1.14(0.83-1.54)	0.41	
Maternal age					
<=25	1		1		0.11
>25	0.89 (0.79-1.01)	0.07	1.05 (0.88-1.26)	0.58	
Mother vital status					
Alive	1		1		0.12
Dead	1.68(1.00-2.79)	0.05	1.52(0.73-3.16)	0.26	
Maternal education					
None	1		1		<0.01
Primary	0.91(0.58-1.41)	0.67	0.84(0.45-1.58)	0.60	
Secondary	0.68(0.44-1.06)	0.09	0.67(0.36-1.25)	0.21	
Tertiary	0.72(0.44-1.17)	0.19	0.69(0.35-1.39)	0.34	
Unknown	0.48(0.31-0.77)	<0.01	0.58(0.31-1.11)	0.30	
Maternal HIV status at child birth					
Negative	1		1		0.04
Positive	0.83(0.71-0.96)	0.02	1.09()0.88-1.36	0.41	
Unknown	0.87(0.75-1.00)	0.07	1.05(0.84-1.31)	0.65	
Parity					
Parity 1	1		1		0.10
Parity 2-4	0.85(0.72-1.00)	0.06	1.00(0.79-1.26)	0.99	
Parity >5	1.17(0.87-1.43)	0.28	0.92(0.58-1.43)	0.70	
Mother Employed					
No	1		1		<0.01

Characteristic	None vs Complete RV		Incomplete vs Complete RV		
Yes	1.30(1.10-1.54)	0.02	1.48(1.17-1.88)	0.01	
Unknown	0.81(0.71-0.93)	0.03	0.88(0.72-1.08)	0.21	
Mother resident in the DSA at child birth					
No	1		1		<0.01
Yes	0.46(0.34-0.61)	<0.01	0.57(0.38-0.87)	0.01	

Table 2: Factors associated with RV uptake among infants in multivariable model.

Characteristic	None vs Complete RV		Incomplete vs Complete RV		
	Odds ratio (95% CI)	**p-value**	**Odds ratio (95% CI)**	**p-value**	**p- value (Overall Model)**
Sex of child					
Female	1		1		0.24
Male	0.99(0.88-1.08)	0.90	1.15(0.97-1.37)	0.12	
Child out migrated from DSA					
Never	1		1		<0.01
Ever	2.26(1.86-2.74)	<0.01	1.42(1.06-1.90)	0.02	
Place of residence					
Urban	1		1		0.05
Peri-urban	0.93(0.72-1.18)	0.99	0.68(0.49-0.94)	0.02	
Rural	1.00(0.78-1.27)	0.55	0.80(0.58-1.11)	0.19	
Maternal age					
<=25	1		1		0.11
>25	0.86 (0.75-0.99)	0.03	1.05 (0.88-1.26)	0.58	
Mother vital status					
Alive	1		1		0.16
Dead	1.65(0.98-2.78)	0.06	1.52(0.73-3.16)	0.26	
Maternal education					
None	1		1		<0.01
Primary	0.82(0.52-1.29)	0.56	0.83(0.44-1.57)	0.60	
Secondary	0.57(0.36-0.89)	0.12	0.60(0.32-1.14)	0.21	
Tertiary	0.55(0.33-0.90)	0.06	0.50(0.25-1.03)	0.34	
Unknown	0.52(0.32-0.83)	0.19	0.64(0.32-1.25)	0.30	
Maternal HIV status at child birth					
Negative	1		1		0.15
Positive	0.84(0.71-0.98)	0.03	1.01(0.81-1.27)	0.92	
Unknown	0.88(0.76-1.02)	0.11	1.01(0.81-1.26)	0.94	
Mother Employed					
No	1		1		<0.01
Yes	1.39(1.16-1.66)	<0.01	1.48(1.14-1.91)	0.02	
Unknown	0.78(0.71-0.93)	0.01	0.81(0.63-1.05)	0.11	
Mother resident in the DSA at child birth					
No	1		1		<0.01
Yes	0.60(0.39-0.91)	<0.01	0.57(0.38-0.87)	0.01	

Table 3: Factors associated with PCV uptake among infants in univariable model.

Characteristic	None vs Complete PCV		Incomplete vs Complete PCV		
	Odds ratio (95% CI)	**p-value**	**Odds ratio (95% CI)**	**p-value**	**p- value (Overall Model)**
Sex of child					
Female	1		1		0.96
Male	0.98(0.87-1.11)	0.80	0.98(0.85-1.13)	0.84	
Child out migrated from DSA					
Never	1		1		<0.01
Ever	2.41(1.96-2.96)	<0.01	1.27(0.98-1.64)	0.07	
Place of residence					
Urban	1		1		0.17
Peri-urban	0.94(0.74-1.21)	0.67	1.18(0.88-1.57)	0.26	
Rural	1.03(0.82-1.31)	0.77	1.07(0.81-1.41)	0.63	
Distance to health facility					
<5km	1		1		0.07
≥5	1.00(0.84-1.20)	0.96	0.81(0.66-0.99)	0.04	
Wealth index					
Lowest	1		1		
Second	1.03(0.84-1.26)	0.75	1.15(0.91-1.45)	0.25	0.73
Middle	0.99(0.81-1.21)	0.94	1.15(0.91-144)	0.25	
Fourth	0.97(0.80-1.19)	0.79	1.14(0.91-1.14)	0.26	
Highest	0.94(0.75-1.16)	0.54	0.95(0.74-1.21)	0.67	
Maternal age					
<=25	1		1		0.29
>25	0.91 (0.80-1.04)	0.16	1.00 (0.86-1.15)	0.58	
Mother vital status					
Alive	1		1		0.05
Dead	1.97(1.14-3.43)	0.02	1.47(0.77-2.80)	0.25	
Maternal education					
None	1		1		<0.01
Primary	0.96(0.61-1.52)	0.86	1.62(0.87-3.03)	0.13	
Secondary	0.72(0.46-1.12)	0.15	1.48(0.80-2.74)	0.21	
Tertiary	0.70(0.42-1.15)	0.19	1.32(0.68-2.57)	0.42	
Unknown	0.54(0.34-0.87)	0.01	1.36(0.73-2.56)	0.34	
Maternal HIV status at child birth					
Negative	1		1		0.04
Positive	0.83(0.71-0.98)	0.03	1.02()0.86-1.22)	0.81	
Unknown	0.83(0.71-0.97)	0.02	0.90(0.76-1.08)	0.26	
Parity					
Parity 1	1		1		0.31
Parity 2-4	0.90(0.75-1.07)	0.22	0.98(0.81-1.19)	0.84	
Parity >5	1.11(0.82-1.51)	0.50	0.87(0.60-1.25)	0.45	
Mother Employed					
No	1		1		<0.01
Yes	1.27(1.06-1.51)	<0.01	1.08(0.88-1.33)	0.46	
Unknown	0.81(0.70-0.94)	<0.01	0.93(0.79-1.09)	0.38	
Mother resident in the					

Characteristic	None vs Complete PCV		Incomplete vs Complete PCV		
DSA at child birth					
No	1		1		<0.01
Yes	0.52(0.38-0.70)	<0.01	0.88(0.60-1.28)	0.01	

Table 4: Factors associated with PCV uptake among infants in a multivariable model.

Characteristic	None vs Complete PCV		Incomplete vs Complete PCV		
	Odds ratio (95% CI)	**p-value**	**Odds ratio (95% CI)**	**p-value**	**p- value (Overall Model)**
Sex of child					
Female	1		1		0.93
Male	0.98(0.86-1.11)	0.72	0.98(0.85-1.14)	0.83	
Child out migrated from DSA					
Never	1		1		<0.01
Ever	2.38(1.93-2.94)	<0.01	1.27(0.98-1.64)	0.07	
Place of residence					
Urban	1		1		0.29
Peri-urban	0.91(0.70-1.17)	0.96	1.16(0.87-1.56)	0.01	
Rural	1.01(0.73-1.29)	0.46	1.11 (0.83-1.48)	<0.01	
Distance to health facility					
<5km	1		1		0.13
≥5	0.92(0.70-1.17)	0.46	0.80(0.64-1.00)	0.39	
<=25	1		1		0.06
>25	1.93 (1.10-3.39)	0.02	1.41(0.74-2.71)	0.30	
Maternal education					
None	1		1		<0.01
Primary	0.93(0.58-1.47)	0.75	1.63(0.87-3.06)	0.13	
Secondary	0.65(0.41-1.02)	0.06	1.45(0.78-2.69)	0.24	
Tertiary	0.56(0.34-0.94)	0.03	1.24(0.63-2.44)	0.53	
Unknown	0.61(0.37-0.99)	0.04	1.46(0.76-2.79)	0.25	
Maternal HIV status at child birth					
Negative	1		1		0.03
Positive	0.80(0.68-0.95)	0.02	0.99(0.83-1.18)	0.94	
Unknown	0.83(0.71-0.98)	0.03	0.90(0.75-1.08)	0.25	
Mother Employed					
No	1		1		<0.01
Yes	1.33(1.10-1.61)	<0.01	1.12 (0.89-1.39)	0.32	
Unknown	0.80(0.67-0.96)	0.01	0.92(0.76-1.12)	0.41	
Mother resident in the DSA at child birth					
No	1		1		<0.01
Yes	0.55(0.34-0.61)	<0.01	0.88(0.60-1.28)	0.01	