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Evaluating measles vaccination coverage in high incidence areas of  
the Western Cape Province, following the mass vaccination  
campaign

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# Part 0: Preamble

## DECLARATION

I, **Gina Leanne Bernhardt** hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Signature:

Signed by candidate

Date: 5 December 2011

# Dedication

I wish to thank the Lord, my strength and refuge; without whom, I am not.

I wish to thank my parents, Wolfgang and Lucille Bernhardt, for their love and support.

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# Abstract

## Background

Measles virus is known to be one of the most contagious of infectious agents and despite considerable progress towards elimination, a number of Sub-Saharan African countries experienced epidemics in 2009-2011, including South Africa, in which there were over 18 000 confirmed cases.

The South African measles vaccination programme started in 1975 with 1 dose schedule, and from 1996-8 has followed the World Health Organization-United Nations Children's Fund strategy. This includes a 2 dose routine vaccination schedule for children at 9 and 18 months of age, supplementary mass vaccination campaigns (MVCs) for children conducted 4 yearly, improved case management and case-based laboratory surveillance. Administrative monitoring of routine vaccination coverage is problematic, and often overestimated, because of denominator and numerator inaccuracies. The potential for a significant outbreak in the Western Cape Province was therefore not recognized.

Over 2000 cases were confirmed in the Western Cape epidemic which began in September 2009 and peaked in March 2010. The Metropole district was mainly affected and over 60% of the cases were under 5 years of age, with 29% aged 6 to 11 months. A MVC, against measles had already been planned; however as a result of the epidemic the targeted age group for measles vaccination was extended from 9 to 59 months, to include children from 6 months to 15 years. This was conducted nationally from 12 to 23 April 2010.

## Aim and rationale

A community survey was conducted in the Western Cape Province after the MVC, as requested by the Provincial Department of Health, to assess vaccination coverage attained by routine and campaign services. The survey targeted children aged 6 to 59 months at the time of the campaign from high incidence areas. These areas represent areas which have increased risk of outbreaks and achieving herd immunity in these populations is a priority.

## Methods

High incidence areas, in which households were consecutively sampled, were identified using routine surveillance data. Caregiver history of campaign vaccination and routine vaccination status from the child's Road to Health Card (RTHC) were collected. Analytic methods include chi-square test, logistic regression and a Monte-Carlo simulation, which was used to estimate pre- and post-campaign immunity.

#### Findings

Of the 8332 households visited from 5 suburbs, 21% participated (1711 of 1800 eligible households). There was no response at 41% (n=3435) of households. Nine percent of the children had a history of measles. Eighty percent of the cases occurred prior to the MVC, with a sharp decline in cases after the MVC. According to caregiver history, 91% were vaccinated in the MVC. Immunity of the children was estimated to have increased from 61% before the MVC to 94% afterwards. The sub-group with a RTHC experienced an increase in immunity from 82% before to 96% after the MVC.

#### Discussion

Routine services are not achieving adequate herd immunity and MVCs remain an important strategy for rapidly increasing coverage and have been proven to decrease measles morbidity and mortality. Careful planning is required to mitigate the potential negative effects of MVCs on the health system. Timely implementation of campaigns in the context of an epidemic is essential to maximize the impact thereof. Routine services need to validate administrative coverage, especially in high risk areas such as informal settlements and immediate action should be taken in areas where coverage fails to achieve herd immunity. Vaccination status as documented on RTHCs is often used as a proxy indicator of population immunity and a risk assessment tool should be developed to model survey data against immunological assays, in order to estimate population immunity.

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GL Bernhardt  
10 May 2012

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# Part A: Protocol

Evaluating measles vaccination coverage in high incidence areas of  
the Western Cape Province, following the mass vaccination  
campaign

*Protocol, 08 July 2010*

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## Background

Immunization is known to be one of the most cost-effective interventions(1) and contributes significantly toward achieving the Millennium Development Goals of reducing Child Mortality by two thirds(2).

### **Predictors of immunization uptake**

Kroeger's variant of Health Care Utilization Model (1983) was useful in categorizing factors associated with health seeking behaviours into (1) predisposing factors, (2) perceptions regarding benefits and burdens, and (3) characteristics of the service/ enabling factors.

Predisposing factors that relate to vaccination coverage include parental education (3) (4), parental marital status (3) , socio-economic status (3-6), mobility (6), parental substance abuse (6)and parity of mother (3,4,7).

Parental perceptions regarding immunization will be affected by knowledge, which itself is a predictor of uptake(8). Other perceptions include the perceived risks associated with immunization versus the potential benefits (or risks associated with non-immunization)(6,8,9). Religious beliefs are also a factor in some communities (6).

Characteristics of the health service include availability of vaccines (3,8), availability of appointments (3), missed opportunities, physical accessibility (including transportation)(3,5,8) , financial accessibility (3). A recent vaccination coverage survey in the Western Cape (10) identified clinic factors as the commonest group of barriers to vaccination, which included missed opportunities, caregivers given incorrect vaccination dates, distance from clinic too far, inconvenient clinic times and unavailability of vaccines. This quantitative survey sampled over 3700 caregivers across the Province, and utilized a valid sampling strategy (modification of WHO 30 by 7) to obtain a representative sample.

### **Immunization Programmes and Strategies**

According to the WHO measles position paper(11), national immunization programmes should reach all children with 2 doses of measles vaccine and that on-time delivery of the first dose is the highest priority

for programmes. Countries, such as South Africa, that are aiming at measles elimination should achieve  $\geq 95\%$  coverage with both doses in every district. The Global Immunization Vision and Strategy (GIVS) document(12), in outlining the new global strategic direction of immunization programmes, has included a call for commitment from all stakeholders to unprecedented efforts to reach the “hard-to-reach”.

Pockets of low coverage result in a build-up of susceptible persons, which are not covered by routine services. This necessitates follow-up supplemental immunization activities (SIAs), approximately every 3-4 years. Importations from neighbouring areas where services have collapsed or coverage is low creates or compounds susceptible pockets.(13)

Regular SIAs are highly effective strategies for protecting children that do not have access to routine health services. Population immunity is rapidly increased by SIA's and thus measles transmission can be interrupted. Follow-up SIA's should be conducted before the number of susceptible children reaches a critical threshold (the size of a birth cohort).(11) SIA's should be accompanied by simultaneous strengthening of routine services, because high measles vaccine coverage through routine services in every new birth cohort is necessary to control measles and sustain achievements over time.(14) The WHO's new recommendations for ongoing measles epidemics includes a recommendation of measles vaccination as an epidemic response intervention.(15)

### **Recent measles outbreak and response**

The South African Region has experienced measles outbreaks since 2009 with some countries reporting outbreaks as early as March 2009. Measles outbreaks have been confirmed in and reported from the following countries in the sub region: South Africa (March 2009), Lesotho (November 2009), Namibia (August 2009), Swaziland (October 2009), Zimbabwe (September 2009).(16)

According to the National Health Laboratory Services, a total of 16 028 laboratory confirmed cases had been reported in South Africa from the beginning of 2009 to 7 June 2010, with cases having been reported in all 9 provinces with the Gauteng and Kwazulu Natal provinces experiencing the highest case loads. The burden of cases in the Western Cape is not directly comparable to other provinces due to the executive decision to temporarily suspend specimen collection for measles surveillance (8 March 2010). The South African response to the measles outbreak included enhanced case-based surveillance and investigation, clinical case management including vitamin A supplementation, outbreak response

vaccination of contacts, and a national mass immunization campaign that was conducted 12-23 April 2010.

### **Western Cape Provincial Context**

The Western Cape Provincial administrative coverage of measles under 1's is 99.8% for 2008/9(17), however, recent unpublished data suggests that measles coverage is closer to 81.8% (95% CI: 77.3-85.7) for children aged 12-23 months (PEARL study (Coetzee D, et al, 2008) conducted in Mitchell's Plain, Gugulethu & Stellenbosch (unpublished). Inadequate coverage is the most likely determinant of the most recent measles outbreak since a coverage of over 93-95% (in the context of random mixing) is required to prevent endemic transmission of measles. Administrative coverage is inaccurate because of (i) challenges in estimating population denominators, particularly for populations with large migrant components (ii) double counting of vaccinations delivered (iii) late vaccination which increases the susceptible pool. In addition, it is known that vaccine efficacy at 9 months is around 85%, which together with inadequate cold chain maintenance further undermines serological immunity.

### **Justification**

During the mass measles/polio immunization campaign (round 1: 12-23 April 2010) special efforts were made to target the "hard-to-reach" populations. Administrative campaign coverage data is unable to accurately reflect the extent to which these populations are covered (for reasons identified above).

In the context of an outbreak, geographically identified case-based surveillance data can be utilized to identify pockets of susceptible individuals. A survey conducted in these areas is able to accurately estimate vaccination coverage in the pockets that have fueled the epidemic.

The Provincial Department of Health in collaboration with City Health, has thus commissioned this survey in order to assess the outcome of the mass immunization campaign in improving measles coverage in hard-to-reach areas as well as to determine factors that could be addressed in order to improve coverage in "hard-to-reach" populations.

## Aim

To determine the effectiveness of the mass vaccination campaign in increasing vaccination coverage in children aged 6 months to <5years from high burden areas in the Western Cape.

## Objectives

- a. To identify areas with a high burden of measles cases and to compare this to the distribution of informal settlements;
- b. To determine measles vaccination coverage in children aged 6 months to under 5 years, from routine and mass campaign activities, and the timeliness of vaccination;
- c. To determine predictors of immunization uptake;
- d. To provide recommendations to improve immunization coverage in these areas;

## Methods

### Study population:

Children 6 months to under 5 years that have lived in the Western Cape Province for at least 6 months prior to the survey in areas with a high burden of measles cases.

Provincial surveillance data will be utilized to identify areas with a high burden of measles cases by plotting the residential addresses of measles cases using GIS (geographic information systems). These are likely to be located in the following sub-districts, which according to surveillance data had the highest measles attack rates (Sept-23 Jun2010):

- Khayelitsha (265/ 100 000)
- Drakenstein (162/ 100 000)
- Mitchell's Plain (163/ 100 000)

If feasible, a map of informal settlements will be layered over a map indicating the distribution of cases to qualitatively assess the degree of correlation between cases and informal housing.

### **Study Design**

A cross-sectional household survey will be conducted in order to determine immunization coverage at one point in time, as well as to investigate predictors of immunization coverage.

### **Sampling and recruitment:**

- A sample size approximately 246 per area was estimated using the following parameters: expected vaccination coverage of 80% ( based on coverage estimates from PEARL study (Coetzee D, et al, 2008) conducted in Mitchell's Plain, Gugulethu & Stellenbosch (unpublished)), alpha error of 0.05, absolute precision of 0.05 and power 0.80)
- Sampling: 246 households will be systematically sampled per demarcated area (identified using Google Earth™). Due to time constraints, absent households will not be revisited, but will be skipped and replaced.
- According to the DHIS population estimates\*, 8.2% of the population in Cape Town and Cape Winelands are between the ages of 6months to under 5 years; the average household size is 3.8 (DHS) thus an average of 0.31 children in this age group are expected per household; thus a minimum of approximately 800 households will need to be visited to obtain the required sample size per area.
- 1 child-caregiver pair will be randomly included per household by means of throwing a dice. Due to time constraints, the grid will only be applied to care-givers who are available for the interview.
- Field work will be conducted by undergraduate medical or other health sciences students from the Universities of Cape Town and Stellenbosch, and possibly clinic staff if available. An interview team will consist of 2 students and will aim to conduct on average 21 interviews per day. At least 3 teams will be allocated per area, and conduct the survey over 4 to 5 days. Each

team will be provided with an escort/translator recruited from the community to facilitate access and ensure the safety of the students.

**Data collection tool:**

- Simplified modification of the questionnaire will be developed from the 2005 Vaccination Coverage household survey(10), and modifications made using a WHO standardized questionnaire.
- Questionnaires will be piloted and be available in English, Afrikaans and Xhosa.
- Questionnaires will be interviewer administered, face-to-face.

**Site preparation and stakeholder engagement:**

- The community will be informed of survey via community health committees; Community Care Workers (CBS staff) will also assist with informing the community of the survey. Where necessary other relevant community bodies will also be informed.
- The research has been commissioned by the Provincial Department of Health. Permission will also be obtained from City Health to conduct the study. Collaboration with clinic staff will be sought and feedback provided at local facilities as well as to City Health and Provincial managers.

**Data management**

- Training will be provided by the research team and a site facilitator/ co-ordinator designated per survey area.
- On a daily basis, co-ordinators will be responsible for verifying data and supervising sampling.
- Data will be double entered into EpiData

- Rules will be generated to detect values outside of the acceptable range
- In the database, skip patterns will be programmed to ensure only appropriate data are recorded

### **Data Analysis**

- The data will be analysed using Stata 10
- Data exploration: categorical variables will be explored by means of proportions and 1- and 2-way frequency tables. Appropriate descriptive measures of central tendency and dispersion will be used for numerical data and graphically explored by means of histograms and box-and-whisker plots.
- Multivariate logistic regression will be performed to model predictor variables of full immunization status.

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## Logistics

### Proposed dates

	Mitchell's Crossroads	Plain:	Khayelitsha: Site B	Wellington
Initial engagement with clinic staff & community	5-9 July 2010		5-9 July 2010	5-9 July 2010
Site visit	20 July 2010		To be determined	To be determined
Pilot	28 July 2010		To be determined	To be determined
Field work	2-5 Aug 2010		To be determined	To be determined

## Budget

Printing questionnaire	PGWC	1200 double-sided copies per site					
	<b>Unit Cost</b>	<b>Phillipi</b>	<b>Site B</b>	<b>Mbekweni</b>	<b>Delft</b>	<b>Du Noon</b>	<b>Per Site Calc</b>
Community host/ translator	R150/person/day	R 2 250	R 4 500	R 4 500	R 4 500	R 4 500	5 persons x 6 days
Site Facilitator	R300/person/day	UCT (Christolene)	?EHP	?Sr Nancy	R 1 800	R 1 800	1 person x 6 days
Site Supervisor	R50/hr	Dr Bernhardt	Dr Cameron/ Berr	R 2 400	R 2 400	R 2 400	1 person x 6 days
Field worker	R40/hr	UCT 4th years	SUN Final years	SUN Final years	R 9 600	R 9 600	5 persons x 6 days
Transport	R2.60/km	UCT	R 1 040	R 1 040	R 1 040	R 1 040	400km/ site
Stationary	R200/site	R 200	R 200	R 200	R 200	R 200	
Cell phone costs	R150/site	R 150	R 150	R 150	R 150	R 150	
Meals	R30/person/meal		R 1 800	R 1 800	R 1 800	R 1 800	12 persons x5 days
20% contingency		R 520	R 1 538	R 2 018	R 4 298	R 4 298	
<b>Totals</b>		<b>R 3 120</b>	<b>R 9 228</b>	<b>R 12 108</b>	<b>R 25 788</b>	<b>R 25 788</b>	

## Internal validity

A modified questionnaire that was used for the previous survey will be utilized. The Road to Health Card will also be used as a valid data source in order obtain accurate date of routine vaccine administration. Response rates will be recorded and deemed acceptable if >80%.

## Ethics

The principles that govern biomedical research involving human subjects will be adhered to, including the Declaration of Helsinki(18). Researchers will ensure that the rights, integrity, and confidentiality of trial subjects will be protected. The risks to respondents involved in this study are minimal, and are outweighed by the anticipated benefits of improved immunization services at community and provincial level. At an individual level, the child participant if not up-to-date with his/her immunizations will be given a referral letter for the local clinic. Participation is voluntary and verbal informed consent will be obtained prior to participation in research. An information sheet about the study will be available in English, Afrikaans and Xhosa. Primary care-givers that are minors will not be excluded from this survey. The minor's assent and consent from the minor's legal guardian will be sought. Their inclusion can be justified because 1. the survey is minimal risk 2. it would assist with identifying the proportion of care-givers that are minors 3. reasons for non-vaccination might be specific for these care-givers. Questionnaires will be anonymised and thus confidentiality will be maintained, and available in commonly spoken languages. Individuals that decide not to participate in the study will in no way be disadvantaged. The findings of the study will be presented at the local level (facility staff and community representatives) as well as to provincial/ district level managers.

Ethics approval will also be sought from University of Cape Town Research Ethics Committee.

## Limitations

- Selection bias: the study will be conducted during normal working hours, thus selection bias will operate in that working parents and children at crèches will not be included; RTHC's of children attending crèches are often kept at the crèche, which will minimize validity of data regarding routine immunizations. The study was commissioned by the Western Cape Department of Health after the mass vaccination campaign had already occurred, and in order to minimize the impact of recall bias, it will be conducted expeditiously. The researchers will therefore not be able to return to absent households.
- Information: The study is conducted retrospectively and is reliant on recall of immunizations received during the campaign and of routine immunizations where the RTHC is not available. Recall bias might thus result in misclassification. Verification of the site of the immunization will assist to minimize misclassification, as has been used in other studies.
- Temporality cannot be determined with cross-sectional surveys, thus one cannot be certain whether certain predictors preceded the outcome of interest.

## Definitions

Household: "individuals living and eating together under the same roof" (19)

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# Part B: Literature Review

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## Objectives

The literature review contextualizes the protocol to assess the effectiveness of the mass measles vaccination campaign in the Western Cape that was conducted in April 2010. The campaign was conducted in the context an epidemic.

The specific objectives were:

1. To review existing knowledge regarding:
  - a. Measles epidemiology;
  - b. The effectiveness of measles control strategies;
  - c. The South African measles control programme and 2009/2010 epidemic.
2. To review the methodology for assessing measles vaccination coverage.

## Search strategy

Extensive literature is available regarding measles. The research topic for this review requires knowledge regarding a range of topics, including epidemiology of measles, measles control strategies, vaccination programmes & policies, measurement of coverage or immunity, and outbreak response. The review was therefore not designed as a systematic review of the literature (which for practical purposes would have meant a very narrow review in terms of content). A pragmatic approach was taken, utilizing information that was acquired from a number of literature searches over a period of time, from March 2010 to December 2011, in order to achieve the purpose of providing a coherent and contextualized summary of relevant information. PubMed was the primary database that was searched and examples of search terms include (“measles vaccination” AND “South Africa”) (“measles outbreak” AND “effectiveness”). Secondly the WHO website was searched and additional sources included reference textbooks and local department of health reports. All types of study designs were included.

## Summary of the literature

### Measles epidemiology

In 1980, before the widespread use of measles vaccine, an estimated 2.6 million measles-related deaths occurred worldwide.(1) Global vaccination coverage of first dose measles reached 82% in 2007 and has resulted in a global decline in measles incidence by two thirds and mortality by 74% from 750 000 in 2000 to 197 000 in 2007.(2) The African region experienced an 89% reduction, accounting for 63% of the global reduction in measles mortality.(3) Globally in 2008, measles accounted for 1% of childhood mortality in under 5's.(4) Despite considerable progress towards measles elimination, measles epidemics occurred in 2009-11 in 28 Sub-Saharan African countries with approximately 200 000 reported cases (1), including South Africa, which had over 18 000 confirmed cases.(5)

Measles virus is known to be one of the most contagious of infectious agents with 12-18 secondary cases estimated to occur from a single case in a completely susceptible population (reproductive index). Outbreaks may therefore occur in populations where herd immunity is below 95%.(6) The incubation period is on average 10-14 days(3), which overlaps the infectious period, which lasts from 4 days prior to the onset of the rash, until 4 days after the onset of the rash(3). Morbidity and mortality from measles is caused by (1) the virus itself, (2) comorbidity with malnutrition or (3) secondary viral or bacterial infections which occur due to measles virus-associated immune suppression.(7) Pneumonia is the commonest cause of measles-associated deaths (8) and subacute sclerosing panencephalitis although uncommon (incidence of 1/10 000 to 1/100 000 cases (9)), is an invariably fatal complication. Vitamin A supplementation has proven to reduce measles-related complications (10).

### The measles vaccine and immunity

A number of live attenuated measles vaccines, often referred to as 'the measles vaccine', have been in use since the 1960's and are equally effective against all wild measles virus genotypes(3). The vaccine is safe and efficacious (3) however effectiveness may be reduced by clinical practices, particularly since the vaccine is light and heat sensitive. The vaccine has been assessed to be one of the most cost-effective public health interventions (11). Routine measles vaccination coverage is used as an indicator of progress towards Millenium Development Goal 4 because it contributes significantly towards mortality reduction and is a marker of access to routine child health services.(1) Measles is considered to be

potentially eradicable because humans are the only reservoir for measles virus, the disease is clinically apparent, sensitive and specific diagnostic tests are available and measles is monotypic requiring therefore only a monovalent vaccine.(8) However, progress is limited by the high reproductive ratio of measles, failure of health systems to achieve adequate coverage and vaccination failures which occur from individual-level factors and poor clinical practices.

Although infants have a high mortality from infection, vaccination before 9 months is not routinely recommended because vaccine efficacy is diminished due to immaturity of the immune system and presence of neutralizing maternal antibodies (12). A review by Cáceres et al (12) described the factors that affect the prevalence of maternal antibodies present in the infant. These include the level of anti-measles antibodies in a pregnant woman, the degree of placental transfer and rate of antibody decay in the infant. Studies have consistently demonstrated that infants of mothers with naturally-acquired immunity have higher antibody levels than infants of women with vaccine-induced immunity (12). Maternal HIV-1 infection and gestational age of the infant are the main factors that impair placental transfer of anti-measles antibodies to infants. There also appears to be lower placental transfer of antibodies in developing compared with developed settings. Maternally acquired antibodies were found to decay to minimal levels by 7-9 months, and the rate of decay did not appear to differ significantly across a variety of settings. Two studies described the levels of maternally acquired anti-measles antibodies in South Africa. Kiepiela et al (1991) (13) found that only 12% (95% confidence interval 1-19%) of infants had protective levels of antibodies at 6 months, and by 9 months all infants were not protected by maternal antibodies. Despite the small sample size (20) and selection bias (term black infants from one township in Durban), the results appear comparable with seroprevalence curves from other studies conducted in a variety of settings.(12) Maternal immunization and maternal and child HIV status were not documented and represent a limitation. The current relevance of this data is uncertain due to the progression of the HIV epidemic and increases in maternal vaccine-induced immunity relative to acquired immunity, caused by changes in implementation of the South African immunization programme.

The results of a number of studies estimated that the median proportion of infants seroconverting following vaccination between 8 and 9 months was 89.6% (interquartile range, 82–95%) compared with 99% (interquartile range, 93–100%) of infants vaccinated between 11 and 12 months.(14) Vaccination

programmes aim to achieve high levels of coverage in individuals 9 months and older, to create sufficient herd immunity that is able to substantially protect younger infants.(8)

Primary and secondary vaccine failure rates are higher in HIV-1 infected children than HIV-uninfected children (8). HIV-1 infection in the mother (15) or child (16) and high population density (17) are associated with a greater proportion of younger cases. The severity of infection and mortality is increased by concomitant immune suppression, including AIDS, malnutrition (18), extremes of age, particularly infants,(8) as well as overcrowded living conditions(3). The WHO recommends an additional vaccination dose at 6 months in refugee camps, hospitals and for HIV-1 infected infants.(19) Measles is also associated with tuberculosis where the cumulative results of a number of studies indicate that about 12% of children with a new diagnosis of pulmonary tuberculosis have a recent history of measles.(8)(8)

#### **Measles control strategies and vaccination policies**

Measles eradication is defined as 'the world-wide interruption of transmission of the virus, and represents the sum of successful elimination efforts in all countries and regions.'(20) Vaccination will need to continue until measles eradication is achieved because of the continued threat of reintroduction of the virus. (21) As of 2008, two of the six WHO regional offices (WHO AFRO, SEARO) have mortality reduction goals (WHO AFRO, SEARO) which aim to achieve coverage targets of  $\geq 90\%$  at the national level and  $\geq 80\%$  in every district. These 2 regions have the highest burden of measles mortality. The remaining four WHO regional offices (AMRO, EURO, EMRO, WPRO) have measles elimination goals, with coverage targets of  $\geq 95\%$  with both doses in every district.(21)

The current WHO-UNICEF comprehensive strategy for reducing measles mortality (22), has been implemented by most WHO member states, including South Africa. The strategy consists of 4 arms, namely (1) achieving sustained high routine first dose immunization coverage (over 90%) to infants, (2) providing of a second opportunity for measles vaccination for all children through routine services or supplementary immunization activities; (3) surveillance of measles and immunization coverage in order to understand the epidemiology of ongoing transmission and (4) improving management of complicated cases, particularly by Vitamin A supplementation.

As of 2008, 192 of 193 WHO member states utilize a 2 dose delivery strategy (3) and timely delivery of the first dose (as soon as possible after protection is lost from maternal antibodies) remains the highest priority for programmes (3). Country policies vary regarding the timing of vaccination, with doses generally offered later and through routine services in countries with longstanding immunization programmes, whereas countries with weaker health systems, deliver the first dose from 9 months and rely on MVCs to deliver the second dose, specifically targeting children that are not reached by routine services(3).

The Pan-American Health Organization (PAHO) has since the 80s used MVCs together with strengthening of routine vaccination to successfully interrupt measles transmission. MVCs ensure vaccination of children who were not reached by routine vaccination programmes (8), increase vaccine efficacy in those that did not initially seroconvert and are effective in rapidly increasing population immunity thereby potentially interrupting endemic transmission(3).

The PAHO 3 prong strategy(23) entails an initial national 'catch-up' campaign targeting individuals aged 1-14 years, sustaining high immunity by routinely vaccinating more than 95% of each new birth cohort ('keep-up') and regular 'follow-up' MVCs targeting children 1-4 years old regardless of previous vaccination status. The interval between regular MVCs is determined by the rate at which susceptible persons accumulate in the population, which depends on vaccination coverage as well as in-migration of susceptible persons. Generally these should be conducted every 3-5 years, which is when the number of susceptible children of pre-school age reaches the size of a birth cohort.(3) These activities require a high degree of commitment, organization and resources (costing more per vaccinated child than routine vaccination (24)(25)) and may weaken the health system by drawing resources from routine health services during the campaign. However, the success of mass campaigns in reducing measles incidence has been well documented (6) and they are considered by experts to be a key innovation that has enabled progress towards measles morbidity and mortality reduction.(26) In addition, campaigns also have the potential to positively impact health systems, by providing opportunities for better collaboration, improved knowledge of immunizations, micro-planning, data quality and surveillance, and increased community demand for immunizations.(27) Since routine services are still seen as the backbone of eradication efforts (1), immunization campaigns should be used as an opportunity to strengthen routine immunization services and the challenges of mass campaigns mitigated with careful planning.

## Vaccination Surveys

Vaccination surveys provide an opportunity to assess the reliability of administrative coverage estimates and to assess the quality of routine and campaign immunization services.(28) Surveys can also increase coverage by increasing public demand for vaccinations. The most frequently utilized sampling methods include the 30 by 7 cluster methodology advocated by the WHO and the lot quality assurance sampling method.(29) The 30 by 7 cluster method aims to estimate vaccination coverage of an area with a precision of 10%. The first stage of sampling selects 30 non-overlapping clusters according to the probability proportionate to the size of the population in the cluster. From a random starting point within each cluster, the first 7 eligible children are included. This method seeks to obtain estimates for the whole area, and not for individual clusters. Lot quality assurance sampling is a stratified random sampling method that originated in the manufacturing industry. The sample from each lot (batch or in this case geographic area) determines the acceptability of the selected lot. The use of a binary outcome allows for smaller sample sizes, and therefore the assessment can be performed more frequently. Data from all the lots may be combined and weighted to estimate population coverage.(29)

Immunization coverage data sources used in surveys include caregiver history, Road to Health Clinic Card (RTHC) and serological data. Coverage surveys estimating routine coverage usually target children 12 to 23 months of age, whereas post-campaign evaluations target the age group that was included in the campaign. Pre- and post-campaign surveys have been used to estimate the impact of MVCs on vaccination coverage.

A Western Cape Province (WCP) vaccination coverage survey (2005)(30) which sampled 3624 children aged 12-23 months estimated 92.7% provincial coverage for first measles vaccination due at 9 months and 60% for the second measles vaccination due at 18 months. The study noted that it was not able to identify 'pockets of low coverage' accurately.

## Outbreak response

Cairns et al (31) conducted a review of studies published between 1995 and July 2009 to determine whether outbreak response vaccination (ORV) should be recommended for measles outbreaks in middle- and low-income countries. ORV can only be assessed by observational studies and commonly measles incidence and the shape of the epidemic curve following ORV is used to assess the impact of the

intervention. Analytic methods have occasionally been used, for example by Guris et al (32) using ecologic data from outbreaks in Micronesia, and demonstrated that the time to reach 80% coverage was significantly associated with the duration of the outbreak. Similarly, in Sudan, measles incidence after an ORV was higher in an area with the lowest coverage.(33) Grais et al(34) used mathematical modeling to estimate the number of cases averted by ORV, and the potential impact of implementing ORV earlier or extending the target age group on the number of cases averted.

Mass vaccination following a measles outbreak was included in the WHO guidelines in 2009(21), as evidenced by reduced morbidity and an interruption in the spread of measles associated with ORV, particularly if it started early, covers a wide age range, and achieves high coverage. The decision to conduct ORV should consider implementation capacity (financial, staff and logistical, including the availability of vaccines and other supplies) and the risk of spread, morbidity and mortality. Timely implementation is critical to minimize the number of severe measles cases and deaths.

### Predictors of vaccination uptake

Kroeger's variant of Health Care Utilization Model (1983) was useful in categorizing factors associated with health seeking behaviours into (1) predisposing factors, (2) perceptions regarding benefits and burdens, and (3) characteristics of the service/ enabling factors.

Predisposing factors that relate to vaccination coverage include parental education (35) (36), parental marital status (35) , socio-economic status (35-38), mobility (38), parental substance abuse (38)and parity of mother (35,36,39).

Parental perceptions regarding immunization will be affected by knowledge, which itself is a predictor of uptake(40). Other perceptions include the perceived risks associated with immunization versus the potential benefits (or risks associated with non-immunization)(38,40,41). Religious beliefs are also a factor in some communities (38).

Characteristics of the health service include availability of vaccines (35,40), availability of appointments (35), missed opportunities, physical accessibility (including transportation)(35,37,40) , financial accessibility (35). A recent vaccination coverage survey in the Western Cape (30) identified clinic factors as the commonest group of barriers to vaccination, which included missed opportunities, caregivers

given incorrect vaccination dates, distance from clinic too far, inconvenient clinic times and unavailability of vaccines. This quantitative survey sampled over 3700 caregivers across the Province, and utilized a valid sampling strategy (modification of WHO 30 by 7) to obtain a representative sample.

### The South African and Western Cape context

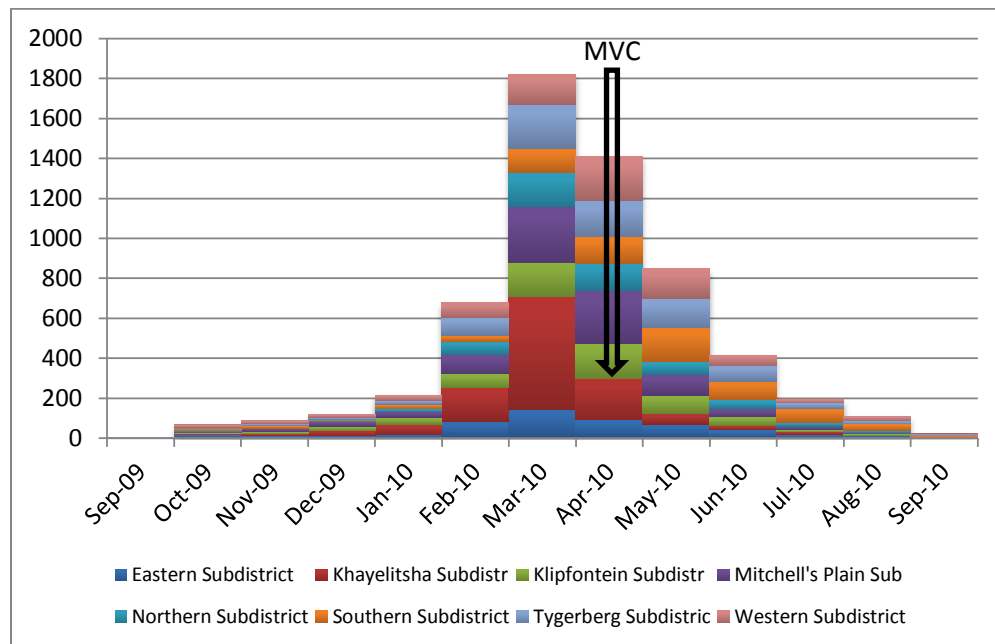
The South African measles vaccination programme started in 1975 with 1 dose schedule (42), and from 1996-8 has followed the PAHO/ WHO-UNICEF strategy (42). MVCs were implemented, starting with a nation-wide catch-up mass campaign covering children 9 months to 14 years in 1996/7(42) and regular 4 yearly follow-up campaigns for children aged 9 months to 4 years. Routine services were also strengthened at that time, including the use of a 2 dose schedule (at 9 and 18 months) and case-based surveillance with laboratory confirmation.

South Africa has an administrative monitoring system for immunization coverage, similar to most countries. The system measures the number of doses administered, as a proportion of the annualized estimated population of eligible children (children under 1 year of age). In South Africa, population estimates are estimated from a 10 yearly census. Estimates are inaccurate, and under-estimated the infant sub-groups because they do not take account of large scale in-migration. This results in inflated coverage estimates, often over 100%. The quality of the numerator is also problematic because of poor information management. The Western Cape province reported measles coverage under 1 year of age as 102.8%, 99.7% and 102.8% for the years 2007/08, 2008/09 and 2009/10 respectively (43). The potential for an outbreak was therefore not anticipated.

The South African epidemic started in the Gauteng province in March 2009 and spread to all provinces despite initial vaccination campaigns in the affected areas and later province-wide.

During this epidemic in 2009/10 the WCP had the third highest number of confirmed cases (more than 2000), despite discontinued laboratory confirmation of cases at the peak of the epidemic.(5) Figure 1 displays the epidemic curve for the Metropole district of the WCP which accounted for 85% of cases. Over 60% of the cases were under 5 years of age, with 29% aged 6 to 11 months. Ninety-six percent of cases had not received a dose of measles vaccine or had an unknown vaccination status. In addition, 41 measles-associated deaths were reported, with a case-fatality ratio of 6.9 per thousand in children under 5 years.(44)

Figure 1. Number of suspect cases reported from Sept 2009-Sept 2010 in the Metropole District of the Western Cape.(45)



A MVC, against measles and polio had already been planned; however as a result of the epidemic the targeted age group for measles vaccination was extended from 9 to 59 months, to include children from 6 months to 15 years. The first round of the campaign was conducted nationally from 12 to 23 April 2010. (A second campaign dose of polio vaccine, Vitamin A and Albendazole were administered in the second round, conducted a month later.) The campaign was conducted predominantly at existing health and educational facilities and crèches. Special efforts were made to reach known 'hard to reach' groups, including informal settlements, immigrant populations and groups known to be opposed to vaccination of children. Over 1.2 million children were immunized in the WCP against measles, and coverage was calculated to be 99% and 76% in children between the ages of 6 and 59 months and 5 and 14 years respectively.(45) Additional outbreak responses in the WCP included strengthening of routine immunization services, implementation of infection control measures at facilities, clinical case management including administration of vitamin A, response vaccination offered to exposed contacts and targeted ORV in high-incidence sub-districts prior to the mass vaccination campaign.

## Needs for further research

Districts need a valid tool for monitoring vaccination coverage, particularly in high risk areas. These areas can be identified in an epidemic by identifying geographic clustering of cases. A community survey is required in the WCP to evaluate pre- and post-campaign coverage in order to assess the extent to which targeted areas were reached by routine services and campaign services, and the need for further 'mop-up' vaccination after the MVC.

Further research is also required to determine the immunity profile of the South African adult population and to model the decay of maternal antibodies, in the context of the HIV epidemic.

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# Part C: Journal Manuscript

Evaluating measles vaccination coverage in high incidence areas of  
the Western Cape Province, following the mass vaccination  
campaign

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# Abstract

## Background

Despite significant advances in measles control, large epidemics occurred in many African countries in 2009-2011, including South Africa. South Africa's control strategy includes 4 yearly mass vaccination campaigns, the last of which was conducted nationally in April 2010 and coincided with the epidemic. Administrative monitoring of vaccination coverage can overestimate coverage, particularly in areas that experience high rates of in-migration, due to inaccurate population estimates.

## Aim

A community survey was conducted in the Western Cape to assess measles vaccination coverage attained by routine and campaign services, in children aged 6 months to 59 months (at the time of the mass campaign), from high incidence areas.

## Methods

High incidence areas, in which households were consecutively sampled, were identified using routine surveillance data. Caregiver history of campaign vaccination and routine vaccination status from the child's Road to Health Card were collected. Analytic methods include chi-square test, logistic regression and a Monte-Carlo simulation, which was used to estimate pre- and post-campaign immunity.

## Results

Of the 8332 households visited from 5 suburbs, there was no response at 41% (n=3435) of households. Ninety-five percent (1711/1800) of eligible households participated. Ninety percent (95% CI 86-94%) of children received a campaign vaccination. Prior to the campaign, 33% of 9-17 month olds had not received a measles vaccination, and this was reduced to 5% after the campaign. Sixty-one percent of children were estimated to have measles immunity before the mass campaign, and this increased to 94% after the mass campaign.

## Discussion

Routine services failed to achieve adequate herd immunity. Mass campaigns can rapidly increase population immunity, however vigilance is required to monitor and sustain adequate coverage, particularly in highly mobile populations.

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## Introduction

Measles is one of the most infectious human viruses and a significant cause of childhood mortality. Population immunity of around 95% is necessary to prevent on-going virus transmission.(1) Significant advances have been made towards measles elimination through a cost-effective vaccine. The current World Health Organization (WHO) strategy for reducing measles mortality (2) has been implemented by most WHO member states, including South Africa since 1996. The strategy consists of 4 arms, namely (1) achieving sustained high routine first dose vaccination coverage to infants, (2) providing a second opportunity for measles vaccination for all children through routine services or mass campaigns, (3) surveillance of measles and vaccination coverage and (4) improving management of complicated cases.

Non-selective mass vaccination campaigns (MVCs) that vaccinate all children within a specified target age group regardless of prior vaccination status, have increased coverage particularly in developing countries where routine health services are weak.(3) MVCs reach children who were not reached by routine programmes,(4), provide a second opportunity for those that did not initially seroconvert and increase population immunity rapidly, potentially interrupting on-going transmission(3). The worldwide impact of MVCs on the incidence of measles has been well-documented (1) and WHO policy has been recently revised to include MVCs as an outbreak response activity (2).

Despite considerable progress towards measles elimination, epidemics occurred recently in 28 Sub-Saharan African countries, including South Africa. In 2009/10 approximately 200 000 cases were reported in Sub-Saharan Africa (5), of which South Africa had over 18 000 confirmed cases (6). The underlying cause of these outbreaks is primarily insufficient coverage, but also poor clinical practices, including cold-chain maintenance.(5)

The South African epidemic started in the Gauteng province in March 2009 and, despite targeted campaigns from May to October 2009(7) in affected areas, spread to the rest of the country. A MVC, against measles and polio had already been planned; however as a result of the epidemic the targeted age group for measles vaccination was extended from 9 to 59 months, to include children from 6 months to 15 years. This was conducted nationally from 12 to 23 April 2010.

Over 2000 cases (6) were confirmed in the 5.5 million (8) people residing in the Western Cape Province. Eighty-five percent of cases occurred in the Metropole district, which houses 65% of the population.

The number of confirmed cases was under-estimated as laboratory confirmation was halted at the peak of the epidemic.(9) The Western Cape epidemic started in October 2009 and peaked in March 2010. Over 60% of cases were under 5 years of age and 29% were in the 6 to 11 month age group. Ninety-six percent of cases in the Metropole district had not received a dose of measles vaccine or had an unknown vaccination status (9). The case-fatality ratio in the under 5's was 6.9 per thousand (9).

Administrative monitoring of vaccination coverage is conducted in all provinces. Due to the under-estimation of population denominators and inaccurate numerators, data from routine immunization programmes and campaigns are often inflated by underestimated official population denominators. The Western Cape reported that measles coverage under one year of age was 102.8%, 99.7% and 102.8% for the years 2007-2009.(10) The potential for an outbreak was thus not anticipated. A community survey was commissioned by the Western Cape Department of Health in 2010 after the MVC to monitor routine and campaign coverage in line with WHO recommendations (11). The aim was to assess the effectiveness of the MVC, particularly in reaching children aged 6 months to 5 years at the time of the campaign, from communities where the incidence of measles had been high and to determine predictors of routine vaccination coverage and measles.

## Methods

A cross-sectional design was used and five high incidence suburbs were purposively selected using provincial surveillance data. Field-mapping was conducted within each suburb to identify high incidence areas. All households within the high incidence areas were consecutively visited and requested to participate in the survey. Within each household 1 caregiver-child pair was randomly selected. Households where there was no response were not revisited due to the limited time available to conduct the survey. A sample of 246 households per suburb was estimated to provide vaccination coverage estimates with an alpha error of 0.05, an absolute precision of 0.05 and power of 0.80, based on a coverage estimate of 80%. A caregiver-child pair was eligible to participate if the child was aged 9 to 62 months (which was equivalent to 6 to 59 months at the time of the campaign), and had resided in the Western Cape for 6 months.

Caregivers were interviewed using a pre-piloted questionnaire, adapted from a previous coverage survey (12), and routine vaccination status was documented from the child's Road to Health Clinic Card (RTHC). Campaign vaccination status was not documented on the child's RTHC, and caregiver history

was therefore relied upon. Local community members were recruited and paid a stipend to accompany field workers in order to facilitate safer access to the communities. Field workers consisted of 3 groups of undergraduate medical students and 1 group of hired field workers. Field work was conducted from 20 July until 30 August 2010.

## Data Analysis

Data analysis was done using STATA v11. Routine vaccinations administered during or after the mass vaccination campaign were not included in the analysis, in order to provide a pre- and post-campaign profile. Children without a RTHC were regarded as 'not vaccinated', because routine vaccination status according to caregiver history was considered unreliable. Homogeneity within high incidence areas was not taken into account as the study did not aim to obtain an overall estimate for the area. Prevalence estimates were calculated with 95% confidence intervals. Associations between independent categorical variables and outcomes were explored using a chi-square test and logistic regression. Timeliness of vaccination was illustrated using a cumulative time-to-event distribution. To facilitate comparability across suburbs for the number of reported barriers to access, this variable was adjusted for sample size per suburb. ([Appendix 8](#))

Population immunity before and after the mass vaccination campaign was modeled based on estimates of waning maternal antibody protection for unvaccinated children aged 6 to 9 months(13), immunity following routine and campaign vaccine dose(s)(14), and immunity following measles infection (assumed complete). The effect of parameter uncertainty on the model estimates was assessed through probabilistic sensitivity analysis in which all parameters were varied simultaneously within the published confidence bounds in a Monte Carlo simulation (1000 runs). Full details of the model and sensitivity analysis are included in [Appendix 8](#).

## Ethical considerations

Verbal informed consent was obtained from all participant caregivers. The Declaration of Helsinki (15) and the South African Medical Research Council Guidelines on ethics for medical research (16) were followed in the conduct of epidemiological research. Ethics approval was obtained from the University of Cape Town's Human Research Ethics Committee.

## Definition of terms

Up-to-date for age: children between the ages of 9 to 17 months who had at least 1 routine measles vaccination and children 18 months and older who had at least 2 routine measles vaccinations according to RTHC.

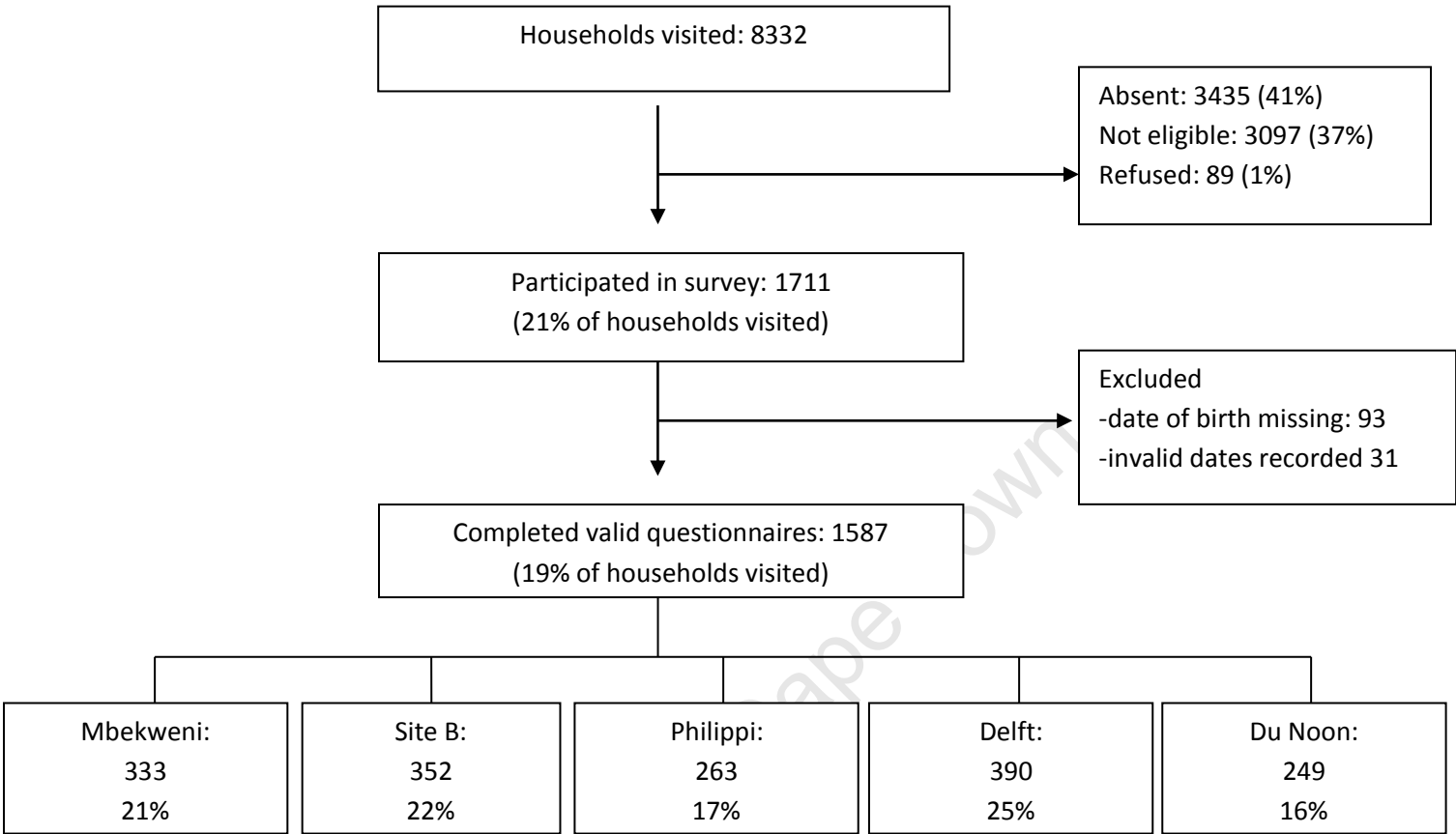
## Results

### Study sites and response rates

The survey was conducted in the following suburbs: Site B Khayelitsha, Philippi, Mbekweni, Delft and Du Noon. Of the 8332 households visited, there was no response at 41% (n=3435). Ninety-five percent (1711 out of 1800) of eligible households participated in the survey. The overall response rate was thus 21%. A total of 1587 completed questionnaires were analysed. (Figure 1)

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**Figure 1. Selection of study participants**



## Demographics

Ninety six percent of primary caregivers were women with a median age of 29 years (range 15 to 86 years) and 93% of primary caregivers reported that they were literate. The mean age of the children was 2.8 years (95% CI 2.7-2.8). (Table 1)

**Table 1. Demographic and measles-related history of study participants.**

	Overall	Mbekweni	Site B	Philippi	Delft	Du Noon
Gender of child: % female (95% CI)	52 (49.9-54.9)	47 (41.4-52.4)	56 (50.8-61.4)	52 (46.2-58.6)	54 (49.3-59.6)	52 (45.2-58.0)
Age of child: mean at time of campaign (95% CI)	2.5 (2.4-2.5)	2.6 (2.5-2.7)	2.6 (2.4-2.7)	2.4 (2.2-2.5)	2.4 (2.3-2.5)	2.4 (2.2-2.5)
Gender of primary caregiver: % female (95% CI)	97 (95.5-97.4)	97 (94.9-98.8)	97 (94.1-98.2)	97 (94.6-98.9)	94 (90.6-95.8)	99 (96.5-99.7)
Age of primary caregiver, years: median (range)	29 (15-86)	30 (15-70)	30 (17-71)	29 (15-69)	29 (16-70)	28 (17-86)
Basic literacy of primary caregiver: % (95% CI)	93 (91.9-94.4)	90 (86.0-92.8)	95 (91.7-96.7)	96 (93.1-98.2)	94 (91.5-96.4)	91 (86.7-94.3)
History of measles: % (n) [95% CI]	9 (142) [7.6-10.5]	6 (20) [3.7-9.1]	13 (44) [9.2-16.4]	11 (28) [7.2-15.0]	7 (28) [4.8-10.2]	9 (22) [5.6-13.1]
History of campaign dose received: % (n) [95% CI]	91 (1448) [89.7-92.6]	93 (311) [90.2-95.8]	92 (324) [88.7-94.6]	90 (237) [85.9-93.4]	90 (351) [86.6-92.8]	90 (225) [86.0-93.7]
Clinic card seen % (n) [95% CI]	75 (1194) [73.0-77.3]	70 (233) [64.7-74.8]	72 (253) [66.9-76.5]	67 (175) [60.5-72.2]	82 (321) [78.2-86.0]	85 (212) [80.1-89.3]

## Measles disease

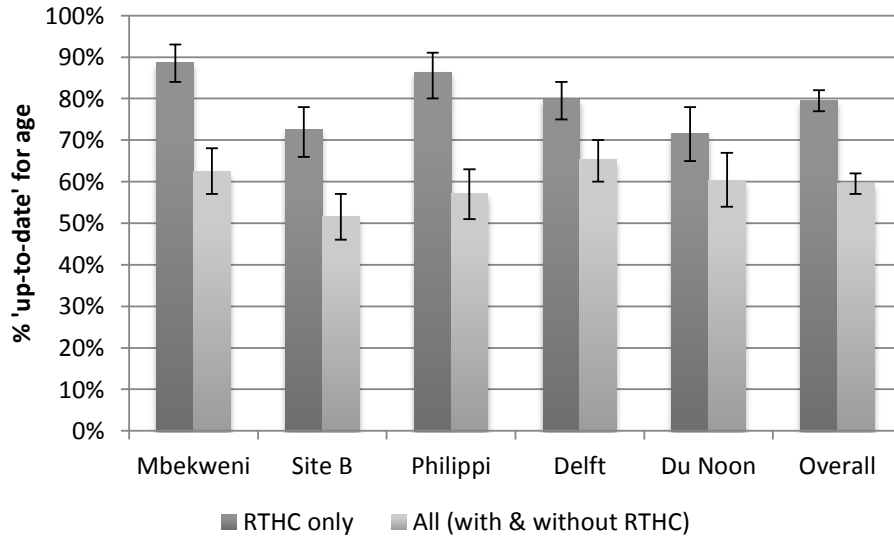
Caregivers reported that 9% (142/1587) of children had measles (Table 1) and 90% (106/118) reported that it occurred between December 2009 and July 2010, with a peak in April 2010. Eighty percent (94/118) occurred prior to the MVC with a sharp decline in the incidence rate after the MVC. ([Appendix 7, Figure B](#))

## Routine Vaccination Services

Seventy-five percent (1194/1587) of caregivers had a RTHC of their child, 22% (n=341) reported that the RTHC was elsewhere and 3% (n=52) were not in possession of a RTHC. Caregivers in Delft (82%) and Du Noon (85%) were significantly more likely to have a card than the other sites (Table 1). Of those without a RTHC, 55% (216/393) of caregivers did not know how many doses of measles vaccine had been administered to their child.

Eighty percent (862 out of 1083) of children older than 9 months with a RTHC were up-to-date for age for measles vaccination. Significant variability existed across study sites as displayed in Figure 2. Fifty-nine percent of all children (with and without a RTHC) 9 months and older prior to the mass campaign were up-to-date-for-age. Significantly more children in the age group 9 to 17 months were up-to-date for age, compared with those over 18 months (RTHC sub-group: 86% [95% CI 81-90] and 78% [95% CI 75-80%] respectively). Routine vaccination status was not significantly associated with any predictor variables, specifically age and literacy of primary caregiver, perceived attitudes of clinic staff, age and gender of child.

Figure 2. Proportion of children up-to-date for age before the MVC, stratified by suburb.

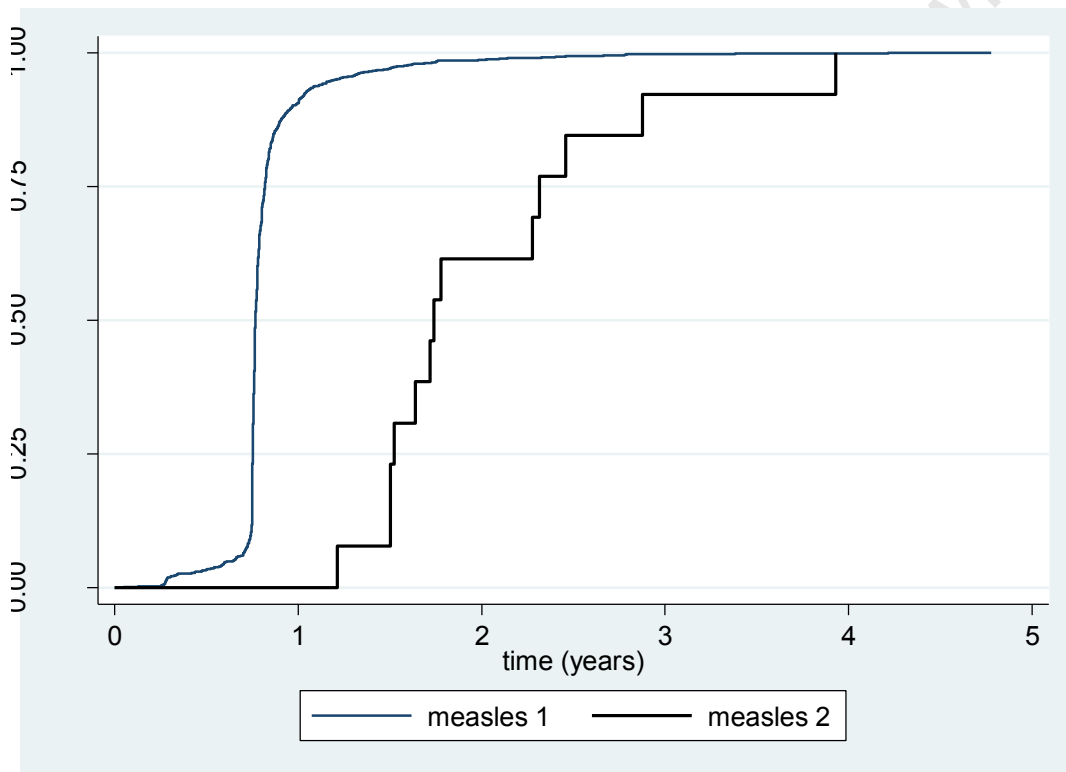


\*Error bars represent 95% confidence intervals

### Timeliness of routine vaccination

Date of vaccination was documented for 68% (987/1449) of those eligible for the first measles dose and 57% (653/1137) of those eligible for the second measles dose. The median time from the due date to vaccination was 8 days (IQR 1-29) for measles 1, and 20 days (IQR 1-78) for measles 2. Figure 3 illustrates the cumulative time to vaccination for the first and second doses, demonstrating delays in the administration of the second dose of measles vaccine.

**Figure 3. Timeliness of first and second measles vaccination, in children with date of vaccination documented on RTHC.**



After adjusting for age, documented routine vaccination coverage prior to the mass campaign was significantly associated with the absence of a history of measles disease in children 9 months and older. One measles vaccination was associated with 49% reduced odds of measles compared with no measles vaccination ( $p=0.003$ ); and 2 measles vaccinations were associated with a 61% reduced odds of measles compared with no measles vaccination ( $p<0.001$ ). Two measles vaccinations were associated with 46% reduced odds of measles compared with 1 measles vaccination ( $p=0.009$ ). ([Appendix 7, Table A](#))

Of caregivers that responded to questions relating to the health services, 85% (1238/1456) reported that the clinic immunization staff had a positive attitude towards them and their child, 8.2% ( $n=118$ ) reported a negative attitude and 6.9% ( $n=100$ ) were neutral. The commonest categories of reasons for caregivers not accessing routine vaccination services were related to a lack of information, followed by personal obstacles. ([Appendix 7, Figure C](#)) The single commonest reason was that the primary caregiver was too busy, followed by the caregiver being unaware of when to return for vaccinations.

## Effectiveness of Campaign

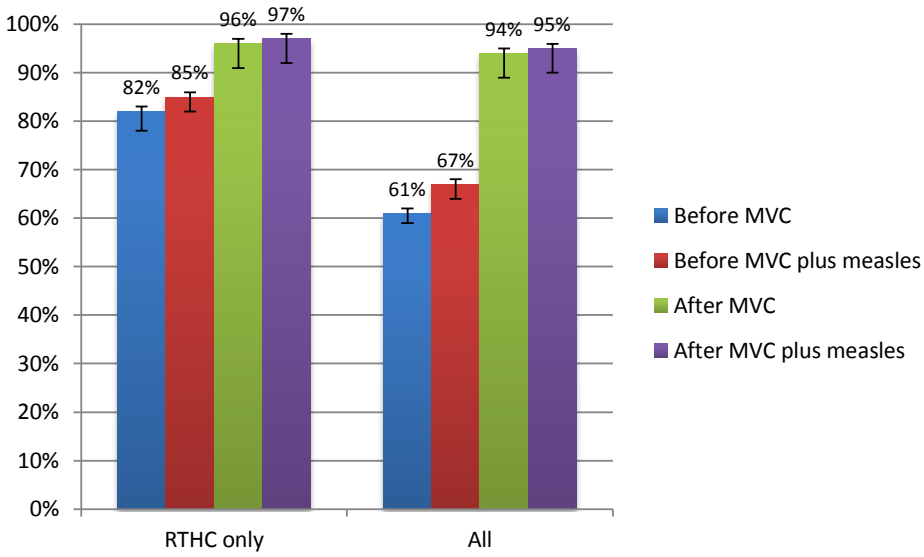
Caregivers reported that 91% of children (1448/ 1587) received a dose of measles vaccine during the MVC. This was not significantly associated with any predictor variables. Prior to the MVC 33% and 30% of children aged 9-17 months and 18 months and older respectively had not had a dose of measles vaccine, whereas after the MVC this was significantly reduced to 5% and 2% respectively. (Table 2)

**Table 2. Proportion of children unvaccinated before and after the MVC, stratified by age group**

	9-17m olds, card only (N=244)		9-17m olds, card plus history (N=312)		18m and older, card only (N=839)		18m and older, card plus history (N=1137)	
	Before	After	Before	After	Before	After	Before	After
% O doses (n)	14 (35)	1 (3)	33 (103)	5 (14)	5 (44)	<1 (2)	30 (342)	2 (26)
[95% CI]	[10-19]	[0.2-4]	[28-39]	[2-7]	[4-7]	[<0.01-0.8]	[2.7-3.28]	[1.5-3.33]
% Change	-	-91	-	-86	-	-95	-	-92

Immunity from vaccinations administered before the campaign was estimated at 82% for those with a RTHC, and increased to 96% after the campaign. For all children (with and without RTHC), estimated immunity from vaccination was 61% before and 94% after the mass campaign. The outbreak of measles alone increased immunity by 3% and 6% for those with a RTHC and all children respectively. (Figure 4)

**Figure 4. Estimated measles immunity of participant children.**



Error bars represent 95% confidence intervals estimated by Monte-Carlo simulation.

## Discussion

### Routine Coverage

Routine vaccination services fail to achieve adequate herd immunity in high risk areas. Lack of information and personal obstacles were the commonest barriers identified by caregivers. This differs from the 2005 Western Cape Provincial vaccination survey(12) where clinic factors (47% of respondents) followed by lack of information (27% of respondents) were identified most frequently. High-risk populations have special access-related needs, and routine services and mass campaigns need to facilitate access for high risk populations.

Vaccinations documented on the RTHC were generally administered on-time, the second dose less so than the first. Timely vaccination ensures that children are not at risk at an early age. Every occasion should be used to vaccinate children when they attend health services as this is a common source of missed opportunities.

### Benefits of Campaigns

MVCs can rapidly increase vaccination coverage amongst high risk populations, as evidenced by the increase in coverage and the decline in measles incidence after the MVC. The data showed that the outbreak would have continued had it not been for the MVC as herd immunity would still have been below the required threshold. The MVC would have had a greater impact if implemented earlier. This is supported by a recent systematic review by Cairns et al (17) that demonstrated a decrease in morbidity associated with rapid outbreak response vaccination.

MVCs have been criticized because they are expensive, logistically challenging and resource-intensive. Human resources are usually drawn from routine primary care services resulting in an interruption of these services and a temporary increase in workload. (18) However these campaigns are a necessary intervention, proven to decrease measles morbidity and mortality. (19) The negative impact on health services can be mitigated by careful planning and conducting the MVC over as few days as is feasible. Campaigns have also had a positive spill-over effects on health systems and routine immunization services, by providing opportunities for better collaboration, improved knowledge of vaccination, micro-planning, data quality and surveillance, and increased community demand for vaccinations. (20)

## Estimating immunity in the population from records of administered doses

Vaccination status as documented on RTHCs is often used as a proxy indicator of population immunity. Tools are lacking to interpret the outbreak potential in light of survey data. A risk assessment tool should be developed to model survey data against immunological assays, in order to estimate levels of neutralizing antibodies. We estimated population immunity using crude assumptions and the methodology requires validation and refinement. The absence of recent data describing the decay of maternal antibodies, the impact of HIV status (maternal and infant), gestational age and maternal measles incidence on the level and attrition of maternally acquired immunity limit these assumptions. Additionally, the effect of HIV status and vaccination practices on vaccine effectiveness was not taken into account.

## Inter-epidemic surveillance and preparedness

The surveillance data from the Western Cape epidemic showed a higher incidence of measles in areas with large informal settlements, consistent with data from other outbreaks. Population density combined with an influx of susceptible persons and decreased access to health care services act synergistically to increase the risk.(21) Residential mobility is highly prevalent in informal settlements (22) and is a determinant of the non-availability of RTHCs(22), and acts as an access-barrier to health care. The sustainability of the impact of MVCs in informal settlements may be limited. Berry et al, in their evaluation of a national MVC in Khayelitsha,(23) found a precipitous drop in vaccination status of immigrants to pre-campaign levels 6 months after a MVC.

Large coverage surveys at a provincial or district level fail to identify specific high risk areas with low coverage. Administrative coverage estimates are also poor and do not account for in-migration in rapidly expanding areas. Lot quality sampling may be used to identify these high risk areas and periodic surveys and mop-up vaccination campaigns should be conducted. In keeping with the vision of the National Department of Health to revitalize Primary Health Care, community health workers are ideally placed to strengthen immunization services and could monitor coverage in high risk areas and facilitate access to routine services.

## Limitations

A notable limitation of this study was non-response (41.2%). Children attending crèches were also not included in the survey. Additionally those who had resided less than 6 months in the Western Cape were considered ineligible, as the study assessed the effectiveness of the campaign in reaching those who were resident at the time of the campaign. Coverage estimates may be overestimated if those selected were more likely to be vaccinated than those who were absent. Additionally, areas that were known to be volatile were avoided and it is likely that coverage in these areas is lower than elsewhere. Vaccination by the MVC is likely to have been overestimated due to recall and social desirability bias. Caregiver knowledge regarding the vaccination schedule was limited and routine coverage in the whole study population was therefore under-estimated as those without a RTHC were classified as unvaccinated. Socio-economic and mobility data were not collected and represents a limitation.

#### Recommendations

A proactive approach is required to prevent future measles outbreaks. A sensitive surveillance system is required to monitor coverage and identify outbreaks. Routine services should monitor coverage especially in high risk areas such as informal settlements, and immediate action should be taken in areas where coverage fails to achieve herd immunity. Community health workers and school nurses are suitably placed in the PHC re-engineering to monitor and promote the uptake of vaccination. All health facilities should contribute by ensuring that missed opportunities for vaccination do not occur. MVCs are an important strategy in the control of measles and careful planning is required to ensure that these are used as opportunities for health systems strengthening. Targeted post-MVC surveys are useful for assessing risk and should routinely form part of MVC planning. Further research is required in developing validated rapid risk assessment methodologies.

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# Part D: Appendices

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## Appendix 1. Questionnaire

Interviewer No's.

Form No.

Date: (dd/mm/yyyy) //

### Measles Coverage Questionnaire in children aged {9 months} – {5 years + 3 months}; Western Cape Department of Health & City Health

The Western Cape department of Health has recently experienced a measles outbreak, and [area] was one of the places with the highest number of cases. In response to this outbreak, the department conducted a mass immunization campaign to immunize children against measles, as well as polio and we would like to assess how well it was able to immunize children that are at risk of getting measles. We would like to ask you a few questions, which will take about 10 minutes of your time. Are you willing to participate?

Screening questions for eligibility:	
1.	How many children are there living in this household that are between the ages of {9 months} and {5 years plus 3 months} of age? <input type="checkbox"/>
2.	Have you been living in the Western Cape for more than 6 months? <input type="checkbox"/> Yes <input type="checkbox"/> No
3.	<input type="checkbox"/> <b>Not eligible:</b> if no children under {5yr plus 3 mnths} or not living in WC for > 6 months, then <b>thank</b> the person for their time and proceed to next household <input type="checkbox"/> <b>Eligible</b> →
4.	<p>We would like to make sure that you understand what this survey entails: no names or personal details will be collected and all the results will be anonymous and confidential (private). Your participation is entirely up to you and you can choose to opt out at any time if you wish. There are no known risks with choosing or not choosing to participate in this study. We hope that this information will help the Department of Health and City Health to improve immunization services in your area and in similar areas in the Western Cape. Your community will benefit from this research and the results of this study will be given to your clinic and to the Provincial department of Health and City Health. You will not receive any payment for your participation.</p> <p>Would you like more information about this survey? → give them copy of information sheet/ read it to them if illiterate. If you have any queries about this research, you can contact Dr Gina Bernhardt (021 483 9292 or 0845100442). Do you have any questions? Do you understand what has been explained to you? Do you agree to participate?</p> <p>Verbal <b>consent</b> given <input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p>How many caregivers are at home now? What are the names of the caregivers? What are the names of [caregiver 1's] children that are between the ages of 9months and 5yrs3mo? What are the names of [caregiver 2's] children that are between the ages of 9months and 5yrs3mo? Etc. Number all eligible children. Throw a dice to see which child will be included in the survey. We will be asking questions about [name of child selected].</p> <p>If eligible but refused → Can I ask what is the reason that you do not wish to participate? _____</p>
Primary care giver	
5.	Are you the primary care giver of [name]? <input type="checkbox"/> Yes <input type="checkbox"/> No
6.	Gender of primary care giver: <input type="checkbox"/> Female <input type="checkbox"/> Male

7.	How old are you? <input type="checkbox"/> <input type="checkbox"/> years
8.	Can you read and write? 1 <input type="checkbox"/> Yes      0 <input type="checkbox"/> No      9 <input type="checkbox"/> Unknown
<b>Child</b>	
9.	Is [name] a girl or a boy?    1 <input type="checkbox"/> Female    2 <input type="checkbox"/> Male
10.	Did [name] ever suffer from measles? 1 <input type="checkbox"/> Yes → Date <sub>(ddmmYYYY)</sub> : <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> 0 <input type="checkbox"/> No                      9 <input type="checkbox"/> Not sure
<b>Mass Immunization Campaign</b>	
11.	Was [name] vaccinated to prevent measles during the <b>mass immunization campaign</b> ? It was held from 12-23 April 2010 and they put a mark on the child's finger. 1 <input type="checkbox"/> Yes → Which <b>area</b> of the body was the injection given?    1 <input type="checkbox"/> Shoulder    2 <input type="checkbox"/> Thigh    3 <input type="checkbox"/> Other    9 <input type="checkbox"/> Unknown 0 <input type="checkbox"/> No                      9 <input type="checkbox"/> Not sure
12.	If YES to question 11 What are the most important reasons why your child got immunized in the campaign? Please take time to think about it and tell us not more than 3 reasons that you think are most important. <b>DO NOT READ THE LIST TO THE PARTICIPANT</b> 1 <input type="checkbox"/> To <b>protect</b> my child against disease 2 <input type="checkbox"/> To keep my child <b>healthy</b> 3 <input type="checkbox"/> I have seen children/ people who have not been vaccinated become <b>sick</b> 4 <input type="checkbox"/> It is my <b>duty</b> to take my child for vaccinations 5 <input type="checkbox"/> The <b>sister</b> /doctor at the clinic told me to get my child vaccinated 6 <input type="checkbox"/> <b>Fear</b> of being shouted at by nurses 7 <input type="checkbox"/> It is <b>normal</b> (everyone takes their child for vaccines) 8 <input type="checkbox"/> Other – specify .
13.	If NO for question 11, What were the <b>most important reasons</b> that [name] was not immunized during the campaign? Please take time to think about it and tell us <b>not more than 3 reasons</b> that you think are most important. <b>DO NOT READ THE LIST TO THE PARTICIPANT</b> Lack of information: 01 <input type="checkbox"/> Unaware of <b>need</b> for vaccination 02 <input type="checkbox"/> Unaware of <b>location/ timing</b> of immunization campaign 03 <input type="checkbox"/> Fear of <b>side-effects</b> 04 <input type="checkbox"/> <b>Wrong ideas</b> about contra-indications (eg. sick children shouldn't be vaccinated when ill) 05 <input type="checkbox"/> Not in <b>area</b> at the time of campaign and unaware that child can go to any clinic for vaccine Lack of motivation: 06 <input type="checkbox"/> No <b>faith</b> in vaccination 07 <input type="checkbox"/> Child <b>already</b> vaccinated 08 <input type="checkbox"/> Previous bad <b>experience</b> (side-effect/ other) 09 <input type="checkbox"/> Child is <b>healthy</b> therefore vaccines not necessary 10 <input type="checkbox"/> Vaccines are <b>harmful</b> 11 <input type="checkbox"/> Vaccines are <b>painful</b> for the child 12 <input type="checkbox"/> <b>Forgot</b> Clinic factors:



18.	Measles 1	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
19.	Measles 2	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
20.	<p><b>If clinic card not seen:</b>  <i>Did your child receive injections to prevent measles, apart from the campaign?</i>  <input type="checkbox"/> Yes      <input type="checkbox"/> No          If YES → How many injections? <input type="checkbox"/>      Don't know <input type="checkbox"/><sub>9</sub>          How old was [name] when the <b>first</b> dose was given? <input type="checkbox"/><input type="checkbox"/>months      <input type="checkbox"/><sub>88</sub>Unknown      <input type="checkbox"/><sub>99</sub>          N/A          How old was [name] when the <b>second</b> dose was given? <input type="checkbox"/><input type="checkbox"/>months      <input type="checkbox"/><sub>88</sub>Unknown      <input type="checkbox"/><sub>99</sub>          N/A  <i>Which <b>area</b> of the body was the last injection given?</i> <input type="checkbox"/><sub>1</sub>Shoulder <input type="checkbox"/><sub>2</sub>Thigh <input type="checkbox"/><sub>3</sub>Other <input type="checkbox"/><sub>9</sub>          Unknown</p>		
21.	<p>If some/ all of the vaccinations have been received:  <i>What are the most important reasons that you take your child for vaccinations?</i>  <i>Please take time to think about it and tell us not more than 3 reasons that you think are most important.</i>  <b>DO NOT READ THE LIST TO THE PARTICIPANT</b>  <input type="checkbox"/><sub>1</sub> To <b>protect</b> my child against disease  <input type="checkbox"/><sub>2</sub> To keep my child <b>healthy</b>  <input type="checkbox"/><sub>3</sub> I have seen children/ people who have not been vaccinated become <b>sick</b>  <input type="checkbox"/><sub>4</sub> It is my <b>duty</b> to take my child for vaccinations  <input type="checkbox"/><sub>5</sub> The <b>sister</b>/doctor at the clinic told me to get my child vaccinated  <input type="checkbox"/><sub>6</sub> <b>Fear</b> of being shouted at by nurses  <input type="checkbox"/><sub>7</sub> It is <b>normal</b> (everyone takes their child for vaccines)  <input type="checkbox"/><sub>8</sub> <b>Other</b> – specify _____.</p>		
22.	<p>If some/ all of the vaccinations are missed:  <i>Could you tell us what are the most important reasons that prevent you from vaccinating your child? Please take time to think about it and tell us not more than 3 reasons that you think are most important.</i>  <b>DO NOT READ THE LIST TO THE PARTICIPANT</b>          Lack of information:  <input type="checkbox"/><sub>01</sub> Unaware of <b>need</b> for vaccination  <input type="checkbox"/><sub>02</sub> Unaware of <b>when</b> to return  <input type="checkbox"/><sub>03</sub> Unaware of need to return for <b>second/ third dose</b>  <input type="checkbox"/><sub>04</sub> Fear of <b>side-effects</b>  <input type="checkbox"/><sub>05</sub> Wrong <b>ideas</b> about contra-indications (eg. sick children shouldn't be vaccinated when ill)  <input type="checkbox"/><sub>06</sub> Not in <b>area</b> at the time when child due for vaccine and unaware that child can go to any clinic for vaccine  <input type="checkbox"/><sub>07</sub> Not aware that if missed the <b>due date</b> that it can still be given later          Lack of motivation:  <input type="checkbox"/><sub>08</sub> <b>Postponed</b> until another time  <input type="checkbox"/><sub>09</sub> No <b>faith</b> in immunization  <input type="checkbox"/><sub>10</sub> Previous bad <b>experience</b> (side-effect/ other)  <input type="checkbox"/><sub>11</sub> Child is <b>healthy</b> therefore vaccines not necessary</p>		

12	<input type="checkbox"/> Vaccines are <b>harmful</b>
13	<input type="checkbox"/> Vaccines are <b>painful</b> for the child
14	<input type="checkbox"/> <b>Forgot</b>
Clinic factors:	
15	<input type="checkbox"/> <b>Place</b> of immunization too far
16	<input type="checkbox"/> <b>Time</b> of immunization too inconvenient
17	<input type="checkbox"/> <b>Waiting</b> time at clinic too long
18	<input type="checkbox"/> Vaccines not <b>available</b> at clinic (eg. clinic has run out of vaccines)
19	<input type="checkbox"/> <b>Vaccinator</b> decided not to vaccinate child (contraindication)
20	<input type="checkbox"/> Told by nurses to <b>come back</b> at another time
21	<input type="checkbox"/> <b>Fear</b> of being shouted at by the nurses because you are late to vaccinate your child already
22	<input type="checkbox"/> Child <b>ill</b> , taken to clinic but nurses did not vaccinate child
Obstacles:	
23	<input type="checkbox"/> Primary care giver too <b>busy</b> (with other children/ household tasks/ work)
24	<input type="checkbox"/> <b>Family</b> problem, including illness of primary caregiver
25	<input type="checkbox"/> Child does not have <b>clinic card</b>
26	<input type="checkbox"/> Child <b>ill</b> , not brought to clinic
27	<input type="checkbox"/> <b>Father</b> did not allow mother to vaccinate child
Other:	
29	<input type="checkbox"/> <b>Religious</b> beliefs – specify _____.
30	<input type="checkbox"/> <b>Other</b> – specify _____.

If some/all immunizations are not up to date, give respondent **referral letter** for the child. *Please take this letter to the clinic so that they can give your child the immunizations that are still needed. Please make sure that all your children are up to date with their immunizations. Thank you for your time. Move*

## Appendix 2. Information Sheet

### **Title of project:**

Evaluating measles vaccination coverage in the Western Cape Province

### **Investigators:**

1. Maternal and Child Health sub-directorate, District Health Services and Programmes, Western Cape Department of Health
2. City Health
3. In collaboration with the Universities of Cape Town and Stellenbosch

This study has been approved by University of Cape Town Faculty of Health Sciences Human Research Ethics Committee and Stellenbosch University Research Ethics Committee (see below for contact details).

### **Purpose and benefits of study:**

There has recently been an outbreak of measles, and [area] was one of the areas that was most affected. We are doing this study to find out how many children have now been vaccinated for measles and to find out why some children have not been vaccinated.

### **Sample size**

We plan to interview around 250 people in [area].

### **Research study design**

We will be collecting information from care-givers of children aged {9 months} to {5 years and 3months}, living in areas that had the highest number of measles cases this year in the Western Cape and who have lived in the Western Cape for more than 6 months. The study will be conducted in a few different areas in during July/ August 2010.

### **Procedure, risks & benefits involved in the study**

You will be asked to answer a few questions which will take approximately 10 minutes, and also to show us your child's Road to Health Card/ clinic card (if you have it). No names or personal details will be collected and all the results will be anonymous and confidential (private). Your participation is entirely up to you and you can choose to opt out at any time if you wish. There are no known risks with choosing or not choosing to participate in this study. We hope that this information will help the department of Health and City Health to improve immunization services in your area and in similar areas in the Western Cape. So your community will benefit from this research and the results of this study will be given to your clinic and to the Provincial department of Health and City Health. You will not receive any payment for your participation.

### **Contact Persons**

If you have any questions, you can ask your interviewer or phone Dr Gina Bernhardt at (021) 483 9292 or 084 5100 442 or [ginabern@pgwc.gov.za](mailto:ginabern@pgwc.gov.za)

University of Cape Town, Faculty of Health Sciences, Human Research Ethics Committee: Ms Lamees Emjedi at (021) 406 6338 or [Lamees.Emjedi@uct.ac.za](mailto:Lamees.Emjedi@uct.ac.za)

### **Declaration**

I have understood the information contained in this letter. I understand the reason for the research and what is required. I have had the opportunity to ask questions and choose to take part in this research study. I understand that I will not be disadvantaged if I decide not to participate.

### Appendix 3. Referral letter

Department of Health  
Western Cape  
Vaccination Research Team  
Date: \_\_\_\_\_

To the Clinic Sister

As part of our research to assess measles vaccination coverage in your area, we have identified this child

\_\_\_\_\_ who is not up to date with his/her immunizations.

Please could you vaccinate this child with the necessary vaccines.

Thank you for your assistance.

Dr Gina Bernhardt

Tel 021 483 9292

Western Cape Department of Health, District Health Services and Programmes,  
Maternal and Child Health Sub-directorate

University of Cape Town

## Appendix 4. Tally sheet

Date(dd/mm/yyyy) / /

Interviewers no.  &

Area: \_\_\_\_\_

### Households visited:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120
121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140
141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160
161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180
181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200

### No-one at home:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

### Not eligible:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

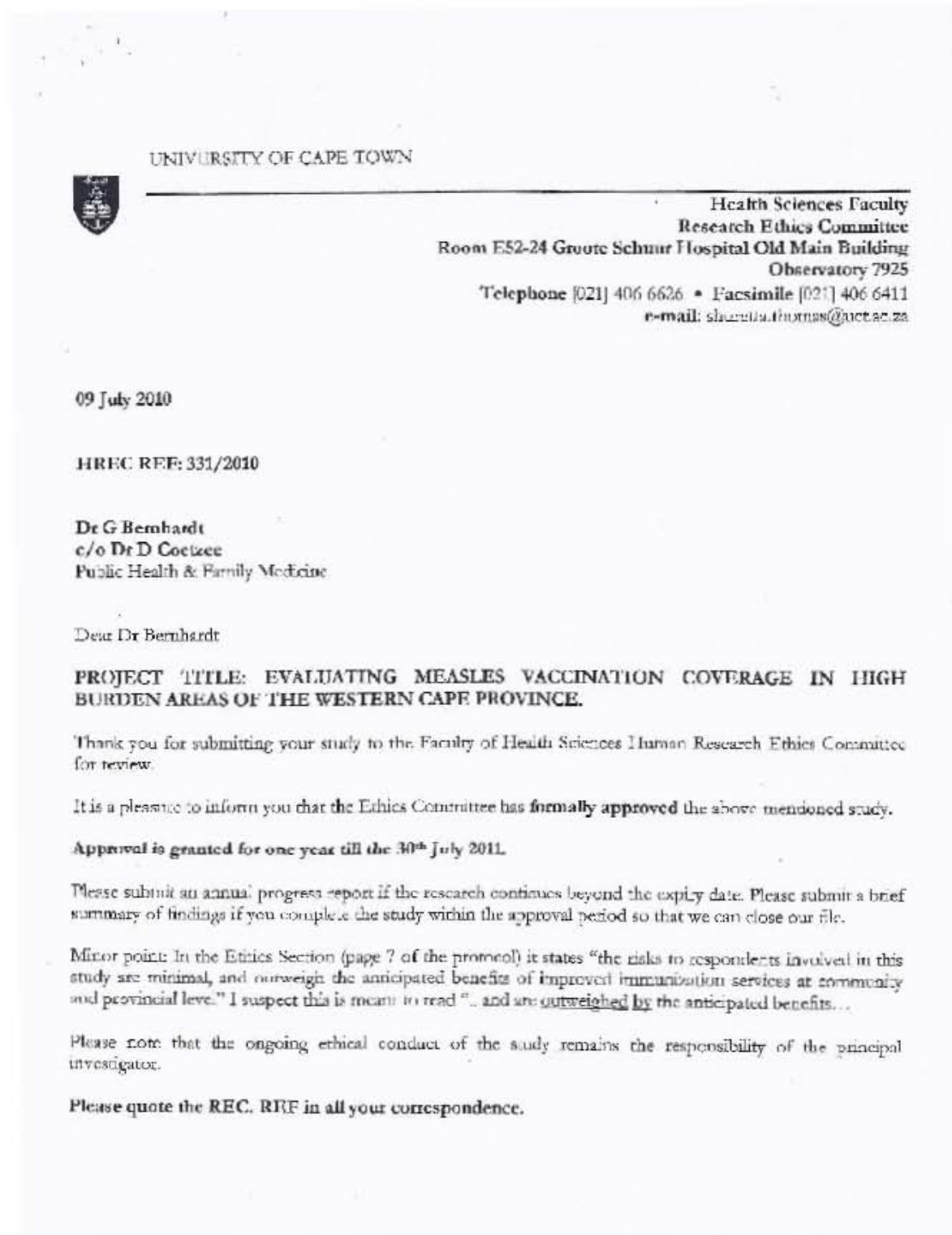
### Refused access:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

### Participated in survey:

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100

## Appendix 5: Ethics Approval Letter



Yours sincerely

**PROFESSOR M BLOCKMAN**  
**CHAIRPERSON, HSF HUMAN ETHICS**

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

## Appendix 6. SAMJ Author Guidelines

<http://www.samj.org.za/index.php/samj/about/submissions#authorGuidelines>

Accessed 2 Dec 2011

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### **RESEARCH ETHICS COMMITTEE APPROVAL**

Evidence must be provided of Research Ethics Committee approval of the research where relevant.

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Authors must declare all sources of support for the research and any association with the product or subject that may constitute conflict of interest.

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Work that is based on or contains reference to ethnic classification must indicate the rationale for this.

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Short items are more likely to appeal to our readers and therefore to be accepted for publication.

**Original articles** of 3 000 words or less, with up to 6 tables or illustrations, should normally report observations or research of relevance to clinical medicine. References should preferably be limited to no more than 15.

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**Review articles** are rarely accepted unless invited.

**Letters to the editor**, if intended for the correspondence column, should be no longer than 400 words with only one illustration or table. The address(es) of the author(s) must accompany correspondence.

**Forum articles** must be accompanied by a short description (50 words) of the affiliation details/interests of the author(s). Refer to recent forum articles for guidance.

**Obituaries** should not exceed 400 words and may be accompanied by a photograph.

## **MANUSCRIPT PREPARATION**

Research articles should have a structured abstract not exceeding 250 words comprising: Objectives, Methods, Outcome measures, Results and Conclusions. For scientific letters/short reports/forum articles, an abstract (summary) of up to 100 words in length should be provided.

Refer to articles in recent issues for guidance on the presentation of headings and subheadings.

### **Qualification and affiliation details of all authors must be provided with submissions.**

Abbreviations should be spelt out when first used in the text and thereafter used consistently, e.g. 'intravenous (IV)...'

Scientific measurements should be expressed in SI units except: blood pressure should be given in mmHg and haemoglobin values in g/dl (Note: litres is denoted with a lower l as in 'ml'). Units should be preceded by a space (except for %), i.e. '40 kg' and '20 cm' but '50%'.

Greater/smaller than signs (> and <) should be placed immediately preceding the relevant number, i.e. 'females >40 years of age'.

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'

Round brackets (parentheses) should be used in the text and not square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

If in doubt, refer to 'uniform requirements' above.

## **ILLUSTRATIONS**

Figures consist of all material that cannot be set in type, such as photographs and line drawings. If any tables or illustrations submitted have been published elsewhere, the author should obtain written consent to republication from the copyright holder and the author(s). **All illustrations/figures/graphs etc. must be of high resolution/quality: 300 dpi or more is preferable but images must not be resized to increase resolution. Raw (unformatted/uncompressed) images must be attached as 'supplementary files' upon submission, and not embedded in the accompanying text document.** JPEG and PNG formats are preferable. Figures may also be provided in high-quality PDF format. For figures/graphs prepared in Microsoft powerpoint/excel, the original workbook may be provided.

## **REFERENCES**

References should be inserted in the text as superscript numbers and should be listed at the end of the article in numerical order (not alphabetical order) - i.e. in order of appearance in the text.

Authors are responsible for verifying references from the original sources.

References should be set out in the Vancouver style. However, please note: references/citations should be manually formatted and inserted into the article – the use of reference manager/formatting add-ins should be avoided.

Approved abbreviations of journal titles must be used; consult the List of Journals in Index Medicus for these details.

Names and initials of all authors should be given unless there are more than six, in which case the first three names should be given followed by et al. First and last page numbers should be given.

Journal references should appear thus:

Price NC . Importance of asking about glaucoma. BMJ 1983; 286: 349-350.

Book references should be set out as follows:

Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975: 96-101.

Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974: 457-472.

Internet references:

World Health Organization. The world health report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: World Health Organization, 2002. <http://www.who.int/whr/2002> (accessed 16 January 2010).

Manuscripts accepted but not yet published can be included as references followed by (in press).

Unpublished observations and personal communications may be cited in the text, but not in the reference list. For personal communications please provide the full name of the source person: e.g. (Prof. Michael Jones, personal communication)

### **PROOFS**

PDFs may be sent to the author before publication to resolve any remaining query.

### **CHANGES OF ADDRESS**

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

### **CPD POINTS**

Authors can earn up to 15 CPD CEUs for published articles. Certificates may be requested after publication of the article.

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3. When available, the URLs to access references online are provided, including those for open access versions of the reference. The URLs are ready to click (e.g., <http://pkp.sfu.ca>).
4. The text is single-spaced; uses a 12-point font; employs italics, rather than underlining (except with URL addresses). Figures consist of all material that cannot be set in type, such as photographs and line drawings. If any tables or illustrations submitted have been published elsewhere, the author should obtain written consent to republication from the copyright holder and the author(s). All illustrations, figures etc. must be of high resolution/quality, preferably jpeg or equivalent but not powerpoint, and preferably attached as supplementary files.
5. **NB: The text adheres to the stylistic and bibliographic requirements in [Author Guidelines](#), which is found in [About the Journal](#).**
6. Research Ethics Committee approval was obtained for the research (this should be indicated in the text of the paper).
7. Authors must indicate any conflict of interest (or competing interests).

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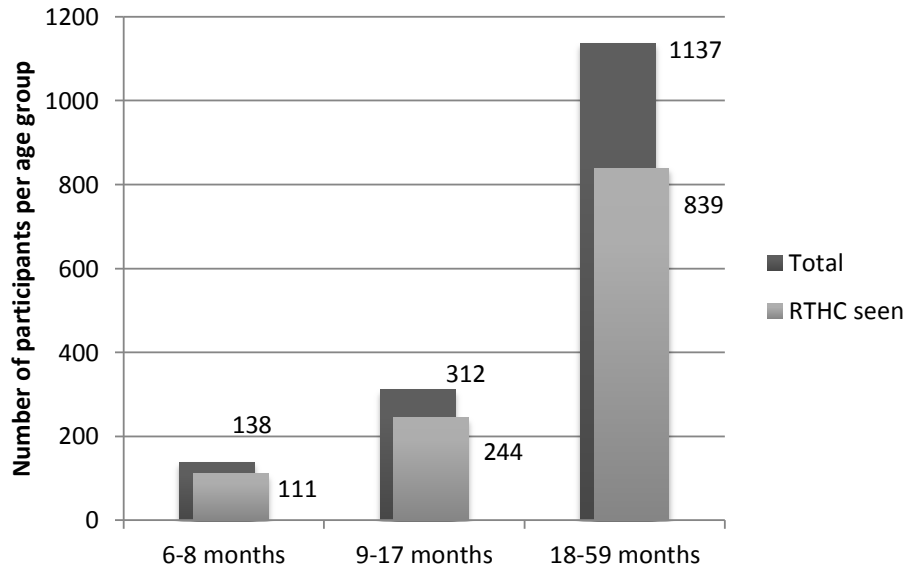
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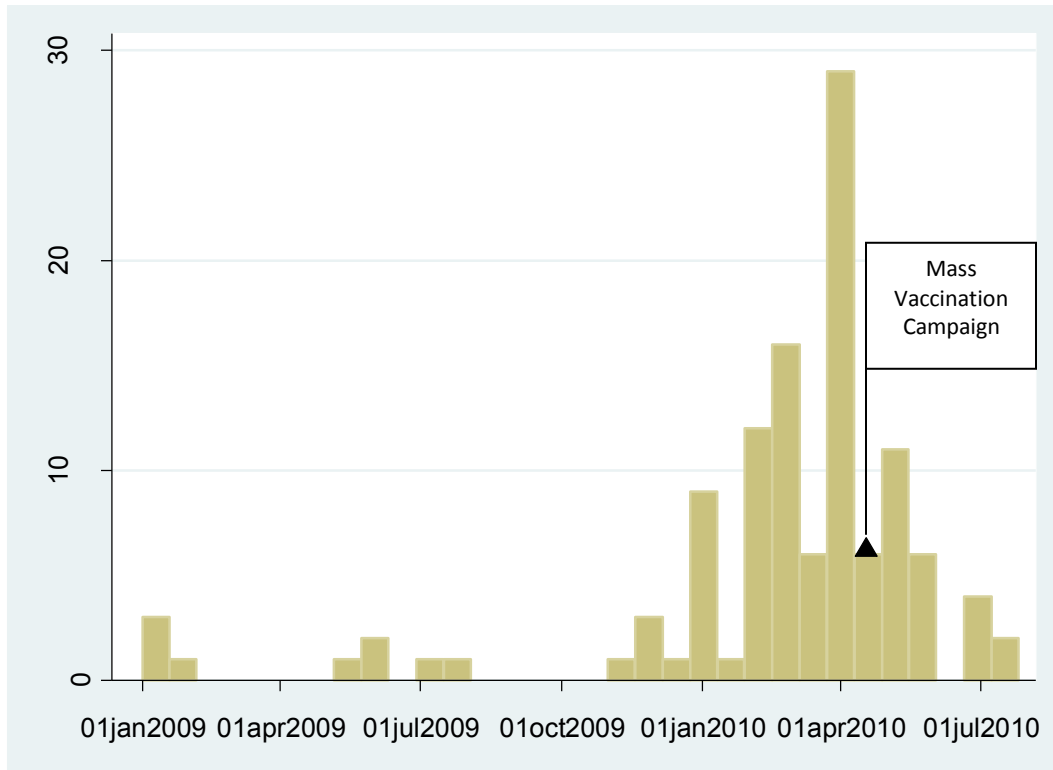
## Appendix 7. Additional tables and figures

Figure A. Distribution of children by age-group



Overall, in 75% of children, the RTHC was seen. Of 1587 participants, 72% were 18-59 months old at the time of the campaign. Of these children, 74% the RTHC was seen. Twenty percent of children were aged 9-17 months and 9% were 6-8 months old at the time of the campaign.

Figure B. Epidemic curve of cases reported by the caregiver



A peak in the reported measles cases occurred in April 2010. Eighty percent (94/118) reported measles cases occurred prior to the MVC with a sharp decline in the incidence after the MVC.

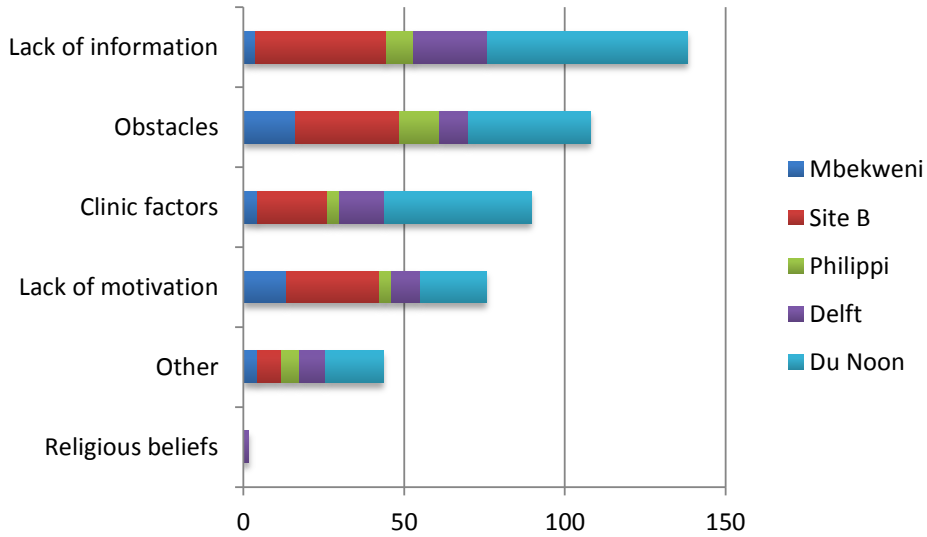
**Table A. Association between number of pre-campaign vaccinations, as documented in the RTHC, and history of measles disease**

	Unadjusted odds ratio (95% confidence interval)	p-value
1 vaccination compared with no vaccinations	0.51 (0.33-0.8)	0.003
2 vaccinations compared with no vaccinations	0.39 (0.24 – 0.61)	<0.001
2 vaccinations compared with 1 vaccination	0.54 (0.34-0.86)	0.009

• Estimated from a logistic regression

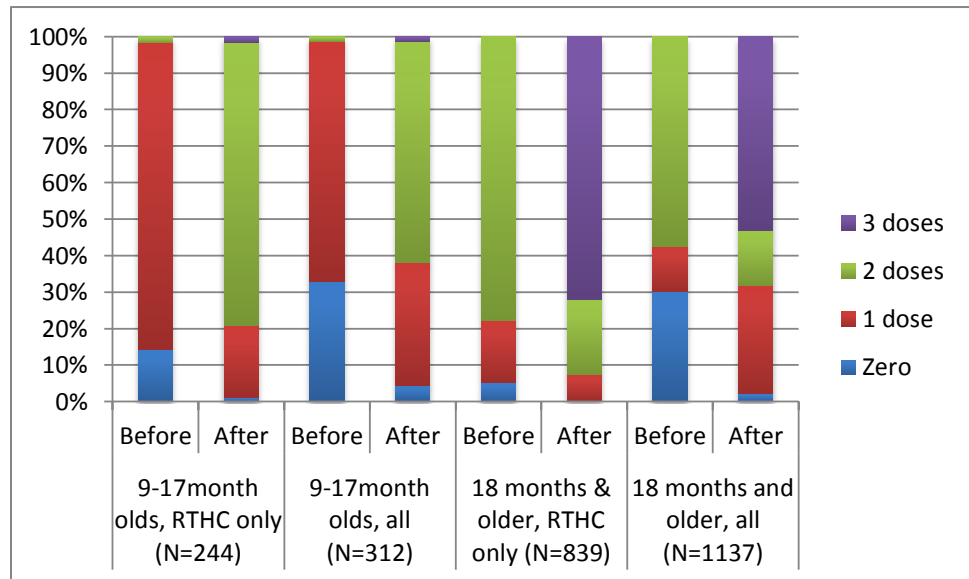
After adjusting for age, documented routine vaccination coverage prior to the mass campaign was significantly associated with the absence of a history of measles disease in children 9 months and older. One measles vaccination was associated with 49% reduced odds of measles compared with no measles vaccination ( $p=0.003$ ); and 2 measles vaccinations were associated with a 61% reduced odds of measles compared with no measles vaccination ( $p<0.001$ ). Two measles vaccinations were associated with 46% reduced odds of measles compared with 1 measles vaccination ( $p=0.009$ ).

**Figure C. Caregiver-reported barriers to accessing routine immunization services, adjusted for sample size per suburb. ([Appendix 8A](#))**



The commonest categories of reasons for caregivers not accessing routine vaccination services were related to a lack of information, followed by personal obstacles.

**Figure D. Measles coverage estimates before and after the mass campaign**



**Table B. Measles coverage estimates before and after the mass campaign**

	9-17m olds, card only (N=244)		9-17m olds, card plus history (N=312)		18m and older, card only (N=839)		18m and older, card plus history (N=1137)	
	Before	After	Before	After	Before	After	Before	After
<b>% 0 doses</b>	14	1	33	5	5	<1	30	2
<b>(N)</b>	(35)	(3)	(103)	(14)	(44)	(2)	(342)	(26)
<b>[95% CI]</b>	[10-19]	[0.2-4]	[28-39]	[2-7]	[4-7]	[<0.01-0.8]	[2.7-3.28]	[1.5-3.33]
<b>% Change</b>	-	-91	-	-86	-	-95		-92
<b>% 1 dose</b>	84	20	66	34	17	7	13	30
<b>(N)</b>	(205)	(48)	(205)	(105)	(142)	(61)	(142)	(335)
<b>% 2 doses (N)</b>	2	77	1	61	78	20	57	15
	(4)	(189)	(4)	(189)	(653)	(171)	(653)	(171)
<b>% 3 doses (N)</b>	0	2	0	1	0	72	0	53
	(0)	(4)	(0)	(4)	(0)	(605)	(0)	(605)

Prior to the MVC 33% and 30% of children aged 9-17 months and 18 months and older respectively had not had a dose of measles vaccine, whereas after the MVC this was significantly reduced to 5% and 2% respectively. In the sub-group analysis of children with a RTHC, 14% and 5% of children aged 9-17

months and 18 months and older respectively had not had a dose of measles vaccine. After the MVC this was reduced to 1% and <1% respectively.

## Appendix 8. Technical Appendices

### A. Formula for adjustment of reported barriers to access

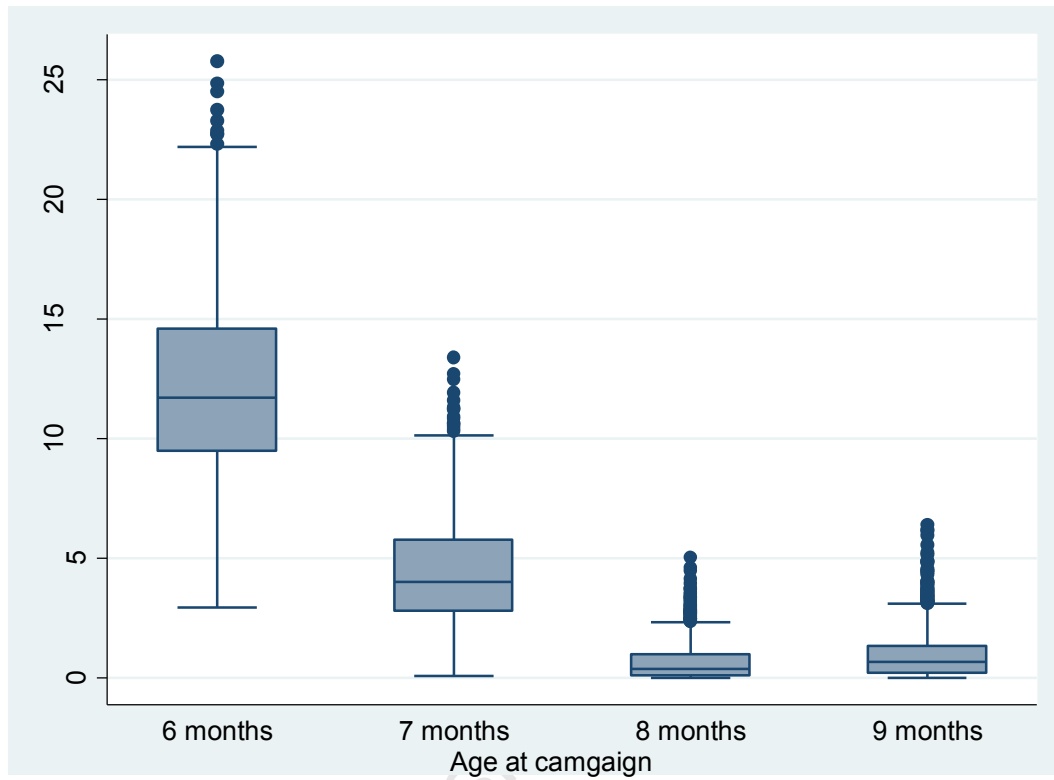
To facilitate comparability across suburbs for the number of reported barriers to access, this variable was adjusted for sample size per suburb. The individual data were multiplied by a factor derived from the following formula: 
$$\frac{\text{Total number of study participants}}{\text{Number of study sites} \times \text{Number of participants per site}}$$

### B. Monte Carlo simulation methods

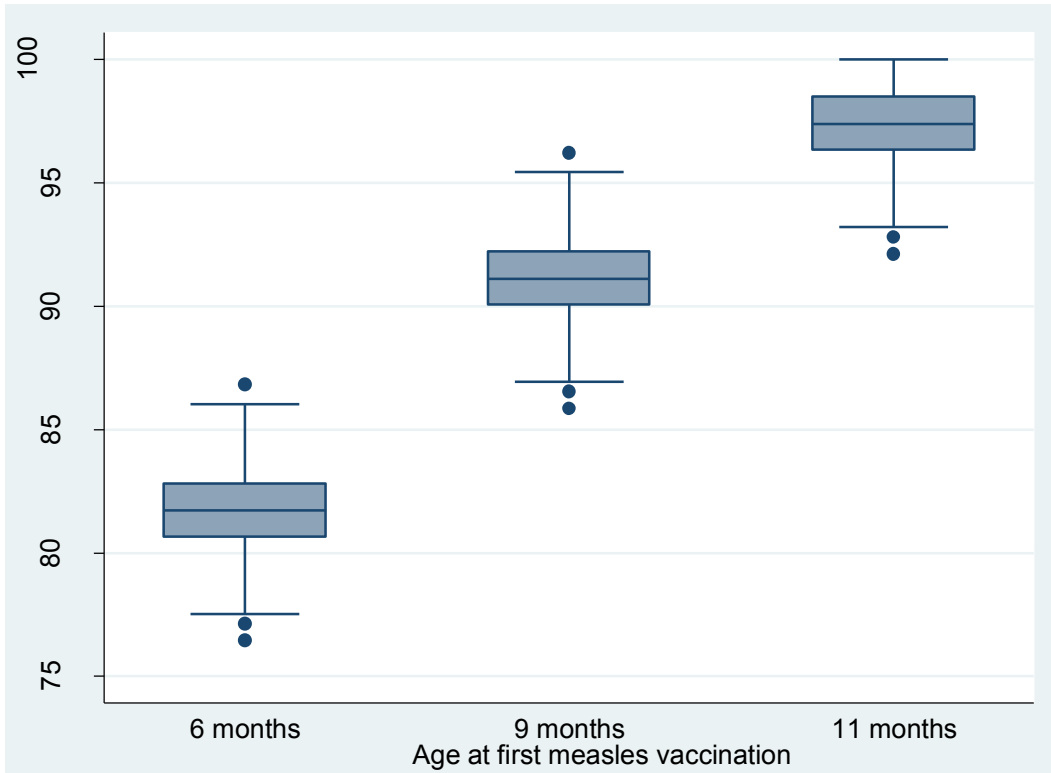
We estimated immunity of the sample population using a Monte-Carlo simulation, with Stata v11.1. A random number was drawn from a probabilistic distribution for 3 parameters for 1000 iterations.

1. The rate of decline of maternally-acquired antibodies for infants less than 9 months who had not been vaccinated was modeled using empirical data from a study by Kiepiela et al (1). A square-root transformation of the outcome ( $y$ ) was used and a linear equation derived using  $m = \frac{\sqrt{y_2} - \sqrt{y_1}}{x_2 - x_1}$  and  $c = \sqrt{y} - mx$ , where  $m$  is the gradient,  $x$  is age in months, and  $c$  is the constant. Random numbers were drawn from a normal distribution with a mean of  $y = (-1.7 \times \text{age at campaign} + 1.195)^2$  and a standard error of 0.055 (calculated for an average  $x$  value:  $\frac{y_{\text{upper95\%}} - y_{\text{lower95\%}}}{2 \times 1.96}$ ). (Figure A)
2. Effect of first vaccination (if only 1 vaccination was administered and given under 1 year) was modeled using estimates from the WHO (2) which summarized the findings of a large number of studies. A linear equation was derived using the following formulae:  $m = \frac{y_2 - y_1}{x_2 - x_1}$  and  $c = y - mx$ . Random numbers were drawn from a normal distribution with a mean of  $y = 0.376 \times \text{age of first vaccination} + 0.63$  with a standard deviation of 0.0166 derived using the formula as for (1). (Figure B)
3. Acquired immunity in children who received the first dose after 1 year of age or received more than one vaccination was drawn from the distribution:  $1 - (-0.02 \times \ln(a))$  (Figure C), where  $a$  is a uniformly distributed random variable on the interval [0,1). Ninety percent of values were over 95%.

**Figure A. Input parameter distribution: waning of maternally-acquired immunity (in child aged 6 to <9 months)**

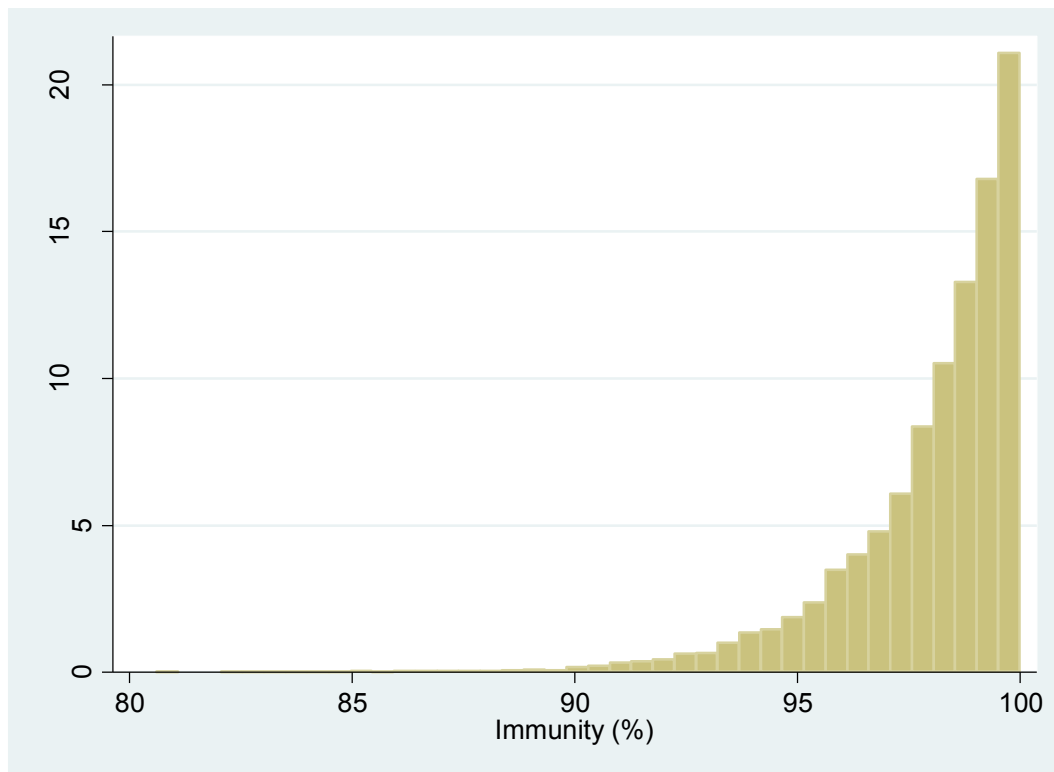


**Figure B. Input parameter distribution: immunity following first vaccination (in child under 1 year of age)**



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Figure C. Input parameter distribution: immunity following vaccination after 1 year of age or more than 1 vaccination.



## References

- (1) Kiepiela P, Coovadia HM, Loening WE, Coward P, Abdool Karim SS. Loss of maternal measles antibody in black South African infants in the first year of life--implications for age of vaccination. *S Afr Med J* 1991 Feb 2;79(3):145-148.
- (2) World Health Organization, Department of Immunization, Vaccines and Biologicals. The immunological basis for immunization series. Module 7: Measles. Update 2009. Geneva, Switzerland: WHO; 2009.