

**FACTORS ASSOCIATED WITH VACCINATION STATUS IN CHILDREN UNDER
5 YEARS OF AGE IN TWO COMMUNITIES IN SOUTH AFRICA**

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Declaration

I declare that this research report is my own work. It is being submitted in partial fulfillment of the requirements for the degree of Master of Science in Epidemiology in the field of Epidemiology & Biostatistics at the University of the Witwatersrand, Johannesburg. This research has not been submitted previously for any degree or examination to any other institution.

A handwritten signature in black ink, appearing to read 'Thandiwe', is written over a horizontal line.

Thandiwe Mthiyane

November 2016

Dedication

I dedicate this work to my mother Ntombiyenkosi Shabalala. Thank you for your support, encouragement and prayers. Thank you for believing in me and supporting my decisions. I am honoured to have you in my life.

Abstract

Background

The vaccination coverage estimates reported for South Africa by WHO are below the 90% target indicating that many children in South Africa remain unvaccinated. Data on proportion of children with delayed vaccination and factors leading to missed and delayed vaccination are limited in this setting. The aim of this study was to describe the vaccination coverage and assess factors associated with missed and delayed vaccination in South Africa.

Methods and material

A secondary data analysis which used data from two Healthcare Utilisation Surveys was conducted in Soweto, Johannesburg in 2012 and in Edendale, Pietermaritzburg in 2013. The analysis was restricted to children aged less than 5 years who had immunisation cards/vaccine histories. Vaccination coverage and proportion of children with delayed vaccination were calculated for each vaccine dose recommended during the first year of life as described in the South Africa Expanded Programme on Immunisation. Pearson's Chi square test and Fisher's exact test were used to compare vaccination coverage across sites. Factors association with delayed and missed third doses of the Diphtheria Tetanus Pertussis vaccine (DTP3) were assessed using univariate and multivariate logistic regression models.

Results

Vaccination coverage was high (above 90%) for most vaccines except for the third dose of the pneumococcal conjugated vaccine (PCV3) and the second dose of rotavirus vaccine, which had coverage of 80.3% and 85.4% respectively. In Edendale, the coverage for all

vaccines appeared to be lower than in Soweto. Vaccination coverage in Soweto ranged from 83.4% to 99.4% and 66.9% to 95.9% in Edendale. In Soweto, DTP3 coverage decreased significantly from 2008 to 2012 ($p < 0.0001$). The highest DTP3 coverage in Soweto was in children aged 48-59 months (98.4%, $p < 0.0001$). In Edendale there was no significant trend observed in coverage by age group or year. A higher proportion of delayed DTP3 vaccination was observed among children aged 12-23 months in Soweto (36.7%, $p = 0.007$) and among children aged 36-47 months in Edendale (42.3%, $p < 0.0001$). Delays were more common in children born in 2010 (47.2%, $p < 0.0001$).

Factors associated with missed vaccination after controlling for other factors were child's age below 12 months (OR 2.7, 95% CI 1.2-5.9) compared to children age 12-23 months, two or more children aged less than 5 years of age in a household (OR 2.5, 95% CI 1.4-4.5) compared to one child and household monthly income less than R500 (OR 2.9, 95% CI 1.03-8.0) compared to a monthly income of more than R2000.

Factors associated with delayed vaccination after adjusting for other factors included being born in 2010 (OR 2.9, 95% CI 1.3-6.3) or 2011 (OR 2.7, 95% CI 1.3-5.8) compared to being born in 2008 and a low level of education for the primary caregiver, where caregivers who completed secondary education was associated with lower odds of delayed vaccination (OR 0.5, 95% CI 0.3-0.9) compared with caregivers who had only primary education.

Discussion

Although most vaccines had high coverage, there were substantial delays in receipt of some vaccines. This difference suggests that both coverage and timely vaccination may be useful as an indicator for immunisation programme performance. Efforts to increase vaccination

coverage and timeliness should take into account caregiver's level of education, number of children aged less 5 years in a household, household income and child's age to improve child health. Vulnerable groups identified in this study should be targeted with improved vaccination services to enhance uptake and timeliness of vaccination.

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ABBREVIATIONS

ANC-antenatal care

BCG- Bacillus Calmette Guerin

CI-confidence interval

DTP- Diphtheria Tetanus Pertussis

EPI- Expanded Programme on Immunisation

GVAP- Global Vaccine Action Plan

HepB- Hepatitis B

Hib- *Haemophilus influenzae* type b

HIV-Human Immunodeficiency Virus

HUS-Healthcare Utilisation Survey

IPV- Inactivated Polio Vaccine

MCV- Measles containing vaccine

OPV- Oral Polio Vaccine

OR-Odds ratio

PCV-Pneumococcal Conjugated Vaccine

Pol-Polio vaccine

Rota-Rotavirus vaccine

RTHC- Road-to-Health Card

UNICEF-United Nations International Children's Emergency Fund

VCT-voluntary counselling and testing

WHO- World Health Organization

CHAPTER 1

1.1 Background

In 2010, of 7.6 million children who died before the age of five years; about two thirds died of vaccine preventable diseases. Sub-Saharan Africa has the highest under-five mortality rate with 103 deaths per 1000 live births in 2010 and 92 deaths per 1000 live births in 2013 (1, 2). One possible factor contributing to the high mortality rate from vaccine preventable diseases may be the failure to complete all age-appropriate doses of vaccines as specified in the World Health Organization (WHO) immunisation recommendations (3). Approximately 17% of global annual under-five mortality could potentially be prevented through increasing routine vaccination coverage; 2.2% prevented through pertussis vaccination, 2.3% through *Haemophilus influenzae* type b (Hib) vaccination, 1.3% through measles vaccination, 0.7% through tetanus vaccination, 5.2% through rotavirus vaccination and 5.4% through pneumococcal vaccination (4, 5).

Despite global improvements in vaccine coverage, it remains lowest in the African continent with only 75% of children having received the third dose of Diphtheria Tetanus Pertussis vaccine (DTP3) in 2013 (6). In South Africa there is variation in vaccination coverage between different provinces and districts, where some areas have high vaccination coverage with figures exceeding 100% for some vaccines which indicates the lack of accurate data (7). While immunisation programmes emphasise high coverage, delays in receipt of vaccines are often not taken into consideration (8) and studies have shown that vaccination delays can occur even in countries with high vaccination coverage (9). Delayed vaccination leaves children susceptible to diseases and reduces herd immunity which prevents the spread of a disease in a population. It is therefore vital not only to assess vaccine coverage but also timeliness of vaccination.

1.2 Literature Review

1.2.1 Vaccination coverage

Vaccination coverage is defined as the proportion of individuals in the target population who are vaccinated (10). According to The Global Vaccine Action Plan, 2011–2020 (GVAP), endorsed by the World Health Assembly in 2012, all countries should aim to reach a target of 90% national coverage for all vaccines and at least 80% coverage in all districts by 2015, with sustained high coverage levels for 3 years by 2020 (11). In South Africa the target of 90% has not been reached for most vaccines in recent years: WHO and UNICEF estimates in 2013 were 65% for DTP3, Hib3 and Hepatitis B Vaccine (HepB3), 84% for Bacillus Calmette Guerin (BCG), 66% for the first dose of measles containing vaccine (MCV1), 66% for the third dose of polio vaccine (Pol3), 58% for MCV2, 64% for second dose rotavirus vaccine (Rota2) and 62% for the third dose of pneumococcal conjugated vaccine (PCV3) (12).

DTP3 coverage at 12 months of age is considered as the main indicator of immunisation programme performance as it reflects the ability of the family to access and utilise immunisation services on multiple visits, and service performance. Globally, DTP3 coverage has remained constant since 2009 with estimated coverage rates reported as 86% in 2014 (13). Although there is great improvement in immunisation services in Africa, large numbers of children remain unvaccinated. In 2013, more than one-third of children who did not receive DTP3 were from Africa and South Africa ranked 9th amongst countries with the largest number of under vaccinated children based on WHO and UNICEF estimates (6). WHO estimates are derived through an annual country review of all available data, including administrative and survey-based coverage data. All these data have their limitations; therefore the quality of these estimates is unknown.

1.2.2 Vaccination coverage estimates from administrative data

Administrative data estimates are calculated from health facility routine data in which the total number of children in the community forms part of the denominator and the number of vaccinations administered during a given period are included in the numerator. These estimates may be useful in monitoring the local health system performance to identify service delivery problems at an early stage (14). Changes in the target population (i.e. through migration, mortality and fertility) can affect the administrative estimates; therefore, the denominator needs to be updated constantly. Administrative data estimates may be overestimated if the denominator includes children who are not part of the target population. For example, in 2009 the DTP3 administrative estimate for South Africa was 107% because of an underestimated target population (12). Therefore, supplementary immunisation data from other sources may be useful to compare with administrative data estimates.

1.2.3 Vaccination coverage estimates from immunisation surveys

Immunisation coverage surveys, such as Demographic and Health Surveys and UNICEF Multiple Indicator Cluster Surveys, produce estimates from a representative sample of households with children in a target age group and may include vaccine doses administered in private health facilities (10, 14). Surveys do not only collect data on vaccine coverage but also collect data on factors that contribute to low vaccine coverage; therefore, household survey data may be useful in assessing both individual and household level factors that are associated with missed and delayed vaccinations. Survey coverage estimates may not be relevant for timely programme interventions as they provide information only on the previous birth cohorts. In addition, they are subject to recall bias and may only be generalisable to populations being surveyed (14).

According to the WHO recommended approach to immunisation surveys, coverage estimates can be calculated using immunisation card information only or card plus verbal history (10). Card only estimates are calculated from vaccine doses which are recorded in the health card only while card plus history estimates are based on all vaccinations including those reported by a mother or caregiver. Coverage estimates by card plus verbal history are usually higher than card only estimates; for example, coverage for fully immunised children in Somaliland in 2008 was 3.2% by card only and 25.8% by card plus verbal history (15). Mothers are more likely to report that children received more vaccine doses than demonstrated by information in the immunisation cards (16). Immunisation cards for older children (aged 4 to 5 years) are more likely to be lost, and hence caregivers usually provide immunisation history verbally for older children (17). Since it may be difficult for a mother to remember the number of vaccines a child received and dates at which they were administered, this may lead to biased coverage estimates. Incorrect estimates could mislead policy makers when setting priorities which can result in disease outbreak if areas with low vaccination coverage are misclassified as having high vaccination coverage. Thus, multiple data sources are required to produce accurate vaccination coverage estimates.

1.2.4 Timeliness of childhood vaccinations

Most children receive all the doses recommended for their age but some do not adhere to these schedules due to different reasons (18). Some children receive their vaccines prior to the recommended schedule while some have delays in receiving vaccines. Vaccine doses administered too close together or too early can lead to suboptimal immune response (19). If a vaccine dose was administered too early it should be considered as invalid and be repeated as age appropriate with correct spacing before any future doses.

In countries where there is a high burden of infectious diseases, timeliness of vaccinations should be improved to reduce susceptibility to vaccine preventable diseases. Previous studies recommended that timely vaccination coverage should be considered as a major indicator of immunisation programme performance because high coverage alone cannot ensure adequate protection of children from infections (16, 20). Since timeliness can only be determined from documented vaccination dates it may be difficult to assess timeliness of vaccinations if there are large numbers of children with verbal vaccine histories only.

1.2.5 Factors associated with delayed vaccination

Previous studies have found that doses given to later age groups are more likely to be delayed compared to birth vaccine doses (21-23). Delays increase with the number of vaccine doses (24, 25), for example, DTP3 vaccination is more likely to be delayed than DTP1. This suggests that older children tend to have more delays in receiving vaccination compared to younger children. Delayed vaccination with birth doses is higher in rural areas than in urban areas (26), possibly due to limited access to healthcare facilities and higher rates of home births in rural areas. Studies have found that delays are more prevalent for DTP3 than BCG (27) likely because BCG is administered immediately after birth reducing the likelihood of delays particularly for children born in health facilities.

Children with many siblings are likely to have delays in receiving vaccinations (28). Similarly, birth order of children is associated with delayed vaccination as the first born child is likely to be vaccinated more on time compared to subsequent children (26). If there is more than one child in a household, caregivers may have limited time and resources for every child to access healthcare appropriately.

Previous utilisation of healthcare services such as tetanus toxoid vaccination and antenatal care of mothers increases the likelihood of timely vaccination for their children (16). Delays

in previous vaccines increase the likelihood of delays in subsequent vaccines, extending the period of vulnerability to diseases. This could result in disease outbreaks if children who experience vaccine delays are from densely populated areas (29).

1.2.6 Factors associated with missed vaccination

Many studies have shown that missed vaccinations are associated with higher mortality and morbidity (24, 30-32), as children who miss vaccinations have a higher risk of developing severe illness. Thus, incomplete vaccination status is one of the risk factors contributing to high mortality in children. The factors that are associated with missed vaccinations include individual, interpersonal, structural and clinic-related factors. Studies have found that children from poor families, whose mothers have no access to media, have low health seeking behaviour and only have primary education, are likely to miss vaccinations (5, 8, 19, 23, 28, 33, 34). In contrast, a study which evaluated the influence of media use on vaccination rates showed that women who watch television daily and those who listen to radio daily are more likely to have their children vaccinated regardless of their socio-economic status (35).

As mentioned the healthcare utilisation behaviour of mothers/caregivers during pregnancy influences the immunisation of their children, as mothers who use antenatal care services may have the opportunity to get advice from health professionals and gain better knowledge of vaccination schedules (36). Children of good ANC attendees are more likely to have frequent check-ups which is associated with complete vaccination (37, 38). Children who do not live with their mothers are less likely to be vaccinated compared to those who live with their mothers (39).

In South Africa, a study conducted in KwaZulu-Natal showed an association between maternal HIV status and vaccination status, with children whose mothers were HIV positive being more likely to miss vaccinations compared to those whose mothers were HIV negative

(40). The beliefs and attitudes of parents also affects the vaccination status of their children as some parents do not vaccinate their children because they think it is unnecessary to vaccinate them, or they are concerned about the side effects of vaccines (41). Children whose mothers understand the importance of immunisation are more likely to be vaccinated compared to children whose mothers have less knowledge regarding the benefits of immunisation (42, 43).

The place of birth of a child is also associated with complete vaccination as children born in health facilities are more likely to be fully vaccinated than those born at home (37, 44, 45). For example, children born at home may miss their BCG vaccine dose. There are also disparities between private and public sectors in providing birth vaccines where private hospitals perform worse than public sector facilities (46).

Studies have found that a short birth interval between subsequent children (47, 48) reduces the likelihood of complete vaccination in children, especially those younger than 18 months of age (39, 47). There are also community related factors that are associated with completeness of vaccination status. For example, community health workers have been found to influence community members by encouraging them to seek healthcare. They also have a better understanding of the community and might bring health services to the people according to their needs (45, 48).

Living closer to a healthcare facility in terms of time travelled (within 30 minutes) (49) or distance (within 5km) (50) was found to reduce the likelihood of a child been unvaccinated compared to those who live further from the facility. Travel costs may also be a problem for children from poor families and may limit access (48). Mothers who live closer are able to come back if there is long queue while those who live far might have transport problems and decide to postpone the vaccination. There are immunisation clinic-related factors resulting in

children missing vaccine, for example; being told by clinic staff to come back another time or given an incorrect return date.

In South Africa only a few studies have explored risk factors associated with vaccination status (6, 40, 41); there is therefore a need for more studies that will look at factors associated with missed and delayed vaccination to advise public health policy.

1.3 Statement of the problem

In South Africa many children miss vaccines or have delays in receiving vaccines even though the Department of Health provides free vaccines for all infants and children under 12 years of age. This leaves children vulnerable to the risk of vaccine preventable disease for a prolonged period of time, potentially resulting in higher morbidity and mortality. According to the WHO immunisation coverage data, only 75% of appropriately aged children in South Africa received DTP3 in 2013 which is below the recommended target of 90%. In addition data on the percentage of children with delayed vaccinations and factors leading to missed and delayed vaccination are limited in this setting.

1.4 Justification

Understanding the factors associated with missed and delayed vaccination may help understand the population of children mostly likely to miss or delay vaccination and help policy makers to target these groups with improved vaccination services. This could possibly help increase vaccination timeliness and vaccine uptake, and therefore reduce deaths caused by vaccine preventable diseases.

1.4 Research Question

What are the factors that are associated with missed and delayed vaccination in children under 5 years of age in two communities of South Africa?

1.5 Study Objectives

1. To describe the vaccination coverage and proportion of children with delayed vaccination for different vaccines in children under 5 years of age in two communities in South Africa enrolled in 2012-2013.
2. To describe the characteristics of children with missed, delayed and timely DTP3 vaccination among children under 5 years of age in two communities in South Africa enrolled in 2012-2013.
3. To determine the factors associated with missed or delayed DTP3 vaccination among children under 5 years of age in two communities in South Africa enrolled in 2012-2013.

CHAPTER 2

This chapter gives a full description of methods used in this study. Since the study was a secondary data analysis, the methods for primary study will also be described.

2.1 Primary study methods

The aim of the primary study was to assess the healthcare utilisation behaviours of defined populations for common illnesses and conditions such as respiratory diseases. The cross-sectional surveys were conducted in areas surrounding two hospital-based sentinel severe acute respiratory infection (SARI) surveillance sites, Chris Hani Baragwanath Hospital and Edendale Hospital. Since immunisation coverage indicates the extent to which children access primary healthcare services, information on vaccination status for children <5 years of age was also collected.

2.1.1 Study setting

This study was based in two sites in South Africa: Soweto and surrounding areas which were assumed to access Chris Hani Baragwanath Hospital for health care and certain areas of Pietermaritzburg which were assumed to access Edendale Hospital for health care. Soweto is an urban township outside Johannesburg, Gauteng Province, with a population of approximately 1.3 million in 2011 (51). Edendale Hospital is located in Pietermaritzburg, KwaZulu-Natal Province and is one of the main public hospitals in the area. The population of Pietermaritzburg was approximately 618,536 in 2011 (51).

2.1.3 Sample size calculation

The sample size was calculated to estimate healthcare utilisation for pneumonia with 95% confidence interval and 10% precision based on the following assumptions in Soweto:

- Cumulative incidence of pneumonia: 2%
- Percent of pneumonia seeking healthcare: 50%
- Non-response rate: 15%
- Household size: 3.5

Based on the above assumptions, we aimed to visit a total of 1614 households in Soweto.

Based on the high refusal rate in the Soweto HUS, the sample size for the Edendale HUS was inflated assuming a higher refusal rate. In Edendale a total of 2382 households were randomly selected.

2.1.4 Sampling method

For the Soweto HUS a list of households within the catchment area was not available, Google Earth (2012) was used to identify boundaries of each residential neighbourhood. Households were selected for participation by a simple random sample of geographic coordinates (latitude and longitude) within the boundaries of what were considered the residential areas of each site. The closest dwelling within 30 m of the randomly selected coordinates was approached for enrolment (52). For the Pietermaritzburg HUS, a complete list of households within the catchment area was available and dwellings were therefore enumerated. Households were then selected by simple random sampling.

2.1.5 Data Collection

The Healthcare Utilisation Surveys were conducted in Soweto in 2012 and in Pietermaritzburg in 2013. Data were collected using standardised questionnaires where members of the household were interviewed about demographic information, medical

conditions and healthcare utilisation. The interviews were conducted in the preferred language of the household by community health workers. The information on vaccination status was recorded from road-to-health cards (RTHCs) and in Soweto from clinic records when RTHCs were missing. Clinic visits for missing data were not done in Edendale.

2.2 Secondary analysis methods

2.2.1 Study design

The study design is cross-sectional.

2.2.2 Data source

Data were provided by the Centre for Respiratory Diseases and Meningitis at the National Institute for Communicable Diseases.

2.2.3 Study population

Children aged <5 years living in Soweto and surrounding areas in 2012 and in Pietermaritzburg in the areas surrounding Edendale Hospital in 2013.

2.2.4 Study sample

All children younger than 5 years of age were sampled from those who participated in the primary study. The primary study was two Healthcare Utilisation Surveys (HUSs).

2.2.5 Inclusion criteria

- **Objective 1**
 - Children with a RTHC or vaccine history from clinic records

- Children aged 1-59 months
- **Objective 2 and 3**
 - Children with a RTHC or vaccine history from clinic records
 - Children aged 18 weeks to 59 months

2.2.6 Exclusion criteria

- **Objective 1, 2 and 3**
 - Unable to provide RTHC or vaccine history
 - Refused consent

2.2.7 Measurement of variables

2.2.7.1 Vaccination coverage (Objective 1)

Vaccination coverage was derived for each vaccine dose administered in the first year of life, by dividing the number of children who received a particular dose of vaccine by the number of children eligible to receive that particular dose. Children who did not have RTHC or vaccine history from clinic records were not included in the denominator. Children were considered as fully immunised if they had received all primary vaccine doses recommended by 12 months of age, therefore vaccine doses recommended at 18 months of age were not included in the analysis (Table 1). The age of a child, calculated using date of birth and survey date, was used to determine whether or not a child was eligible to receive a specific vaccine dose.

- For all vaccine doses recommended at birth, the numerator was children aged 1-59 months who received a vaccine dose and the denominator was all children aged 1-59

months. We assumed that most children received their birth vaccines immediately after birth.

- For all vaccine doses recommended at 6 weeks, the numerator was children aged 10 weeks-59 months who received a vaccine dose and the denominator was all children aged 10 weeks-59 months. We used 10 weeks as our minimum age to capture children who might have received their vaccinations late (after 4 weeks of the recommended age). Since PCV and rotavirus vaccines were introduced in the South Africa's EPI schedule in April and August 2009 respectively, children born before 15 February 2009 were excluded in the analysis that involved PCV and children born before 15 June 2009 were excluded from the analysis of rotavirus vaccine. Oral polio vaccine (OPV) and Inactive polio vaccine (IPV) at 6 weeks were considered as a single dose (OPV/IPV Dose 1) in the analysis.
- For all vaccine doses recommended at 10 weeks, the numerator was children aged 14 weeks-59 months who received a vaccine dose and the denominator was all children aged 14 weeks-59 months. We used 14 weeks as our minimum age to capture children who might have received their vaccinations late (after 4 weeks of the recommended age).
- For all vaccine doses recommended at 14 weeks, the numerator was children aged 18 weeks-59 months who received a vaccine dose and the denominator was all children aged 18 weeks-59 months. We used 18 weeks as our minimum age to capture children who might have received their vaccinations late (after 4 weeks of the recommended age). Children born before 15 February 2009 were excluded in the analysis that involved PCV and children born before 15 June 2009 were excluded from the analysis of rotavirus.

- For all vaccine doses recommended at 9 months, the numerator was children aged 10-59 months who received a vaccine dose and the denominator was all children aged 10-59 months. We used 10 months as our minimum age to capture children who might have received their vaccinations late (after 4 weeks of the recommended age). Children born before 15 February 2009 were excluded in the analysis that involved PCV.

Table 1: South Africa's Expanded Programme on Immunisation (EPI) Schedule in 2012-2013

AGE OF CHILD	VACCINE NEEDED
At birth	OPV(0) Oral Polio Vaccine
	BCG Bacillus Calmette Guerin
6 weeks	OPV(1) Oral Polio Vaccine
	RV (1) Rotavirus Vaccine
	DTaP-IPV//HIB(1) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine & <i>Haemophilus influenzae</i> type b combined
	Hep B(1) Hepatitis B Vaccine
	PCV(1) Pneumococcal Conjugated Vaccine
10 weeks	Hep B(2) Hepatitis B Vaccine
	DTaP-IPV//HIB(2) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine & <i>Haemophilus influenzae</i> type b combined
14 weeks	RV (2) Rotavirus Vaccine
	DTaP-IPV//HIB(3) Diphtheria, Tetanus, acellular Pertussis, Inactivated Polio Vaccine & <i>Haemophilus influenzae</i> type b combined
	Hep B(3) Hepatitis B Vaccine
	PCV(2) Pneumococcal Conjugated Vaccine
9 months	Measles Vaccine(1)
	PCV(3) Pneumococcal Conjugated Vaccine

0-birth dose, 1-first dose, 2-second dose, 3-third dose

2.2.7.2 Delayed vaccination coverage (Objective 1)

Delayed vaccination coverage was calculated by dividing the number of children who received a vaccine dose after 4 weeks of the recommended age by the total number of

children who received that particular dose. The age at vaccination was used to determine whether or not the vaccine dose was delayed.

- For all vaccine doses recommended at birth, the numerator was children aged 1-59 months who received their vaccine dose after 4 weeks of birth and the denominator was all children aged 1-59 months who received a vaccine dose.
- For all vaccine doses recommended at 6 weeks, the numerator was children aged 10 weeks-59 months who received a vaccine dose after 10 weeks and the denominator was all children aged 10 weeks-59 months who received a vaccine dose. Children born before 15 February 2009 were excluded in the analysis that involved PCV and children born before 15 June 2009 were excluded from the analysis of rotavirus. Oral polio vaccine (OPV) and Inactive polio vaccine (IPV) at 6 weeks were considered as a single dose (OPV/IPV Dose 1) in the analysis.
- For all vaccine doses recommended at 10 weeks, the numerator was children aged 14 weeks-59 months who received a vaccine dose after 14 weeks and the denominator was all children aged 14 weeks-59 months who received a vaccine dose.
- For all vaccine doses recommended at 14 weeks, the numerator was children aged 18 weeks-59 months who received vaccine dose after 18 weeks and the denominator was all children aged 18 weeks-59 months who received a vaccine dose. Children born before 15 February 2009 were excluded from the analysis that involved PCV and children born before 15 June 2009 were excluded from the analysis of rotavirus.
- For all vaccine doses recommended at 9 months, the numerator was children aged 10-59 months who received a vaccine dose after 10 months and the denominator was all children aged 10-59 months who received a vaccine dose. Children born before 15 February 2009 were excluded from the analysis that involved PCV.

2.2.7.3 DTP3 vaccination status (Objective 2)

DTP3 which was considered to be the main indicator of immunisation programme performance was used to generate the outcome which was then categorised into three groups, timely, delayed and missed DTP3 vaccination. Children were considered eligible to have received DTP3 if they were 14 weeks of age or older.

2.2.7.3.1 Definitions of vaccination status

- Timely vaccination – a vaccine dose was considered as timely if it was received within 4 weeks of the recommended age.
- Delayed vaccination– a vaccine dose was considered as delayed if it was received 4 weeks or more after the recommended age.
- Missed vaccination– a vaccine dose was considered as missed if an age appropriate dose was not received at all by the time of the survey.

2.2.7.4 Delayed DTP3 vaccination (Objective 3)

The outcome was either delayed or timely DTP3 vaccination and was restricted to children who received DTP3 vaccination.

2.2.7.5 Missed DTP3 vaccination (Objective 3)

The outcome was binary categorised as either missed or not missed and was measured among all children who were eligible to receive DTP3.

2.2.7.6 Independent variables

- **Site:** The study site was defined as either Soweto or Edendale.

- **Number of children <5 years:** The total number of children aged <5 years in a household was categorised into two groups namely households with only one child and households with two or more children.
- **Sex:** This was defined as either male or female.
- **Household income:** The minimum monthly household income was categorised into 3 groups: Less than R500, R500-R1999 and R2000 or above.
- **Primary caregiver:** The main person looking after a child was defined as a parent if it was either the mother or father taking care of the child, and as “other” if someone else other than a parent was the primary caregiver. The “other” group included grandparents, aunts, crèche and other family members.
- **Education:** The highest level of education of the primary caregiver was defined as primary, secondary or tertiary. The primary education group included no high school and some high school education. The secondary education group included those who completed matric (Grade 12) or an equivalent and some tertiary education or college. The tertiary education group included completed tertiary qualifications and postgraduate education.
- **Age:** The age of a child was calculated from date of birth to the survey date and was categorised into 5 groups: 0-11 months, 12-23 months, 24-35 months, 36-47 months and 48-59 months.
- **Year of birth:** For each study site, children born after the survey date (after 2012 in Soweto and 2013 in Edendale) were not included in any analyses.
- **Maternal HIV status:** This was defined as positive, negative and unknown based upon VCT records, medical records, clinic records, the child’s RTHC or verbal report.

- **Building material:** Type of building material was grouped into two categories as either built from bricks (formal) or no bricks (informal) which included tin, mud bricks, wood or traditional.
- **Toilet:** The type of toilet facilities available in a household was defined as either a flush toilet or no flush toilet which included no toilet or a pit latrine/bucket system (private or communal).
- **Household assets:** These included car, computer, television set, radio, electricity supply, fridge, bicycle, land and domestic worker. Each item was categorised as yes (been present) or no (not present).
- **Source of energy used for cooking:** This included electric/gas stove, paraffin stove and open wood fire/coal fire. Each item was categorised as yes (been present) or no (not present).

2.3 Data analysis and Management

STATA version 13 (StataCorp LP, Texas USA) was used to perform all the analyses.

2.3.1 Data management for secondary analysis

Frequency tables were used to check for missing and miscoded data. The responses of different variables were compared to check if they were logical. For example, a date of birth that is later than survey date, or a two months old infant who has received all the vaccine doses recommended at 24 months. The response for a variable was regarded as missing if it was not possible to correct it, i.e. if both date of birth and a vaccination date for birth doses were missing.

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2.3.2 Descriptive analysis

Frequencies were generated using cross-tabulation to describe the characteristics of children and vaccination coverage by study site.

2.3.3 Analytical analysis

2.3.3.1 Comparison of characteristics of children with timely, delayed and missed DTP3 vaccination

The characteristics of children with timely, delayed and missed DTP3 vaccination were compared using Pearson's chi square test and Fisher's exact test. A p-value of <0.05 was considered statistically significant.

2.3.3.2 Factors associated with delayed and missed DTP3 vaccination

Two separate logistic regression models were conducted to assess the association between independent variables and the outcomes. A univariate analysis was performed to examine the association between each independent variable and the outcome. All variables with a p-value of <0.20 in the univariate analysis were included in the multivariate model. Variables which were non-significant (p-value ≥ 0.05) were removed one at a time using backward elimination and the Wald test was used to confirmed their significance in the model before removing them. A variance covariance estimator (vce) approach was used to account for correlation among children within each household and potential multi-collinearity among independent variables was assessed prior to fitting the multivariate model.

2.4 Ethical consideration

The Healthcare Utilization Surveys received approval from the University of the Witwatersrand and University of KwaZulu-Natal Human Research Ethics Committees and

the primary caregiver provided written consent for participation on behalf of the household.

For the secondary data analysis, ethics approval was also obtained from the University of the Witwatersrand Human Research Ethics Committee on the 10th February 2016 (M151164).

CHAPTER 3

This chapter provides detailed results found in this study.

3.1 Study participants

Of a total of 2382 households randomly selected in Edendale, 144 (6%) were non-residential (Figure 1). Of the remaining 2232 (94%) that were visited, 134 (6%) refused participation and 168 (8%) did not have a primary caregiver home after 3 attempted visits for interview. A resultant 1936 (86.5%) households with a total of 9750 members were surveyed in Edendale. Among the surveyed households, 514 (26.5%) had at least one child aged less than 5 years. In Soweto, of 1713 selected households, 191 (1.2%) were non-residential. Of the 1522 (88.8%) households visited, 207 (13.6%) refused participation and 342 (22.5%) did not have primary caregiver home after 3 attempted visits for interview. A resultant 973 (63.9%) households with a total of 4364 members were interviewed in Soweto. Among the surveyed households, 248 (25.5%) had at least one child aged less than 5 years. A total of 1061 children aged less than 5 years were enrolled from both sites, 705 (66.4%) from Edendale and 356 (33.6%) from Soweto.

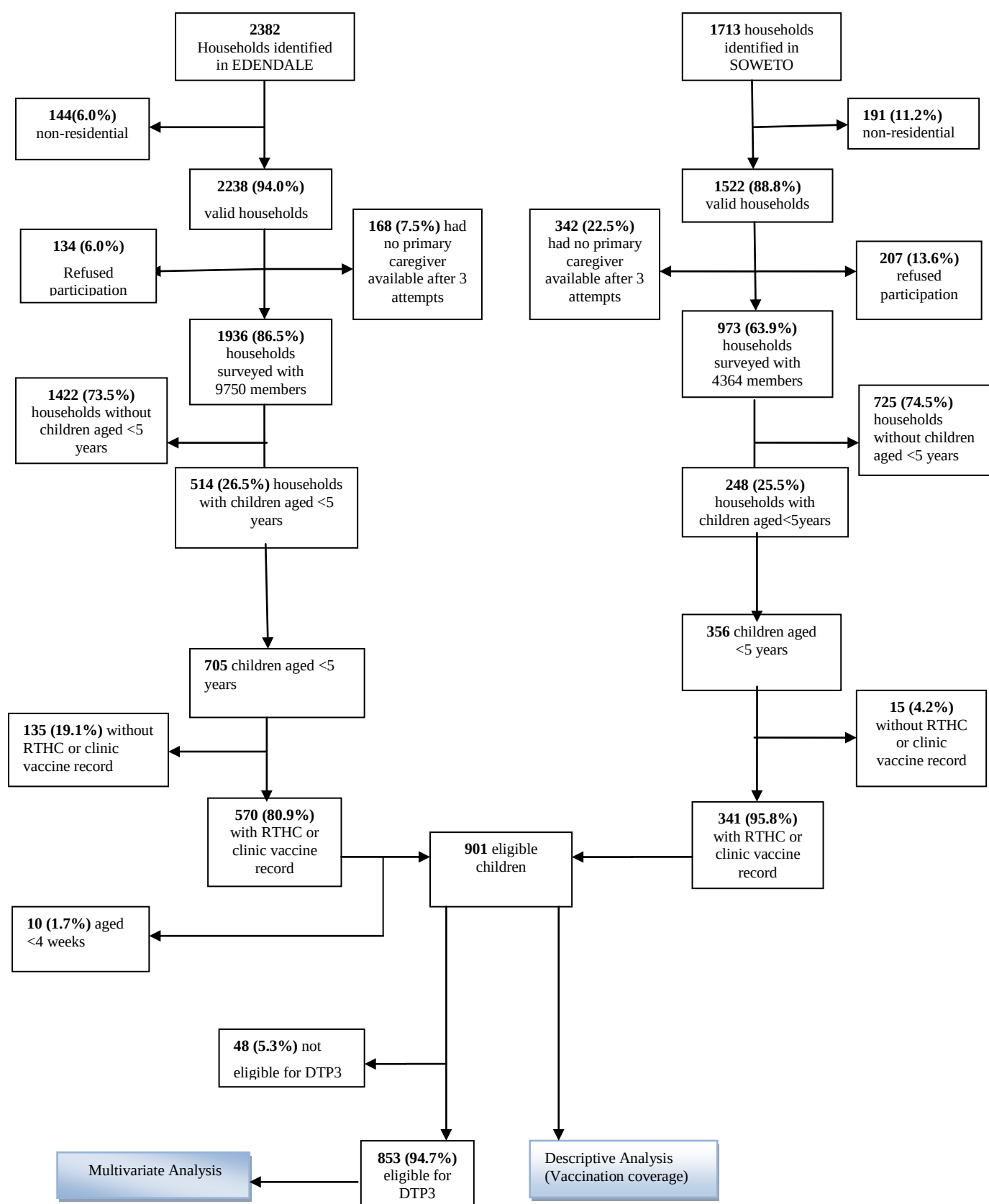


Figure 1. Flow diagram of households and children from Edendale and Soweto included in the healthcare utilisation surveys, South Africa, 2012-201

3.2 Characteristics of participants

Table 2 shows the characteristics of households and children under 5 years of age by study site. The study sites differed with regards to a number of characteristics. In Soweto households were significantly more likely to have a monthly income between R500-R1999 ($p<0.0001$) and primary caregivers who had completed secondary education ($p<0.0001$) compared to households in Edendale. More households in Edendale (98.8%) owned cellphones compared to Soweto (91.9%, $p<0.0001$). A high proportion of children in Soweto (83.9%) lived in households made of bricks and had flush toilets (78.2%); this differed significantly from Edendale ($p <0.0001$) where lower proportions of children lived in formal brick houses (49.4%), or had flush toilets (23.7%). In contrast, children in Edendale were significantly more likely to come from households that owned land ($p<0.0001$). In Edendale households were more likely to report owning assets, such as a bicycle, fridge, radio and electricity than households in Soweto, although not all of these differences were significant.

Table 2. The characteristics of households and children <5 years of age by study site (Soweto and Edendale), 2012-2013

Characteristics of children				
Characteristic	Edendale N=705 n (%)	Soweto N=356 n (%)	TOTAL N=1061 n (%)	p-value
Child's Age				
<12 months	151 (21.6)	63 (17.7)	214 (20.2)	0.194
12-23 months	139 (19.5)	90 (25.3)	229 (21.6)	
24-35 months	138 (19.8)	66 (18.5)	204 (19.2)	
36-47 months	134 (19.2)	73 (20.5)	207 (19.5)	
48-59 months	143 (19.9)	64 (18.0)	207 (19.5)	
Child's Sex				
Male	36 (51.5)	179 (50.3)	542 (51.1)	0.710
Female	342 (48.5)	177 (49.7)	519 (48.9)	
Characteristics of households				
	Edendale N=514	Soweto N=248	TOTAL N=762	p-value
Primary caregiver				
Parent	342 (66.5)	170 (68.6)	512 (67.2)	0.580
Other	172 (33.5)	78 (31.4)	250 (32.8)	

Education of primary caregiver¹				
Primary	264 (54.9)	142 (57.5)	402 (55.8)	
Secondary	22 (4.6)	80 (32.4)	102 (14.0)	
Tertiary	195 (40.5)	25 (10.1)	220 (30.2)	<0.0001
Number of children <5y				
Only child	369 (71.8)	164 (66.1)	533 (70.0)	
Two or more	145 (28.2)	84 (33.9)	229 (30.0)	0.110
Maternal HIV²				
Positive	92 (21.5)	45 (19.5)	137 (20.2)	
Negative	356 (79.5)	186 (80.5)	542 (79.8)	0.745
Household income³				
Less than R500	17 (4.8)	29 (14.0)	46 (8.2)	
R500-R1999	186 (52.5)	116 (56.0)	302 (53.8)	
>=R2000	151 (42.7)	62 (30.0)	213 (38.0)	<0.0001
Domestic worker				
No	500 (97.3)	239 (96.4)	739 (97.0)	
Yes	14 (2.7)	9 (3.6)	23 (3.0)	0.494
Cellphone				
No	6 (1.2)	20 (8.1)	26 (3.0)	
Yes	508 (98.8)	228 (91.9)	736 (97.0)	<0.0001
Television				
No	31 (6.0)	17 (6.9)	48 (6.3)	
Yes	483 (94.0)	231 (93.1)	714 (93.7)	0.661
Radio				
No	117 (22.8)	67 (27.0)	184 (24.1)	
Yes	397 (77.2)	181 (73.0)	578 (75.9)	0.199
Computer				
No	430 (83.7)	214 (86.3)	644 (84.5)	
Yes	84 (16.3)	34 (13.7)	118 (15.5)	0.347
Car				
No	383 (74.5)	186 (75.0)	569 (74.7)	
Yes	131 (25.5)	62 (25.0)	193 (25.3)	0.885
Bicycle				
No	476 (92.6)	345 (96.9)	716 (94.0)	
Yes	38 (7.4)	11 (3.1)	46 (6.0)	0.024
Electricity				
No	9 (1.7)	8 (3.2)	17 (2.2)	
Yes	505 (98.3)	240 (96.8)	745 (97.8)	0.196
Own land				
No	392 (76.3)	237 (95.6)	629 (82.5)	
Yes	122 (23.7)	11 (34.4)	133 (17.5)	<0.0001
Building material				
No Bricks	260 (50.6)	40 (16.1)	300 (39.4)	
Bricks	254 (49.4)	208 (83.9)	462 (60.6)	<0.0001
Flush toilet				

No	392 (76.3)	54 (21.8)	446 (58.5)	
Yes	122 (23.7)	194 (78.2)	316 (41.5)	<0.0001
Fridge				
No	39 (7.6)	32 (12.9)	71 (9.3)	
Yes	475 (92.4)	216 (87.1)	691 (90.7)	0.018
Electric/gas stove				
No	14 (2.7)	10 (4.0)	24 (3.2)	
Yes	500 (97.3)	238 (96.0)	738 (96.8)	0.333
Paraffin stove				
No	504 (98.0)	239 (96.4)	743 (97.5)	
Yes	10 (2.0)	9 (3.6)	19 (2.5)	0.163
Coal fire				
No	506 (98.4)	347 (99.6)	753 (98.8)	
Yes	8 (1.6)	1 (0.4)	9 (1.2)	0.167

¹ Proportions calculated out of 481 for Edendale and 247 for Soweto due to missing data

² Proportions calculated out of 448 for Edendale and 231 for Soweto due to missing data

³ Proportions calculated out of 354 for Edendale and 207 for Soweto due to missing data

3.3 Availability of immunisation card or vaccination history from the clinic

Of the 1061 enrolled children, immunisation cards or vaccine history from the clinic were available for 911 (86%) children; 341 (95.8%) in Soweto and 570 (80.9%) in Edendale. Of a total of 24 children in Soweto for whom immunisation cards were not available, 9 (37.5%) had their vaccine histories found from an immunisation clinic, while vaccine histories could not be confirmed from the appropriate facility for 15 (62.5%) children. Of the 9 children whose vaccine histories were found from a clinic, 5 (55.5%) had lost their cards and 4 (44.4%) children had their cards in another city. Of the 15 children for whom vaccines histories could not be found from the appropriate facility, 6 (40.0%) had lost their cards, 5 (33.3%) had their cards in another city/country and 2 had their vaccines from a private practitioner. In Edendale, 135 (19.1%) children did not have RTHCs or vaccine histories; however, this number may be overestimated because clinic vaccine records were not checked. Table 3 compares the characteristics of children for whom immunisation cards or vaccine history were available and those who did not have cards or vaccine history. A greater proportion of children (90%) who did not have immunisation cards or vaccine history were

from Edendale and more than half (58.7%) were males. Almost half of children (47.9%) for whom immunisation cards were not available had primary caregivers with only primary education and 47.5% were from households that had a monthly income between R500 and R1999.

Table 3. The characteristics of children <5 years of age by immunisation card status in Soweto and Edendale, 2012-2013

Characteristic	RTHC or vaccine history N=911	No RTHC or vaccine history N=150	p-value
Site			
Edendale	570 (62.6)	135 (90.0)	<0.0001
Soweto	341 (37.4)	15 (10.0)	
Age			
Less than 12 months	195 (21.4)	19 (12.7)	0.054
12-23 months	199 (21.8)	30 (20.0)	
24 -35 months	176 (19.3)	28 (18.7)	
36-47 months	171 (18.8)	36 (24.0)	
48-59 months	170 (18.7)	37 (24.6)	
Sex			
Male	454 (49.8)	88 (58.7)	0.045
Female	457 (50.2)	62 (41.3)	
Primary caregiver			
Parent	619 (68.0)	94 (62.7)	0.202
Other	292 (32.0)	56 (37.3)	
Education¹			
Primary	492 (56.4)	69 (47.9)	<0.0001
Secondary	131 (15.0)	11 (7.6)	
Tertiary	250 (28.6)	64 (44.4)	
Number of children <5y			
Only Child	468 (51.4)	65 (43.3)	0.068
Two or more	443 (48.6)	85 (56.7)	
Maternal HIV Status²			
Positive	175 (20.9)	13 (13.1)	0.069
Negative	663 (79.1)	86 (86.9)	
Household Income³			
Less than R500	51 (7.6)	7 (5.9)	0.030
R500-R1999	393 (58.5)	56 (47.5)	
>=R2000	228 (33.9)	55 (46.6)	
Domestic worker			
No	879 (96.5)	146 (97.3)	

Yes	32 (3.5)	4 (2.7)	0.596
Cellphone			
No	34 (3.7)	2 (1.3)	
Yes	877 (96.3)	148 (98.7)	0.580
Television			
No	56 (6.2)	11 (7.3)	
Yes	855 (93.8))	139 (92.7)	0.133
Radio			
No	216 (23.7)	39 (26.0)	
Yes	695 (76.3)	111 (74.0)	0.543
Computer			
No	776 (85.2)	120 (80.0)	
Yes	135 (14.8)	30 (20.0)	0.105
Car			
No	687 (75.4)	106 (70.7)	
Yes	224 (24.6)	44 (29.3)	0.215
Bicycle			
No	858 (94.2)	141 (94.0)	
Yes	53 (5.8)	9 (6.0)	0.930
Electricity supply			
No	22 (2.4)	4 (2.7)	
Yes	889 (97.6)	146 (97.3)	0.853
Own land			
No	745 (82.1)	125 (83.3)	
Yes	163 (17.9)	25 (16.7)	0.711
Building material			
No bricks	356 (39.1)	60 (40.0)	
Bricks	555 (60.9)	90 (60.0)	0.830
Flush Toilet			
No	521(57.2)	98 (65.3)	
Yes	390 (42.8)	52 (34.7)	0.061
Fridge			
No	84 (9.2)	14 (9.3)	
Yes	827 (90.8)	136 (90.7)	0.965
Electric/Gas stove			
No	31 (3.4)	7 (4.7)	
Yes	880 (96.6)	143 (95.3)	0.440
Coal fire			
No	895 (98.5)	150 (100.0)	
Yes	14 (1.5)	0 (0.0)	0.240
Paraffin stove			
No	888 (97.5)	14 (96.0)	
Yes	23 (2.5)	6 (4.0)	0.283

¹ Proportions calculated out of 873 for RTHC and 144 for No RTHC due to missing data

² Proportions calculated out of 838 for RTHC and 99 for No RTHC due to missing data

³Proportions calculated out of 672 for RTHC and 118 for No RTHC due to missing data

3.4 Vaccination coverage

Vaccination coverage for different vaccines is described in Table 4. For most vaccines, the coverage was high (above 90%) across both sites except for PCV3 and rotavirus 2 which had coverage of 80.3% and 85.4% respectively. There were substantial differences in vaccination coverage between study sites; in Edendale coverage for all vaccines appeared to be lower than in Soweto. Vaccination coverage in Soweto ranged from 83.4%-99.4% and 66.9%-95.9% in Edendale. Significant differences in vaccination coverage between study sites were observed for PCV1, BCG, measles and DTP1. For OPV/IPV, significant differences in vaccination coverage were observed for the first three doses; and for HepB the difference in coverage was significant for all three doses. Table 4 also shows the proportion of children who received their vaccine doses late. Delays were more common in Edendale compared to Soweto for PCV2, PCV3, measles, HepB2 and HepB3.

Table 5 shows the DTP3 coverage by birth year and age group. In Soweto, DTP3 coverage decreased significantly from 2008 to 2012 ($p<0.0001$). The highest coverage in Soweto was in children aged 48-59 months (98.4%, $p<0.0001$). In Edendale there was no significant trend observed in coverage by age group or year. Delayed DTP3 vaccination differed by year and age group in Edendale and by age group in Soweto. A higher proportion of delayed DTP3 vaccination was observed among children aged 12-23 months in Soweto (36.7%, $p=0.007$) and among children aged 36-47 months in Edendale (42.3%, $p<0.0001$). Delays were more common in children born in 2010 in Edendale (47.2%, $p<0.0001$).

Table 4. Vaccination coverage among children under 5 years of age in Soweto and Edendale, 2012-2013

VACCINE	Due age of vaccines	VACCINATION COVERAGE				DELAYED VACCINATION			
		Soweto n=341	Edendale n=560	TOTAL N=901	p-value	Soweto n=338	Edendale n=533	TOTAL N=871	p-value
PCV (%)									
Dose 1	6 weeks	248/254 (97.6)	481/515 (93.4)	729/769 (94.8)	0.013	28/248 (11.3)	42/481 (8.7)	70/729 (9.6)	0.267
Dose 2	14 weeks	228/243 (93.8)	448/494 (90.7)	676/737 (91.7)	0.146	40/228 (17.5)	109/448 (24.3)	149/676 (22.0)	0.044
Dose3	9 months	183/219 (83.6)	338/430 (78.6)	521/649 (80.3)	0.133	84/183 (45.9)	190/338 (56.2)	274/521 (52.6)	0.024
Rotavirus (%)									
Dose1	6 weeks	215/230 (93.4)	443/ 474 (93.5)	658/704 (93.6)	0.993	21/215 (9.8)	37/443 (8.4)	58/658 (8.8)	0.548
Dose 2	14 weeks	181/219 (82.7)	393/ 453 (66.9)	574/672 (85.4)	0.248	29/ 181 (16.0)	72/ 393 (18.3)	101/574 (17.6)	0.502
BCG (%)									
Birth dose	Birth	341/ 344 (99.1)	534/561 (95.2)	868/898 (96.7)	0.001	12/340 (3.5)	12/530 (2.3)	24/870 (2.8)	0.266
Measles (%)									
Dose 1	9 months	294/303 (97.0)	415/466 (89.1)	709/769 (92.2)	<0.0001	127/294 (43.2)	238/415 (57.4)	365/709 (51.5)	<0.0001
DTP+HIB (%)									
Dose 1	6 weeks	331/338 (97.9)	525/551 (95.3)	856/889 (96.3)	0.043	31/331 (9.4)	49/525 (9.3)	80/856 (9.4)	0.987
Dose 2	10 weeks	320/ 333 (96.1)	509/538 (94.6)	829/871 (95.2)	0.320	61/320 (19.1)	107/509 (21.0)	168/829 (20.3)	0.495
Dose 3	14 weeks	297/327 (90.8)	478/530 (90.2)	775/853 (90.8)	0.758	76/297 (25.6)	146/478 (30.5)	222/775 (28.7)	0.138
OPV/IPV (%)									
Birth Dose (OPV)	Birth	341/344 (99.1)	538/561 (95.9)	879/905 (97.1)	0.005	13/341 (3.8)	10/538 (1.9)	23/879 (2.6)	0.077
Dose 1 (OPV/IPV)	6 weeks	336/338 (99.4)	527/551 (95.6)	863/889 (97.1)	0.001	19/336 (5.7)	33/527 (6.3)	52/863 (6.0)	0.715
Dose 2 (IPV)	10 weeks	325/333 (97.6)	505/538 (93.9)	830/871 (95.3)	0.012	55/325 (16.9)	95/505 (18.8)	150/830 (18.1)	0.490
Dose 3 (IPV)	14 weeks	301/ 327 (92.1)	476/530 (89.8)	777/853 (91.1)	0.274	72/301 (23.9)	127/476 (26.7)	199/777 (25.6)	0.390
Hep B (%)									
Dose 1	6 weeks	335/338 (99.1)	525/ 551 (95.3)	860/889 (96.7)	0.002	16/ 335 (4.8)	35/525 (6.7)	51/ 860 (5.9)	0.252
Dose 2	10 weeks	330/333 (99.1)	506/538 (94.1)	836/871 (96.0)	<0.0001	26/ 330 (7.9)	70/506 (13.8)	96/836 (11.5)	0.008
Dose 3	14 weeks	314/327 (96.0)	483/530 (91.1)	797/853 (93.4)	0.006	47/314 (15.0)	102/ 483 (21.1)	149/797 (18.7)	0.030

Table 5. DTP3 coverage and delayed vaccination among children aged <5 years by age group and year of birth in Soweto and Edendale, 2012-2013

Coverage by birth year n (%)	DTP3 coverage							
	Birth year	2008	2009	2010	2011	2012	2013	p-value
	Edendale	15/16 (93.8)	92/105 (87.6)	106/113 (93.8)	93/106 (87.7)	107/116 (92.2)	65/74 (87.7)	0.491
	Soweto	64/65 (98.5)	64/68 (94.1)	59/64 (92.1)	84/94 (89.4)	18/28 (64.3)		<0.0001
	Total	79/81 (97.5)	156/173 (90.2)	165/177 (93.2)	177/200 (88.5)	125/144 (86.8)	65/74 (87.7)	0.095
Coverage by age group n (%)	Delayed DTP3 vaccination							
	Birth year	2008	2009	2010	2011	2012	2013	p-value
	Edendale	4/15 (26.7)	17/92(18.5)	50/106 (47.2)	36/93 (38.7)	26/107 (24.3)	13/65 (20.0)	<0.0001
	Soweto	11/64 (17.2)	13/64 (20.3)	16/59 (27.1)	30/84 (35.7)	6/18 (33.3)		0.083
	Total	15/79 (19.0)	30/156 (19.2)	66/165 (40.0)	66/177 (37.3)	32/125 (25.6)	13/65 (20.0)	<0.0001
Coverage by age group n (%)	DTP3 coverage							
	Age group(months)	<12	12-23	24-35	36-47	48-59	p-value	
	Edendale	81/92 (88.0)	102/112 (91.1)	101/113 (89.4)	97/103 (94.2)	97/110 (88.2)	0.556	
	Soweto	33/45 (73.3)	79/87 (90.8)	59/65 (90.8)	65/68 (95.6)	61/62 (98.4)	<0.0001	
	Total	114/137 (83.2)	181/199 (90.9)	160/178 (89.9)	162/171(94.7)	158/172 (91.9)	0.014	
Coverage by age group n (%)	Delayed DTP3 vaccination							
	Age groups (months)	<12	12-23	24-35	36-47	48-59	p-value	
	Edendale	16/81(19,8)	29/102 (28.4)	41/101 (40.6)	41/97 (42.3)	19/97 (19.6)	<0.0001	
	Soweto	10/33 (30.3)	29/79 (36.7)	18/59 (30.5)	8/65 (12,3)	11/61 (18.0)	0.007	
	Total	26/114 (22.8)	58/181 (32.0)	59/160 (36.9)	49/162 (30.3)	30/158 (19.0)	0.004	

3.5 Characteristics of children with delayed or missed DTP3 vaccination

Of 853 children who were eligible for DTP3 vaccination, 551 (64.6%) were vaccinated on time, 221 (25.9%) had delayed vaccinations and 81 (9.5%) missed vaccinations. Table 6 shows the characteristics of children with delayed or missed DTP3 vaccinations. Children who were born in 2011 (OR 5.1, 95% CI 1.2-22.4), 2012 (OR 6.0, 95% CI 1.3-26.8) and 2013 (OR 5.5, 95% CI 1.1-26.2) were more likely to miss vaccination compared to children born in 2008. Children aged less than 12 months (OR 2.0, 95% CI 1.1-3.9) and children from households with two or more children aged less than 5 years (OR 2.0, 95% CI 1.2-3.2) were 2 times more likely to miss vaccinations compared to children aged between 12-23 months or those who had no siblings aged less than 5 years. Children who did not have television sets in their homes were more likely to have missed (OR 3.0, 95% CI 1.5-6.3) or delayed receiving vaccinations (OR 1.9, 95% CI 1.1-3.6) compared to children who had television in their homes. Children born in 2010 (OR 2.8, 95% CI 1.4-5.8) or 2011 (OR 2.5, 95% CI 1.3-5.1) were more likely to have delayed vaccinations compared to children who were born in 2008.

Table 6. Comparison of characteristics of children <5 years of age with timely, delayed and missed DTP3 vaccination in Soweto and Edendale, 2012-2013

CHARACTERISTIC	Timely vaccination	Delayed vaccination		Missed vaccination	
	n(%)	n(%)	Unadjusted OR (95% CI) ¹	n(%)	Unadjusted OR (95% CI) ²
Study site					
Edendale	219 (39.7)	76 (34.4)	1	29 (35.8)	1

Soweto	332 (60.3)	145 (65.6)	0.8 (0.6-1.1)	52 (64.2)	0.9 (0.5-1.5)
Age group					
<12 months	88 (16.0)	26 (11.8)	0.6 (0.4-1.1)	23 (28.4)	2.0 (1.1-3.9)
12-23 months	123 (22.3)	58 (26.2)	1	18 (22.2)	1
24-35 months	100 (18.2)	59 (26.7)	1.3(0.8-2.0)	17 (21.0)	1.1 (0.5-2.2)
36-47 months	113 (20.5)	49 (22.2)	0.9 (0.6-1.5)	9 (11.1)	0.6 (0.3-1.2)
48-59 months	127 (23.0)	29 (13.1)	0.5 (0.3-0.8)	14 (13.1)	0.9 (0.4-1.8)
Birth year³					
2008	63 (11.8)	15 (6.9)	1	2 (2.5)	1
2009	125 (23.0)	29 (12.8)	1.0 (0.4-2.1)	17 (21.0)	4.4 (1.0-19.5)
2010	99 (18.2)	66 (30.1)	2.8 (1.4-5.8)	10 (12.3)	2.6 (0.6-12.2)
2011	111 (20.4)	66 (29.7)	2.5 (1.3-5.1)	23 (28.4)	5.1 (1.2-22.4)
2012	93 (17.1)	32 (14.6)	1.5 (0.7-3.1)	19 (23.5)	6.0 (1.3-26.8)
2013	52 (9.5)	13 (5.9)	1.1 (0.4-2.6)	10 (12.3)	5.5 (1.1-26.2)
Sex of a child					
Male	276 (50.1)	114 (51.6)	1	40 (49.4)	1
Female	273 (49.9)	107 (48.4)	0.9 (0.7-1.3)	41 (50.6)	1.0 (0.6-1.7)
Primary caregiver					
Parent	278 (67.5)	146 (66.7)	1	46 (56.8)	1
Other	179 (32.5)	73 (33.3)	1.0 (0.7-1.4)	35 (43.2)	1.6 (1.0-2.7)
Education of primary caregiver					
Primary	289 (54.3)	125 (59.8)	1	49 (63.6)	1
Secondary	88 (16.5)	23 (11.0)	0.6 (0.4-1.0)	9 (11.7)	0.7 (0.3-1.4)
Tertiary	155 (29.1)	61 (29.2)	0.9 (0.6-1.3)	19 (24.7)	0.7 (0.4-1.3)
No of children <5 y					
Only child	289 (52.5)	115 (52.0)	1	29 (35.8)	1
Two or more	262 (47.5)	106 (48.0)	1.0 (0.7-1.4)	52 (64.2)	2.0 (1.2-3.2)
Maternal HIV					
Positive	116 (22.4)	34 (17.4)	1	11 (15.9)	1
Negative	401 (77.6)	162 (82.6)	0.7 (0.5-1.1)	58 (84.1)	1.4 (0.7-2.9)
Household income					

Less than R500	28 (6.9)	13 (8.0)	1.1 (0.5-2.5)	7 (11.5)	2.6 (1.0-6.8)
R 500 to R1999	238 (58.9)	91 (56.2)	0.9 (0.6-1.4)	38 (65.6)	1.8 (0.9-3.4)
R2,000 or more	138 (34.2)	58 (35.8)	1	13 (22.9)	1
Domestic worker					
No	19 (3.4)	9 (4.1)	1	1 (1.2)	1
Yes	532 (96.6)	212 (95.9)	1.2 (0.4-3.6)	80 (98.8)	0.3 (0.1-2.4)
Cellphone					
No	532 (96.5)	214 (96.8)	1	75 (92.6)	1
Yes	19 (3.5)	7 (3.2)	1.1 (0.5-2.6)	6 (7.4)	0.4 (0.2-1.2)
Television					
No	527 (95.6)	203 (91.9)	1.9 (1.1-3.6)	69 (85.2)	3.0 (1.5-6.3)
Yes	24 (4.4)	18 (8.1)	1	12 (14.8)	1
Radio					
No	417 (75.7)	174 (78.7)	1	61 (73.3)	1
Yes	134 (24.3)	47 (21.3)	1.2 (0.8-1.7)	20 (24.7)	0.9 (0.5-1.6)
Computer					
No	78 (14.2)	32 (14.5)	1	13 (16.1)	1
Yes	473 (85.8)	189 (85.5)	1.0 (0.6-1.7)	68 (83.9)	1.2 (0.6-2.2)
Car					
No	139 (25.3)	57 (25.8)	1	14 (17.3)	1
Yes	412 (71.8)	164 (74.2)	1.0 (0.7-1.5)	67 (82.7)	0.6 (0.3-1.2)
Bicycle					
No	27 (4.9)	18 (8.1)	1	3 (3.7)	1
Yes	524 (95.1)	203 (91.9)	1.7 (0.9-3.4)	78 (96.3)	0.6 (0.2-2.0)
Electricity supply					
No	537 (97.5)	217 (98.2)	1	4 (4.9)	1
Yes	14 (2.5)	4 (1.8)	1.4 (0.4-4.5)	77 (95.1)	0.4 (0.1-1.5)
Land owner					
No	95 (17.2)	45 (20.4)	1		1
Yes	456 (82.8)	176 (79.6)	1.2 (0.8-1.9)	71 (87.7)	0.6 (0.3-1.3)
Building material					

Not Bricks	341(61.9)	127 (57.7)	1	50 (61.7)	1
Bricks	210 (38.1)	94 (42.5)	0.8 (0.6-1.1)	31 (38.3)	1.0 (0.6-1.7)
Flush Toilet					
No	236 (42.8)	94 (42.5)	1	36 (44.4)	1
Yes	315 (57.2)	127 (57.5)	1.0 (0.7-1.4)	45 (55.6)	1.1 (0.7-1.7)
Fridge					
No	502 (91.1)	204 (92.3)	1	69 (85.2)	1
Yes	49 (8.9)	17 (7.7)	1.2 (0.7-2.1)	12 (14.8)	0.5 (0.3-1.1)
Electric/gas stove					
No	527 (95.6)	217 (98.2)	1	78 (96.3)	1
Yes	24 (4.4)	4 (1.8)	2.5 (0.9-7.0)	3 (3.7)	0.9 (0.3-3.4)

¹Delayed vaccination versus timely vaccination

²Missed vaccination versus not missed vaccination

³Children born in 2007 were excluded due to low frequency

3.6 Factors associated with missed DTP3 vaccination among children aged <5 years on multivariable analysis

Table 7 shows the factors associated with missed DTP3 vaccination on multivariable analysis. Children from households with two or more children aged less than 5 years of age (OR 2.5, 95% CI 1.4-4.5) and children from households that had a monthly income less than R500 (OR 2.9, 95% CI 1.03-8.0) were more likely to miss vaccinations compared to children from households with only one child aged less than 5 years or from households that had a monthly income of more than R2000. Children younger than 12 months were nearly three times more likely to miss vaccination compared to children age 12-23 months (OR 2.7, 95% CI 1.2-5.9). We explored whether the factors associated with missed vaccination differed by economic status and found that there was no difference (data not shown).

Table 7. Factors associated with missed DTP3 vaccination in children aged <5 years in Soweto and Edendale on multivariate analysis, 2012-2013

Factors	Adjusted OR (95%CI)¹	p-value
Age group		
<12 months	2.7(1.2-5.9)	0.013
12-23 months	1	
24-35 months	1.0 (0.5-2.3)	0.947
36-47 months	0.6 (0.2-1.5)	0.190
48-59 months	0.9 (0.4-2.2)	0.863
Number of children<5y		
Only child	1	
Two or more	2.5 (1.4-4.5)	0.003
Household income		
Less than R500	2.9 (1.03-8.0)	0.043
R500-R1999	1.6 (0.8-3.0)	0.213
R2000 or more	1	

¹Missed vaccination versus not missed vaccination

3.7 Factors associated with delayed DTP3 vaccination in children aged <5 years on multivariable analysis

Table 8 shows the factors associated with delayed vaccination in children <5 years on multivariable analysis. Children whose mothers completed secondary school education were less likely to have delayed vaccination compared to children whose mothers had only primary education (OR 0.5, 95% CI 0.3-0.9). Children born in 2010 (OR 2.9, 95% CI 1.3-6.3) or 2011 (OR 2.7, 95% CI 1.3-5.8) were more likely to have delayed vaccination compared to children born in 2008. Negative maternal HIV status was marginal significantly associated with higher odds of delayed vaccination (OR 1.6, 95% CI 1.0-2.5). We explored whether the factors associated with delayed vaccination differed by economic status and found that there was no difference (data not shown).

Table 8. Factors associated with delayed DTP3 vaccination in children <5 years of age in Edendale and Soweto on multivariate analysis, 2012-2013

Factors	Adjusted OR (95%CI)¹	p-value
Birth year		
2008	1	
2009	0.8 (0.4-2.0)	0.677
2010	2.9 (1.3-6.3)	0.008
2011	2.7 (1.3-5.8)	0.011
2012	1.3 (0.5-3.0)	0.567
2013	1.0 (0.4-2.7)	0.986
Education of primary caregiver		
Primary	1	
Secondary	0.5 (0.3-0.9)	0.023
Tertiary	0.8 (0.5-1.2)	0.285
Maternal HIV infection		
Positive	1	
Negative	1.6 (1.0-2.5)	0.050

¹Delayed vaccination versus timely vaccination

3.8 Reasons given by caregivers for their children having missed or delayed any vaccines

Table 9 shows reasons given by caregivers for their children having missed or delayed any vaccines. The most common reasons were that the clinic had been out of stock of the relevant vaccine (30.3%) and that there was no one available to take the child to the clinic for immunisation (12.6%). Table 10 shows the distribution of vaccine stock outs by year of birth as were reported by caregivers. Of a total of 321 children whose primary caregivers reported having missed or delayed any vaccines due to vaccine stock outs, 94 (29.3%) were born in 2010. Other reasons were that the RTHC was lost or destroyed (1.3%), child was ill at the time of immunisation (1.1%) and caregiver did not feel that it was necessary for a child to have all their scheduled vaccines (0.6%).

Table 9. Most common reasons given by caregivers for their children having missed or delayed any vaccines

Reason	n(%)
Clinic was out of stock of relevant vaccine	321 (30.3)
No one available to take child to clinic for immunisation	134 (12.6)
RTHC was lost/destroyed	13 (1.2)
Child was ill at the time of immunisation visit	12 (1.1)
Caregiver felt it was unnecessary to vaccinate	6 (0.6)
Other reasons	10 (0.8)

*Percentages calculated out of 1061 children aged less 5 years

Table 10. The distribution of vaccine stock outs by child's year of birth, as reported by caregivers

Year of birth	n (%)
2008	20 (6.2)
2009	77 (24.0)
2010	94 (29.3)
2011	75 (23.4)
2012	38 (11.8)
2013	17 (5.3)
Total	321 (100.0)

3.9 Challenges experienced by caregivers in accessing immunisation services for the children

Table 11 shows challenges experienced by caregivers in accessing immunisation services for the children. The challenges reported by caregivers included unfriendly staff, restricted opening hours of clinics, long distance to travel to the clinic, unable to get leave from work to take a child to the clinic and transport costs to reach the clinic for immunisation services.

Table 11. Challenges experienced by caregivers in accessing immunisation services for the children.

Challenge	n(%)
Unfriendly staff	37 (3.5)
Opening hours of clinic	15 (1.4)
Long distance to travel to clinic	9 (0.8)
Unable to get leave from work to take child to clinic	3 (0.3)
Cost of transport to travel to clinic	2 (0.2)
Other	5 (0.7)

*Percentages calculated out of 1061 children aged less 5 years

CHAPTER 4

4.1 Overview of study findings

In this study we investigated factors associated with delayed and missed vaccinations in children less than 5 years of age using data from two Healthcare Utilisation Surveys. Our results show that low monthly income and having two or more children aged less than 5 years in a household was associated with missed vaccinations. Children younger than 12 months of age were more likely to miss vaccinations. We found that being born in 2010 or 2011 was associated with higher odds of delayed vaccination. Children whose mothers completed secondary education were less likely to have delayed vaccination. These findings can hopefully guide policy makers with regards to different strategies that could be implemented to improve timeliness and coverage of vaccines.

4.2 Vaccination coverage

Vaccination coverage was high for most vaccines except for PCV3 and Rota2 which had coverage of 80.3% and 85.4% respectively. In Edendale, vaccination coverage was lower than in Soweto which may reflect variability in coverage between provinces or districts as differences are shown in provincial administrative coverage data (7). The proportion of children who were reported not to have a RTHC or vaccine history may have been overestimated in Edendale as the interviews were done by lay community health workers and not nurses; and clinic records were not checked. It is also likely that some vaccine doses were not recorded as not all copies of RTHC were available in Edendale to verify the information. We observed differences in coverage for some vaccine doses that were given at the same visits or as a combined injection. This was possibly due to vaccine stock outs for vaccines given at the same visit and inadequate recording at the clinic level with the introduction of

new vaccines in 2009 which were not accommodated by old RTHCs in the case of combination vaccines. The new RTHC with spaces for Pentaxim, Rota and PCV was introduced in 2011 and this may have affected the recording of the vaccination information especially for children born before 2011. There are a number of estimates of vaccination coverage for South Africa, including the WHO and South African Department of Health administrative estimates (12). These systems give differing results due to use of different methodology (14). Our vaccination coverage estimates were intermediate between these two estimates giving us confidence in the validity of our findings. As we used a survey approach it is possible that our results may be more accurate than the other methods.

Coverage was high for birth doses at both sites as most children in South Africa are born in healthcare facilities (96.8% in Gauteng and 82.4% in KwaZulu-Natal in 2014 (53)), and receive their birth vaccines immediately after birth. A study in Ethiopia that assessed the relationship between facility delivery and infant immunisation found higher BCG coverage among children born in a healthcare facility versus children born at home (54). Similarly in Guinea, children born in healthcare facilities were more likely to be vaccinated with BCG compared to children born at home (55).

We observed a decrease in DTP3 coverage after new changes in the SA immunisation programme i.e. the change to a combined vaccine (DTaP-IPV/Hib) and the introduction of new vaccines (Rotavirus and PCV) all in 2009. These accumulative changes may have affected service delivery to some degree. Stock outs affect vaccine delivery; in 2010, for example, the Department of Health reported Pentaxim delivery issues that resulted in shortage of this vaccine in health facilities (44).

4.3 Factors associated with missed vaccination

We found that children younger than 12 months of age were more likely to miss vaccination compared to children in the older age groups, possibly because many children receive their vaccines late. We cannot determine from our study whether these children would receive missed vaccines in the second year of life or not, as they were evaluated at a single point in time. Our finding of a higher rate of missed vaccines in younger children, is similar to previous studies which found that children aged 18-23 months were less likely to miss vaccinations compared to children aged 12-17 months (39, 56), implying that many children do not get vaccinated in the first year of life.

Similar to previous studies (23, 48, 57) children in our study from households that had two or more children were more likely to miss vaccinations. This suggests that higher numbers of children in a household reduces the odds of being vaccinated. A possible reason for missing vaccines in households with many children, may be that the primary caregiver might not have time or resources to take children to the clinic unless they are sick and not just for routine vaccination visits.

Children from households that had a lower income were more likely to be unvaccinated. These findings are consistent with previous studies (23, 34, 58). In Ethiopia, a study that assessed immunisation coverage and its determinants found that children in households with a family income greater than 1000 ETB (or 52 US dollar) were more likely to be fully vaccinated(49). The reason in our setting could be that even though healthcare is free for children aged <5 years, poor families may have challenges with transport costs to seek regular health care.

4.4 Factors associated with delayed vaccination

Similar to previous studies, we found that children whose primary caregiver had completed secondary education were less likely to have delayed vaccination (26, 56, 59, 60). Caregivers who are educated are more likely to know the number of vaccine doses a child should receive and the age at which these doses should be received. They might also know the importance of timely vaccination.

Contrary to a previous study in KwaZulu-Natal that assessed the impact of maternal HIV on childhood vaccination status and found that children of HIV-infected mothers had delayed vaccines (40), we found that negative maternal HIV status was associated with delayed vaccination. In our study HIV status was self-reported if it was not documented on the RTHC or available from clinic records, and many mothers had an unknown HIV status; it is therefore possible that we may have underestimated maternal HIV positive status. In addition maternal HIV prevalence estimated in this study was lower than the reported antenatal prevalence rates. In our study maternal HIV prevalence was 21.5% in Edendale and 19.5% in Soweto, as compared to 37.4% in KwaZulu-Natal and 29.9% in Gauteng (61). It is possible that positive self-reported maternal HIV status could be associated with better healthcare seeking behaviour which may affect the vaccination status of children. A study in Zimbabwe that explored predictors of utilisation of maternal health services and women's health seeking behaviour found that the knowledge of HIV status encouraged the use of maternal health services (62).

In our study children born in 2010 or 2011 were more likely to have delayed vaccinations. A study in Burkina Faso found an association between year of birth and delayed vaccination which was related to changes in vaccination programme performance over time (59). This association could be confounded by the performance of health system which varies over time

due to isolated stock outs and introduction of new vaccines. Among the reasons that were given by caregivers for their children having missed or delayed any of the vaccines, was vaccine stock outs as the most common reason (30.3%). In addition, a study in Malawi that assessed the predictors of uptake, timeliness and availability of new vaccines (Rotavirus and PCV) found an association between vaccine stock-out and delayed vaccination (63).

4.5 Limitations

Our study has several limitations. Firstly, household characteristics such as income, education of primary caregiver and maternal HIV status were self-reported and could introduce misclassification bias. Secondly, different strategies used for vaccination history data collection in the different sites might have influenced response rates. In Soweto, nurses were able to obtain vaccine histories from clinic records if immunisation cards were not available, whereas in Edendale vaccine histories were collected by community health workers who did not have access to clinic records. Participants may have felt uncomfortable when asked to share sensitive information such as HIV status with community health workers when compared with nurses and may have therefore been more likely to withhold RTHCs with a documented HIV positive status in Edendale. Thirdly, characteristics of children without immunisation cards/vaccine histories were different from children who had immunisation cards/vaccine histories and there are likely to be some differences in vaccination status between these groups. Assuming that children without RTHCs were unvaccinated, a sensitivity analysis showed that factors associated with missed vaccinations did not differ, however some factors became insignificant, possibly due to misclassification of vaccination status. Households that agreed to participate could be different from those that refused participation, increasing the potential for selection bias. As we only included children with

RTHCs in the analyses, vaccination coverage in the community may have been overestimated. Lastly, our study used data from one urban site and one peri-urban site; therefore, these results may not be generalisable to more rural populations.

4.6 Strengths

Despite the limitations, the study also has several strengths. Vaccination coverage estimates only included children with documented vaccination histories, so estimates were not affected by recall bias. Household survey design in which households were randomly selected allowed us to get information on the characteristics of households and individuals. Our sample included children of different age groups from two sites which allowed us to compare coverage estimates between these groups and sites, and also examine changes in vaccination coverage over a number of years. This study adds important data on vaccination coverage using a survey approach and on factors associated with missed and delayed vaccination.

4.7 Recommendations

To address the problem of delayed vaccination, health workers should always remind caregivers of subsequent vaccination dates and special attention should be paid to children from households with primary caregivers who have a low level of education to ensure that they understand regarding vaccination dates.

Health system managers should address issues of delivery to prevent unnecessary delays that occur when children are turned away from clinic due to vaccine stock-out.

Primary caregivers who are HIV negative may not frequently make use of health facilities; thus, mass media interventions should be used to educate caregivers on the importance of timely vaccination and to improve their healthcare seeking behaviour.

Since a high proportion of children who missed vaccinations come from households with low income and a high number of children aged less than 5 years, increasing the number of mobile clinics and mass vaccination campaign in high-risk populations may address the problem of missed vaccinations.

4.8 Conclusions

Although most vaccines had high coverage, there were substantial vaccination delays. This suggests that both coverage and timely vaccination should be used as an indicator for immunisation programme performance. Factors associated with delayed and missed vaccination were different. These findings suggest several strategies to improve timeliness and vaccination coverage. Efforts to increase vaccination coverage and timeliness should take into account caregiver's level of education, household income, number of children aged less than 5 years in a household and child's age to improve child health. Policy makers should target vulnerable communities with improved vaccination services and enforce vaccination promotion programmes to increase uptake and timeliness of vaccination.

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APPENDIX 1: Plagiarism Declaration Form

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I **Thandiwe Mthiyane** (Student number: **1120178**) am a student

registered for the degree of **MSc in Epidemiology** in the academic year **2016**.

I hereby declare the following:

- ❖ I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- ❖ I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- ❖ I have followed the required conventions in referencing the thoughts and ideas of others.
- ❖ I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.

Signature:  Date: **28/11/2016**

APPENDIX 2: Ethics Clearance Certificate



R14/49 Miss Thandiwe Mthiyane

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M151164

NAME: Miss Thandiwe Mthiyane
(Principal Investigator)
DEPARTMENT: School of Public Health
University of Witwatersrand

PROJECT TITLE: Factors Associated with Vaccination Status in Children
Under 5 Years of age in two Communities in South Africa

DATE CONSIDERED: 27/11/2015

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Prof Cheryl Cohen

APPROVED BY: 
Professor P Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 10/02/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004, 10th floor, Senate House/2nd Floor, Philip Tobias Building, Parktown, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**


Principal Investigator Signature

Date 11/02/2016

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES