

**Vaccination coverage at seven months of age in Limpopo Province, South Africa:  
a cross-sectional survey**

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## **INTRODUCTION**

The expansion of routine childhood vaccinations has led to significant reductions in childhood morbidity and mortality globally. The World Health Organization (WHO) estimates that vaccines for just four diseases—diphtheria, tetanus, pertussis, and measles—prevent 2 to 3 million deaths each year. However, coverage rates remain low in some settings, and there are still 1.5 million deaths annually from vaccine-preventable diseases (1). While there have been large studies on attitudes towards vaccination in sub-Saharan Africa, such as a recent survey of attitudes towards COVID-19 vaccination in fifteen African Union countries, there has been less study on the vaccination attitudes of caregivers of infants in sub-Saharan Africa (2). This is problematic because South Africa has had issues with childhood vaccination coverage. At the time this study was conducted, for a variety of routine childhood immunizations, the WHO and United Nations Children's Fund (UNICEF) estimated only 66-78% of South African children are vaccinated on the recommended schedule, although the South African government's coverage estimates were higher for each vaccine (84-96%) (3).

Knowledge and attitudes about vaccines among new or expecting mothers have been studied in some sub-Saharan African countries (e.g. Uganda, Nigeria), with some evidence that mothers with more positive views of vaccines are more likely to have their children vaccinated (4-5). There is a need for further study of how new mothers' knowledge and attitudes may contribute to vaccination coverage in South Africa specifically. A study of nurses providing immunizations in Limpopo Province identified caregiver non-compliance with the recommended vaccination schedule as a major contributor to poor vaccination coverage, although it was not determined how much of this non-compliance was due to limited knowledge, negative attitudes, or structural factors (e.g. long wait times at clinics) (6).

In addition to caregivers' knowledge of and attitudes towards vaccines, structural factors may affect vaccine coverage in South Africa. For instance, community health workers (CHWs) have been shown to increase vaccination coverage in other parts of sub-Saharan Africa (7). Conversely, barriers to vaccination reported by caregivers in other parts of sub-Saharan Africa include distance to clinic, hours of service at clinic, and long queues at the clinic (8-10). In South Africa, people receive vaccinations at government primary care clinics for free, thus the direct cost of the vaccination should not be a barrier to caregivers having their children vaccinated. However, stock-outs (i.e. shortages of at least one vaccine on the day of contact) would prevent parents from having their children receive that vaccine.

In this study, we evaluated some of the behavioral and structural factors which have influenced vaccine coverage among a cohort of 317 caregiver-child dyads in Limpopo Province, South Africa.

## **METHODS**

### **Setting**

This study took place in the town of Tzaneen in Mopani District, Limpopo Province, South Africa. Mopani has a population of 1.1 million people, around 80% of whom live in rural areas (11). Tzaneen is located 180 km from the Zimbabwe border, 250 km from the Botswana border and 170 km from the Mozambique border. The Greater Tzaneen municipality has a population of 390,095, with a population density of 120 persons/km<sup>2</sup> (12). The two largest ethnolinguistic groups in Tzaneen are speakers of Sepedi (Northern Sotho) and Xitsonga.

### **Sampling**

This cross-sectional study was nested within a larger, two-year-long child development intervention trial (SANCTR: reference number 4407/ PACTR201710002683810) (13). In this trial, a package of CHW interventions, largely centered on promoting positive mother-child interactions, is being tested to see what effects they may have on children's physical and neurocognitive development during the first two years of life. Overall, 1107 caregiver-child dyads have been enrolled in the trial and are being followed for two years. Children were enrolled from birth and randomized to either intervention (i.e. curriculum integrated into existing CHW protocol with monthly visits to the household) or control arm (i.e. standard protocol). At enrollment, information on household demographics, child health, and caregiver well-being were collected through face-to-face interviews. At endline (two years of age), the impact of the intervention on child health and physical and neurocognitive development will be assessed. A subsample of 317 caregiver-child dyads is participating in a sub-study. Participants in the sub-study visit a testing center in the town of Tzaneen for neurocognitive measurements, principally eye-tracking and electroencephalography (EEG), when children are aged 7, 16, and 25 months. A cross-sectional survey on vaccine knowledge and attitudes was administered to caregivers when children visited the testing center for their 7-month assessment. The other data presented in this paper are secondary data from the larger child development study. For our study, 'caregiver' was defined as the adult family member who brought the child in for testing, which in this study tended to be mothers (Table 1).

### **Data Collection**

Data collection forms were used to gather demographic information from the caregivers, as well as the children's vaccination data. Caregiver and child demographic information was collected at the time of enrollment in the study. The vaccination data were acquired from the

Road to Health Card (distributed by the National Department of Health) that caregivers were asked to bring to the testing center. This card lists the age-appropriate vaccinations that children should receive according to recommendations from the South African Expanded Programme on Immunisation (EPI) (14). Health care workers record the date the vaccination was given and the batch number in the card.

The survey vaccine questions were based largely on questions developed by WHO's SAGE Working Group on Vaccine Hesitancy, as well as questions from the Parent Attitudes about Childhood Vaccines survey (15-17). The survey questions were written in English and then verbally translated into the local languages, Xitsonga and Sepedi, by local research staff, who administered the survey to the study participants. The study team agreed on appropriate wording for the translations during the training and piloting phase. The results of these surveys, as well as general demographic data, were entered into an electronic REDCap database (Vanderbilt University, Nashville, USA) by local research staff (18).

Ethical clearance for the main intervention trial, in which this survey was nested, was obtained from the institutional review boards of Boston University, University of the Witwatersrand, and the Limpopo Department of Health. Written informed consent for study participation was obtained from caregivers in the local languages, Sepedi and Xitsonga, with the help of local research staff who served as interpreters.

### **Variables**

To measure caregivers' views on vaccines, a simple vaccine positivity index was created. During the survey, caregivers were asked to agree or disagree with seven different statements concerning vaccinations, with the options 'Strongly agree', 'Agree', 'Not sure', 'Disagree', or 'Strongly disagree.' For the five statements in which agreement indicated a more positive view

about vaccination, ‘Strongly agree’ and ‘Agree’ were both coded 1. For the two statements in which agreement indicated a more negative view about vaccination, ‘Strongly agree’ and ‘Agree’ were both coded -1. The caregivers’ responses to the seven statements were summed to create a vaccination positivity index, which could range from a low of -2 (uniformly negative views about vaccination) to 5 (uniformly positive views about vaccination). A continuous wealth index was constructed based on principal component analysis of household asset data per the methodology described in Filmer & Pritchett (19). Participants reported whether their household owned 27 key assets (e.g. a radio, a television, a refrigerator, etc.), selected based on the questions from the 2014/2015 South Africa Living Conditions Survey (20).

### **Analysis**

All data were analyzed using R (R Foundation for Statistical Computing, Vienna, Austria). The primary outcome of interest was ‘full coverage,’ or whether a child had received their recommended vaccinations by 7 months of age. ‘Full coverage’ was defined for this study as having received Bacillus Calmette-Guérin tuberculosis vaccine at birth; oral polio vaccine at birth and 6 weeks of age; diphtheria and tetanus toxoids, acellular pertussis adsorbed, inactivated poliovirus, *Haemophilus influenzae* type B, and hepatitis B vaccines at 6, 10, and 14 weeks; and rotavirus vaccine (RV) at 6 weeks. National guidelines recommends that by 6 months of age, infants should have received all of these vaccinations at the timeframes indicated, as well as pneumococcal conjugate vaccine (PCV) at 6 weeks and 14 weeks, RV at 14 weeks, and measles vaccine at 6 months (14). We excluded PCV in our definition of ‘full coverage’ because it appears that PCV was not available during the study period due to stock-outs, a factor outside of the control of caregivers whose inclusion in our model would make it difficult to elucidate any other factors correlated with immunization status. Measles vaccine was also excluded because

the recommended date of administration (6 months) and the 7-month assessment visit were so close in time, and did not give caregivers adequate time to present at the clinic and receive the vaccination before assessment. Additionally, RV is recommended at both 6 weeks and 14 weeks, but the 14-week vaccination was not asked about in our survey, so was necessarily excluded from our definition.

Demographic characteristics are summarized using frequencies for categorical variables and means with standard deviation for continuous variables. We present the proportion of children who had received each vaccination at any point before 7 months of age and not necessarily by the time recommended by the government (e.g. a child who at age 3 months had received a vaccine recommended at 1 month would be counted as having coverage of this vaccine). We also used logistic regression to identify factors associated with ‘full coverage’ by age 7 months.

## **RESULTS**

Table 1 shows demographic information for the caregivers at the time of study enrollment. The majority (88%) of the caregivers who brought children to the 7-month assessment were the same as those who completed the baseline enrollment survey. Most caregivers (83%) who brought the child to their 7-month assessment were the child’s mother. The average age of caregivers in this study is 31.8 years old (SD 10.4 years), with an average of 10.2 years of schooling completed (SD 2.6 years). Twelve percent of caregivers were employed outside of the home and 42% were married. Additionally, 31% of caregivers surveyed were first-time mothers. While just 29% of caregivers reported clean water on site at home, over 99% of households reported owning a cell phone. Many caregivers (45%) reported that a CHW had

visited in the past month, and 38% reported that the CHW had spoken with them about vaccines at their most recent visit.

The vaccination status of children enrolled in the study was based on Road to Health Cards, which all caregivers were asked to bring to each study visit and which 99% of caregivers brought to their 7-month visit. Of note, while vaccination coverage was generally high in this population, coverage was lower for measles (87%) and very low for PCV (36%) (Table 2). In total, only 29% of children were up-to-date on all vaccinations they were supposed to have received by age 6 months. However, coverage of all vaccines besides PCV was 70%. Furthermore, looking at coverage for all vaccines besides both PCV and measles (i.e. ‘full coverage’), this rose to 76%. Notably, coverage for individual vaccinations in the study population was higher than the most recent WHO and UNICEF estimates for South Africa as a whole at this time of this study (3), as seen in final column of Table 2.

Overall, for the vaccination positivity index, which ranges from -2 (most negative) to 5 (most positive), the mean was 4.1 (SD=1.1), indicating that caregivers generally had positive feelings about vaccines (Figure 1). For instance, 99% agreed it is important for themselves and their children to get recommended vaccinations. Of note, though, a number of caregivers did not feel confident the clinic would have the vaccinations they require when they need them (23%). Additionally, one in five caregivers felt they were not provided enough information about vaccines, their safety, and how they work (20%).

While several caregivers indicated that barriers for accessing childhood vaccinations included the distance from their home to the clinic (12%) and time needed to reach and wait at the clinic (11%), by far the most commonly cited barrier was that the vaccine was out-of-stock at the clinic (50%) (Figure 2). A higher proportion of caregivers whose children did not receive



PCV reported vaccines were out-of-stock compared to caregivers whose children did receive PCV (53% and 41%, respectively;  $p=0.026$ ). Thus, it appears stock-outs are a major factor driving low PCV coverage. Of note, none of the caregivers indicated vaccine cost was a barrier for them.

Table 3 shows the results of a logistic regression model exploring which factors contributed to whether or not a child achieved ‘full coverage’ of recommended vaccinations by 7 months of age. Vaccine positivity index of caregiver, total barriers reported by caregiver, CHW discussion of vaccines at most recent visit, wealth index of household, caregiver age, caregiver parity, and caregiver employment were all found to be statistically insignificant in relation to whether or not a child had achieved ‘full coverage.’ There was a positive association between ‘full coverage’ and both caregiver education (in years of schooling;  $p=0.01$ ) and the dummy variable of whether or not a CHW had visited in the past month ( $p<0.001$ ). 37 participants were excluded from the logistic regression model due to missing values for one or more variables included in the model. Participants dropped from the final analysis due to missing data were not systematically different from those who were included (Appendix 1).

## **DISCUSSION**

This analysis yielded four main findings. First, caregivers generally expressed positive attitudes about vaccination. Second, vaccination coverage rates were high except for PCV. Third, low PCV coverage appeared to be related to stock-outs at government clinics. Fourth, recent CHW visits and caregiver education were both associated with higher probability of achieving ‘full coverage’ by 7 months of age.

Attitudes towards vaccinations were generally positive among the caregivers in the study population, but it appears structural factors determined vaccination coverage more than behavioral factors (e.g. knowledge and beliefs about vaccines). In particular, vaccine stock-outs were a common problem among this population, particularly for PCV. South Africa first introduced PCV to its recommended EPI vaccine schedule in 2008, in the form of the older formulation PCV7, before introducing the newer formulation PCV13 in 2011 (14). The introduction of PCV dramatically reduced rates of invasive pneumococcal disease among South Africa children younger than 2 years old (21). It is currently recommended infants receive 3 different PCV shots, at 6 weeks, 14 weeks, and 9 months of age. However, when PCV was first introduced in South Africa, there were reports of widespread stock-outs, with several reports of continued PCV13 stock-outs in South African government clinics since then. For instance, one study in the Tshwane Health Province of Gauteng Province found 65% of surveyed clinics had experienced a stock-out of PCV13 in the previous 12 months, with similarly high stock-out rates for other vaccines like rotavirus and DTaP-IPV/Hib (22). In Limpopo Province specifically, the Stop Stock Outs Project has uncovered notable vaccine stock-outs; in 2014, for example, 28% of clinics reported they did not have any DTaP-IPV/Hib vaccine in stock (23). For PCV13 in particular, high prices pose a major barrier to access in South Africa, since the country spends more than 30% of its annual vaccination budget on PCV13 alone (24).

The most statistically significant finding of the regression model was a positive association between ‘full coverage’ and a CHW visit in the past month. This appears to support previous findings which link CHW programs in South Africa with higher rates of vaccination coverage (25). Additionally, there was a significant positive association between ‘full coverage’ and the number of years of schooling completed by the caregiver. This appears to support

previous research which found maternal education has a positive association with child vaccination (26). It is plausible that caregivers with a higher level of education were better able to understand the instructions given to them about when to bring their children in for vaccination, although further study is needed to better understand the mechanism behind this association. It is interesting to note that, although not statistically significant, CHW discussion of vaccines with caregiver at last visit was associated with a decreased likelihood of 'full coverage.' It is plausible this is because CHWs were more likely to discuss vaccines with caregivers whose children were not up-to-date on vaccinations; however, given the lack of statistical significance, further study is needed on this topic.

There are several limitations of this study. Surveyed caregivers were all enrolled in a larger child development study and thus may not be representative of the full population of caregivers in Limpopo Province, because caregivers who participated in this study may be better integrated into the formal health system than other caregivers in this area. Another limitation is that this study only gathered data on whether children had received their first RV and PCV at 6 weeks of age, even though by 6 months of age they should all have received two RV and two PCV (at 6 weeks and 14 weeks for each vaccine). Therefore, it is difficult to accurately assess complete coverage of the PCV and rotavirus vaccine series because coverage of the second vaccine in each series (at 14 weeks) was not recorded. Additionally, the generally positive attitudes about vaccines expressed by caregivers may in part be due to a social desirability bias, whereby respondents expressed these positive views about vaccines because they believed it was what surveyors wanted to hear. Furthermore, the possible barriers to vaccination which we investigated was not exhaustive, and many other conceivable barriers (e.g. immigration status, religious beliefs, behaviors of local healthcare workers, etc.) were unexplored and may warrant

further investigation. Finally, because of the descriptive nature of this cross-sectional study, it is not possible to demonstrate causation from the associations described. Therefore, any conclusions from this study must be treated with caution and further study is warranted in order to better understand the relationships between vaccination coverage and stock-outs, CHW programs, caregiver education, and other variables described in this paper.

## **CONCLUSIONS**

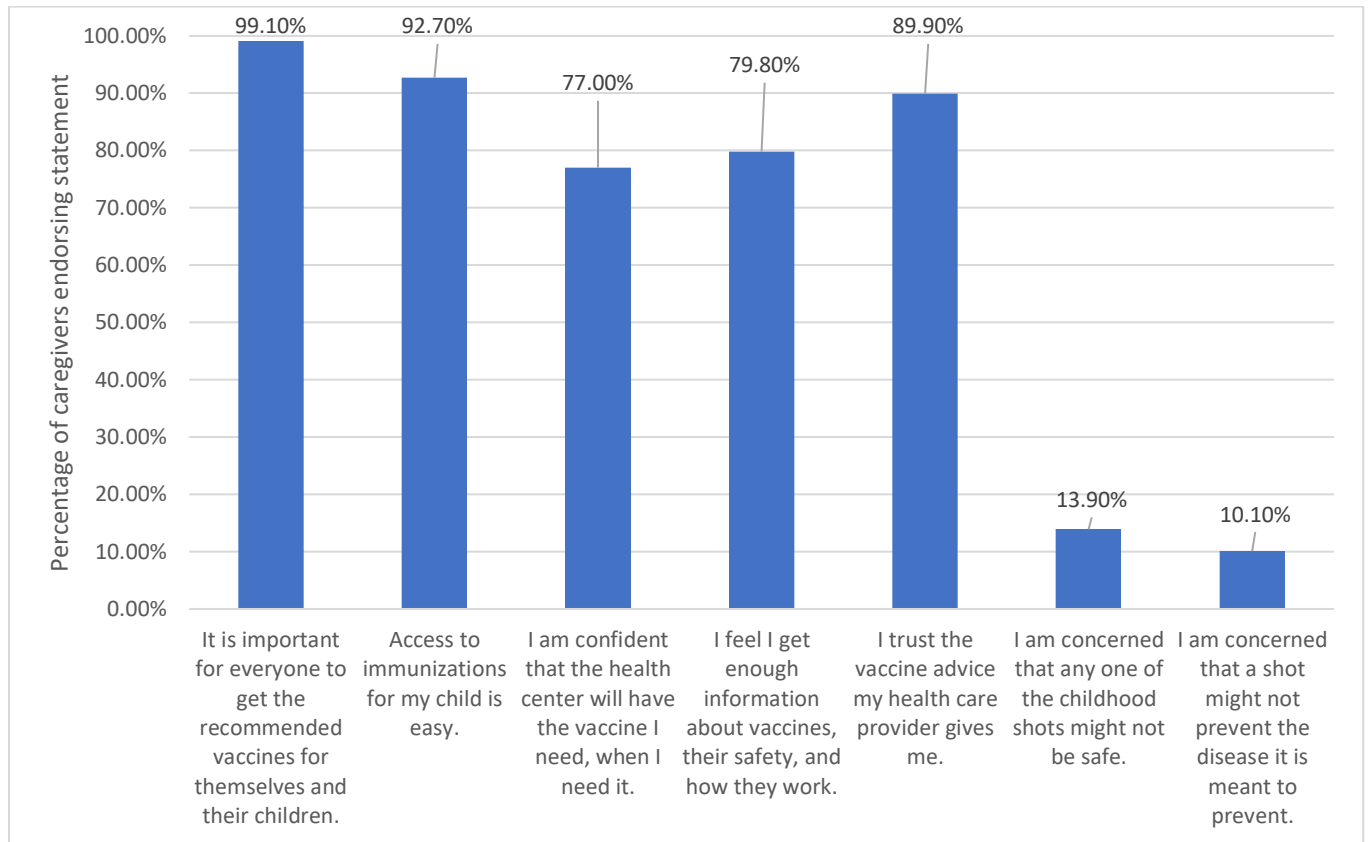
Overall, it appears that structural factors (e.g. vaccine availability at clinics) play a much larger role in determining a child's vaccination status than behavioral factors (e.g. caregiver attitudes about vaccines) in this study population. To improve vaccination rates among infants in Limpopo Province, it is important to prevent vaccine stock-outs, with a particular emphasis on PCV. For this reason, the supply chain of PCV in South Africa should be closely studied in order to identify and address the root causes of PCV stock-outs, with a goal of preventing future stock-outs in those regions of the country with relatively low coverage, like Mopani District. Additionally, given the positive association between caregiver education and vaccination coverage, expanded educational opportunities for women and girls in Limpopo Province may augment vaccination coverage in Limpopo Province. Finally, given the strong positive association between vaccination coverage and recent CHW visits, expanded support for CHW programs, including home visits to recent mothers, may be another means for promoting vaccination among infants in Limpopo Province. However, given the descriptive nature of this cross-sectional study, it is difficult to prove causation between any of these associations, and further study of this subject is warranted before policy prescriptions can be confidently made.

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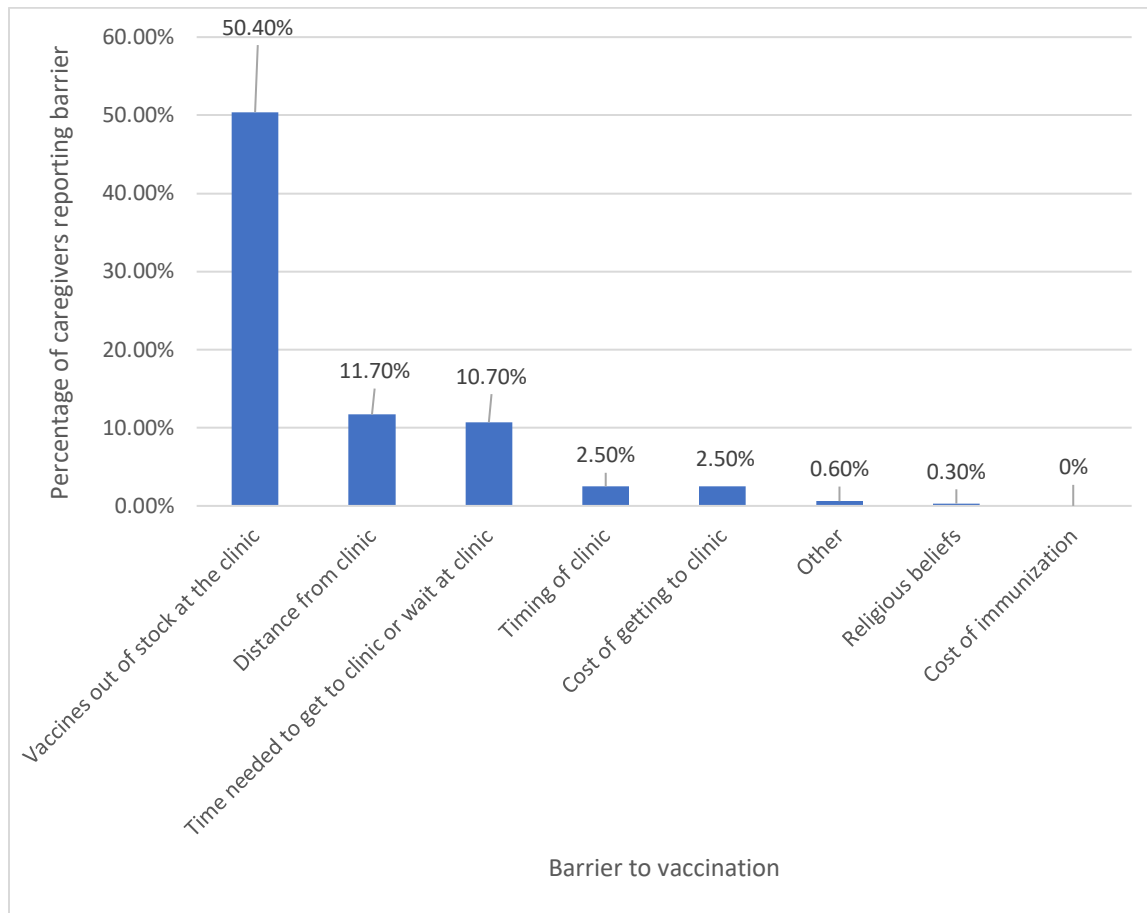
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**Figure 1. Results of Survey on Attitudes Towards Vaccination (N=317)**



\*The variables here were combined into a vaccine positivity index, scored by +1 for agreement with the first 5 statements (positive statements about vaccines) or -1 for agreement with the final 2 statements (negative statements about vaccines). The mean vaccine positivity index score was 4.1, with a standard deviation of 1.1.

**Figure 2. Results of Survey on Barriers to Vaccination (N=317)**



\*In total, 206 caregivers (65.0%) reported at least one barrier to vaccination. A mean of 0.8 barriers to vaccination were reported (SD 0.7).



**Table 1. Demographic Characteristics of the Study Population (N=317).\***

<b>Caregiver Characteristics (n)**</b>	<b>n (%)</b>
Age of caregiver (years) (n=310)	31.8 (10.4)***
Relationship of caregiver to child	
Mother	263/317 (83.0%)
Father	2/317 (0.6%)
Aunt	13/317 (4.1%)
Grandmother	37/317 (11.7%)
Sister	2/317 (0.6%)
Education of caregiver (years of schooling completed) (n=309)	10.2 (2.6)***
Caregiver is employed	36/312 (11.5%)
Parity of caregiver (including current child and any stillbirths)	
1	98/313 (31.3%)
2	82/313 (26.2%)
3	76/313 (24.3%)
4+	57/313 (18.2%)
Marital status	
Married	127/303 (41.9%)
Single	163/303 (53.8%)
Divorced	6/303 (2.0%)
Widowed	7/303 (2.3%)
<b>Household Characteristics</b>	<b>n (%)</b>
Household assets	
Clean water on site (borehole or piped water)	91/314 (29.0%)
Farmland	186/312 (59.6%)
Cell phone	312/314 (99.4%)
Motor vehicle	69/314 (22.0%)
Community health worker (CHW) visited in the past month	141/317 (44.5%)
CHW spoke with caregiver about vaccines at last visit	119/316 (37.7%)

\*Totals may not add up to 317 for all variables due to missing values.

\*\*Caregiver characteristics were based on information provided by caregivers during baseline survey at time of study enrollment. 87.4% of all caregivers who brought child to their 7-month assessment were the same caregiver who completed baseline enrollment survey.

\*\*\*Mean (SD)

**Table 2. Vaccination Status of Children (N=317).\***

Vaccine	Recommended time	n (%) received	South Africa baseline****
BCG**	Birth	288/310 (92.9%)	74%
OPV 0**	Birth	306/312 (98.1%)	N/A
DTaP-IPV/Hib/HBV 1**	6 weeks	286/313 (91.4%)	78%
OPV 1**	6 weeks	302/311 (97.1%)	N/A
PCV 1**	6 weeks***	111/308 (36.0%)	N/A
RV 1**	6 weeks***	292/310 (94.2%)	N/A
DTaP-IPV/Hib/HBV 2**	10 weeks	285/310 (91.9%)	N/A
DTaP-IPV/Hib/HBV 3**	14 weeks	294/313 (93.9%)	66%
Measles	6 months	272/311 (87.5%)	75%
Up to date on all vaccines		87/299 (29.1%)	N/A
Up to date on all vaccines besides PCV		211/302 (70.0%)	N/A
Up to date on all vaccines besides PCV and measles (i.e. 'full coverage')		229/303 (75.6%)	N/A

\*Totals may not add up to 317 for all variables due to missing values, including because they did not bring their Road to Health Card to the appointment (n=4) and were thus not included in this portion of the analysis.

\*\*BCG=Bacillus Calmette-Guérin tuberculosis vaccine; OPV=oral polio vaccine; DTaP-IPV=diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine; HBV=hepatitis B virus vaccine; Hib=*Haemophilus influenzae* type B vaccine; PCV=pneumococcal conjugate vaccine; RV=rotavirus vaccine

\*\*\*PCV and RV recommended at 6 and 14 weeks, but data were only collected on the 6-week vaccination.

\*\*\*\*South Africa vaccination coverage is based on 2016 WHO and UNICEF estimates (3). N/A used to indicate vaccinations whose coverage was not estimated by the WHO and UNICEF.

**Table 3. Factors Predicting Whether Child Was Up-To-Date On Surveyed Vaccinations Besides PCV And Measles (n=280).\***

<b>Variable</b>	<b>Mean (SD)</b>	<b>Adjusted OR (95% CI)</b>	<b>P-value</b>
Vaccine positivity index of caregiver	4.1 (1.1)	1.00 (0.96-1.05)	0.989
Total barriers reported by caregiver	0.8 (0.7)	1.01 (0.94-1.08)	0.831
Did CHW discuss vaccines at last visit	119 (37.7%)**	0.89 (0.79-1.01)	0.069
Did CHW visit in the past month	141 (44.5%)**	1.24 (1.10-1.41)	<0.001***
Wealth index of household (z-score)	139.8 (80.3)	1.00 (1.00-1.00)	0.572
Caregiver age	31.8 (10.4)	1.00 (0.99-1.01)	0.616
Caregiver parity	2.4 (1.3)	0.99 (0.95-1.03)	0.728
Is caregiver employed	36 (11.5%)**	1.00 (0.85-1.17)	0.967
Caregiver education (years of schooling)	10.2 (2.6)	1.03 (1.01-1.05)	0.012***

\* Regression model excludes 37 caregivers from total study population (317) due to missingness of values for one or more variables included in the logistic regression model. For the 280 caregivers included in the model, 213 infants (76.1%) were up-to-date on all surveyed vaccinations besides PCV and measles. Please see Appendix 1 for comparison of sample groups included and excluded from the regression model.

\*\* n (%) with outcome

\*\*\* Statistically significant (p < 0.05)

**Appendix 1. Comparison of Samples Included and Excluded From Logistic Regression Model (N=317)\***

<b>Variable</b>	<b>280 participants included in regression model – mean (SD)</b>	<b>37 participants excluded from regression model – mean (SD)</b>
Vaccine positivity index of caregiver	4.1 (1.1)	4.4 (0.8)
Total barriers reported by caregiver	0.8 (0.7)	0.9 (0.7)
Did CHW discuss vaccines at last visit	106/280 (37.9%)**	13/36 (36.1%)**
Did CHW visit in the past month	126/280 (45.0%)**	15/27 (55.6%)**
Wealth index of household (z-score)	0.2 (1.0)	0.3 (1.0)
Caregiver age	31.3 (10.0)	36.9 (12.4)
Caregiver parity	2.4 (1.3)	2.6 (1.4)
Is caregiver employed	32/280 (11.4%)**	4/32 (12.5%)**
Caregiver education (years of schooling)	10.3 (2.5)	9.8 (2.8)
Up-to-date on vaccines	213/280 (76.1%)**	16/23 (69.6%)**

\*From the total study population of 317, there were 37 participants excluded from the logistic regression model due to missing values for one or more variables included in the model.

\*\*n (%)