Original Paper

Title: Individual level determinants for not receiving immunization, receiving immunization with delay, and being severely underimmunized among rural western Kenyan children

Authors: Dustin G Gibson[1], PhD, MS; Benard Ochieng[2],MS; Eunice W Kagucia[1], MHS; David Obor[2], MS; Frank Odhiambo[2], PhD; Katherine L O'Brien[1], MD, MPH; Daniel R Feikin[1,3], MD, MPH

[1]Johns Hopkins Bloomberg School of Public Health, Department of International Health, Baltimore, MD, United States

[2]Kenya Medical Research Institute/Centers for Disease Control and Prevention Public Health and Research Collaboration, Kisumu, Kenya

[3]Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA, United States

Corresponding Author:
Dustin Gibson, PhD
Johns Hopkins Bloomberg School of Public Health
615 North Wolfe Street, E8650
Baltimore, MD 21205
Phone: (919)-943-1095
Email: dgibso28@jhu.edu

Keywords: vaccination coverage, vaccination timeliness, fully immunized child, FIC, underimmunization, immunization, vaccination, Kenya

Abstract Word Count: 297/300

Text Word Count: 2982/3000

Tables: 6

Figures: 0

Supplemental files: 0

Citations: 47

Abstract

Background: Estimating vaccination coverage and delays are important because these measures can identify at risk sub-populations who can be targeted with interventions and public health policies. This paper sought to determine estimates and risk factors for children in rural western Kenya who did not receive immunization, received immunization with delay, or were severely underimmunized.

Methods: Caregivers of children aged 12-23 months old were surveyed for immunization history using written records from the immunization booklet. Risk factors for not receiving immunization, delayed immunization, and severe underimmunization were calculated using log-binomial regression. Children were categorized as delayed if a given immunization was received greater than four weeks from the age-appropriate scheduled date. Severely underimmunized children were those who were fully unvaccinated for more than 90 days and had three or more vaccines delayed or not given.

Results: Immunization coverage for pentavalent1, pentavalent3, measles, and fully immunized child (FIC; BCG, three doses of polio, three doses of pentavalent, and measles vaccines) were 99%, 94%, 83%, and 80%, respectively. Approximately, 10%, 24%, and 29%, of children were delayed for pentavalent1, pentavalent3, and measles, respectively. Each model produced a unique combination of risk factors with only advanced maternal age as a risk factor common to all models. Children with delayed receipt of pentavalent1 were at risk for not receiving pentavalent3 (RR: 5.20; 95%CI 3.48, 7.77), measles vaccine (RR: 1.48; 95%CI 1.12, 1.95), and not achieving FIC (RR: 1.88; 95%CI 1.51, 2.34) compared with children who received pentavalent1 on time.

Conclusions: Immunization coverage among 12-23 month old children was high, yet a substantial proportion of children were vaccinated with delay. Although vaccine coverage and timeliness are often conceptualized as separate measures, the finding that delayed pentavalent1 receipt was a strong risk factor for not receiving future immunizations indicates the two measures are intertwined.

1. Introduction

Few interventions available to public health practitioners rival the cost-effectiveness of vaccines for reducing childhood morbidity and mortality.[1] Numerous studies have identified risk factors for being unimmunized[2-5] and receiving vaccines with delay.[6,7] Estimating vaccination coverage and delays are important because these measures can identify at risk sub-populations which can be targeted with interventions and public health policies.[8-11]

In Kenya, the Division of Vaccine and Immunization (DVI) recommends children receive bacillus Calmette–Guerin (BCG) and polio vaccines at birth, three doses of polio and pentavalent (diphtheria, tetanus toxoid, pertussis, hepatitis B, and *Haemophilus influenzae type b* antigens) vaccines at 6, 10, and 14 weeks of age, and measles vaccine at 9 months of age[12]. Kenya added pneumococcal conjugate vaccine (PCV) and rotavirus vaccine to their national immunization plan in 2011 and 2014, respectively.

Coverage estimates for three doses of pentavalent (pentavalent3), or DTP3 in countries where pentavalent is not available, in children 12-23 months old is a common indicator of a country's health and vaccine system strength.[13,14] Data from successive Kenyan Demographic and Health Surveys found improvements in DTP3 coverage of infants 12-23 months old from 2003 (72%) to 2009 (86%).[15] Although the DTP series should be completed by 14 weeks of age, if all doses are received on time and in most low-income countries, the standard coverage measure is DTP vaccination by 12-23 months of age, which does not differentiate timely or delayed receipt.

Delayed vaccination has been associated with increased cases of pertussis[16,17], hepatitis B[18], and *Haemophilus influenzae* type b[19], all which have high morbidity and mortality in early infancy. Furthermore, timely vaccination heightens population herd immunity levels[20], thereby protecting those who are too young to be vaccinated, have medical contraindications, or who do not produce an adequate immunological response.

Vaccination delays are prevalent across lower income countries. Two systematic reviews identified a median delay of 6.2 and 6.3 weeks for DTP3 across 76 lower and middle-income countries (10 countries were included in each review).[6,7] In Kenya, the median estimated delay in DTP3 was 3.2 weeks, a value lower than the global median, but 25% of Kenyan children had DTP3 delays greater than 7.5 weeks.[7]

The objectives of this study were to determine the proportion and risk factors of children in rural Western Kenya: (1) not receiving immunization; (2) receiving immunizations with delay; and (3) being severely underimmunized.

2. Methods:

2.1 Study Design

During March and April of 2013, a cross-sectional survey was conducted in Gem District, Siaya County, Kenya to ascertain immunization coverage in children 12-23 months old. Gem District is nested within the study area of the Kenya Medical Research Institute (KEMRI) and Centers for Disease Control and Prevention (CDC) Health and Demographic Surveillance System (HDSS). The HDSS follows a population of approximately 220,000 residents living in 54,869 households from 385 villages. HDSS residents are defined as living within the study area for at least four months or individuals that are born to residents. Approximately 45% of the population is aged 15 years and younger [21] Most of this rural population belongs to the Luo ethnic group with subsistence farming as the primary occupation. The survey's primary purpose was to collect immunization coverage for sample size calculations of the Mobile Solutions for Immunizations (M-SIMU) randomized controlled trial (ClinicalTrials.gov NCT01878435).

The HDSS provided a census of enumerated HDSS-consented households from 120 villages with children aged 12-23 months. Using this list of eligible households, HDSS community interviewers approached all eligible mothers, sought consent, and administered the survey.

The study protocol received ethical clearance from the Scientific Steering Committee (SSC), the KEMRI-Nairobi Ethical Review Committee (SSC#2409), Johns Hopkins University Bloomberg School of Public Health, and CDC.

2.2 Data Collection and management

KEMRI/CDC staff conducted surveys using smart-phones programmed with the Open Data Kit (ODK) application. Staff members asked the caregiver of children aged 12-23 months if the maternal and child health (MCH) booklet was available, and if so, immunization dates were recorded. If no MCH booklet was present, immunization history was collected verbally (data excluded from present analysis). A multiple correspondence analysis of household assets (livestock and valuable goods), cooking fuel and water sources, and household head's source of income was conducted to assign socio-economic status (SES) quintiles to each participant [22]. SES was then dichotomized to lower 40% and upper 60% SES. Straight-line distances from a child's household to the nearest health facility were calculated using ArcView Geographic Information Systems (GIS; Esri, Redlands, CA).

2.3 Primary outcome definitions

The three primary outcomes for regression analyses were: (1) Not receiving immunization; (2) Receiving delayed immunization; and (3) being severely underimmunized. Not receiving immunization and delayed immunization estimates were restricted to pentavalent1 (delayed only), pentavalent3, measles vaccine, and fully immunized child (FIC; not receiving-immunization only), defined as receiving BCG, three doses of polio vaccine, three doses of pentavalent vaccine, and one dose of measles vaccine. Not receiving immunization was the vaccine-specific proportion of children who were not vaccinated when surveyed at ages 12-23 months of age, independent of timeliness. Not achieving FIC was defined as the proportion of children who were not immunized for at least one vaccine by the time of survey.

Delayed vaccination was defined as the vaccine-specific proportion of children who were immunized greater than four weeks from the DVI recommended age.[23] For pentavalent1, pentavalent3

and measles, children were delayed if vaccination occurred after 10 weeks, 18 weeks, and 10 months (303 days), respectively. Delayed immunization was the vaccine-specific proportion of children who were delayed in vaccination over all children that received vaccination. Catch-up schedules for pentavalent series vaccine were not included in primary analyses.

Severe underimmunization was defined as children who, cumulatively across five vaccines (BCG, the three pentavalent vaccines, and measles), had greater than 90 days of underimmunization (either not receiving immunization at all or receiving it with delay) in the first 12 months of life and were delayed for at least three of the five aforementioned vaccines. Days delayed began to accumulate after the four week window had lapsed. The 90 days of underimmunization and the number of vaccines delayed were both required for a child to be considered underimmunized.

2.4 Data Analysis

The age at vaccination was calculated by subtracting the child's birth date from vaccination date. Vaccinations received were then dichotomized into delayed and timely as defined above.

For severe underimmunization, vaccination data were censored at 12 months of age. For BCG, pentavalent1-3, and measles vaccines, the number of days underimmunized (delayed or not receiving vaccination) were summed to produce the total number of days underimmunized in the first 12 months of life. Children who received vaccination within 4 weeks of scheduled date were given 0 days of underimmunization for that vaccine. Days underimmunized were not double counted if underimmunized vaccines overlapped. For example, if a child did not receive BCG and measles vaccine, but received all other vaccines on time, the child would be underimmunized 337 days for BCG (365-28 days) and 62 days for measles (365-303; where 303=10 months). Since BCG and measles underimmunization periods overlapped, the child would be considered underimmunized for 337 days. The number of vaccines delayed and not given was summed for each child. Children with three or more such vaccines were considered severely underimmunized if the total number of days underimmunized was greater than 90 days.

Crude risk ratios with 95% confidence intervals for each primary outcome were obtained by log-binomial regression. Initial multivariable models were created using an automated forward-stepwise selection of variables with an alpha of 0.05. Variables that were significant in any of the initial multivariable models were then manually entered into a final regression model for each vaccine to make comparisons of risk factors across the models easier. Eight children (0.4% of the sample with written immunization history) who did not receive pentavalent1 vaccine were excluded from regression models for risk factors of not receiving vaccination (pentavalent3, measles and FIC). These children were excluded because of the inclusion of the timely/delayed pentavalent1 variable in regression analyses and because children who do not receive pentavalent1 vaccine cannot be considered vaccinated for pentavalent3 vaccine. Analyses were performed using STATA/IC, version 11.2 (Stata Corp, College Station, Texas) with an alpha of 0.05.

3. Results

A total of 2632 households were visited. Excluded from present analysis were 75 (2.8%) children with unknown birthdate or not within 12-23 months of age, 690 (26.2%) children with no immunization booklet, 57 (2.2%) children who could not be located, and 129 (4.9%) children with illegible or incomplete records. The final analysis included 1681 (63.9%) children aged 12-23 months with vaccination history inscribed in their MCH booklet. Overall, demographic characteristics between those who had written immunization history and those who verbally reported (excluded from analysis) were similar. However, there were higher proportions of households with one child under five years old and of older children in those who verbally reported (Table 1).

3.1 Not receiving Immunization

Antigen-specific vaccination coverage measured at 12-23 months was high for all vaccines (Table 2). Approximately 99%, 94%, 83%, and 80% of children received pentavalent1, pentavalent3, measles, and were a FIC, respectively. Multivariable analyses for factors associated with not receiving vaccination, as compared to receiving vaccination, showed unique combinations of risk factors for each

vaccine. However, only children who received pentavalent1 delayed were significantly associated with not receiving vaccination in all three models (Table 3). Specifically, children with delayed pentavalent1 receipt, as compared to those with timely pentavalent1, were 5.2 (95%CI: 3.5, 7.8), 1.5 (95%CI: 1.1, 2.0) and 1.9 (95%CI: 1.5, 2.3) times more likely to not be vaccinated for pentavalent3, measles, and FIC, respectively. In sensitivity analyses where the time window for delays was decreased from four to two weeks, children who received pentavalent1 two weeks late were 4.6 (95%CI: 3.0, 6.9), 1.3 (95%CI: 1.1-1.7), and 1.6 (95%CI: 1.3, 1.9) times more likely to not receive pentavalent3, measles, and be fully immunized, respectively.

Caregiver's marital status, socio-economic status, and the child's gender were not significant in any of the initial models for not receiving immunization, receiving immunization with delay, and being severely underimmunized. In addition, the number of children under five years old in the house, the number of individuals in the house, and distance to the clinic were not significantly associated with any of the models for not receiving vaccination.

3.2 Receiving Immunization with Delay

Vaccine-specific estimates of coverage were notably lower when incorporating timely definitions. Approximately 10%, 24% and 29% of children received pentavalent1, pentavalent3, and measles delayed as compared to the DVI immunization schedule, respectively (Table 2). The median delay was 18 days for pentavalent1 (IQR: 5, 51 days), 21 days for pentavalent3 (IQR: 9, 65 days) and 26 days for measles (IQR: 9, 66 days).

Similar to models of not receiving vaccination, multivariable models of delayed vaccination, as compared to timely vaccination, found a unique pattern of risk factors specific to each vaccination. However, the only socio-demographic variable significantly associated in each of the delayed immunization models was maternal age; where mothers aged 30 years or more, as compared to mothers aged 15-24 years old, were more likely to have children delayed for pentavalent1 (RR: 1.6; 95%CI: 1.1, 2.2), pentavalent3 (RR: 1.6; 95%CI: 1.0, 1.9), and measles vaccine (RR: 1.6; 95%CI: 1.0, 1.9), (Table 4).

Demographic variables for maternal literacy, marital status, socio-economic status, maternal mobile phone ownership, and child's gender were not significantly associated with delayed pentavalent1, pentavalent3, or measles vaccine.

3.3 Severe Underimmunization

Underimmunization (i.e. children who were not vaccinated or vaccinated with delay) was prevalent. Approximately 38% of children achieved FIC without delay in any vaccination (Table 5). In the first twelve months of life, and cumulatively for BCG, pentavalent1-3, and measles vaccines, children spent a median of 16 days underimmunized (IQR: 0, 66 days). Of the 62% of children who were underimmunized for at least one vaccine, the median number of cumulative days underimmunized increased to 62 days (IQR: 21, 115 days), or 18% (62/337 days) of vaccination-eligible days.

Approximately 14% of children were severely underimmunized. Multivariable analyses found that the oldest mothers, mothers with less than eight years of education, mothers with difficulty or inability to read English, and mothers who do not own a mobile phone were significant risk factors for children who were severely underimmunized as compared to children who were not severely underimmunized (Table 6).

4. Discussion

Immunization coverage levels in the study community have increased substantially over the past decade, likely a result of the substantial global commitment to improving immunization delivery systems.[24-26] In 2003, pentavalent3, measles, and FIC coverages were 68%, 50%, and 41%, respectively.[27] In 2013, vaccination coverage estimates were, 94%, 83%, and 80%, respectively. These coverages were very similar to the estimates by other investigators in 2011, suggesting that immunization coverage levels may be plateauing in rural western Kenya.[28]

Timely vaccination estimates are just recently gaining traction in low-income countries as an important public health metric to monitor over time and as another measure to assess the vaccine delivery system's strength.[27,29-32] Although high immunization coverage by 12-23 months of age was observed, there were substantial proportions of children whose vaccinations were delayed. Similar to coverage estimates, there have been secular improvements in study-site specific estimates of timely vaccination. The proportion of children who received timely pentavalent3 and measles vaccination improved from, respectively, 27% and 18% in 2003 to 76% and 71% in 2013[27].

The regression models found a distinct set of risk factors, by vaccine, for not receiving immunization and delayed immunization. Finding different socio-demographic risk factors for each vaccine may result from differences in the recommended ages of vaccination; with the pentavalent series clustered in the first four of months of life and a single dose of measles vaccine at 9 months of age. In all vaccine-specific models, children with oldest mothers were at significant or trending towards highest risk for not being immunized, being immunized with delay, or being severely underimmunized, which hints at a potential subset of the population to target vaccination-promoting interventions. We did not collect information on the birth order of child, which has been found to be associated with underimmunization in several studies[27,33], and therefore may confound our results. However, the number of children under 5 years old in the household were included in regression models, which may serve as a proxy for birth order.

Immunization coverage and timeliness have usually been conceptualized as separate measures. In this study, the distinction between timeliness and coverage is blurred by the finding that delayed pentavalent1 vaccination was strongly associated with pentavalent series dropout and moderately associated with not receiving measles vaccination or being fully immunized. This finding has been demonstrated in the United States, but to our knowledge, has not been previously documented in resource-constrained settings.[34-37] In this setting, delayed pentavalent1 vaccine could be used as an early warning system to alert practitioners that this child is at higher risk for drop-out of the EPI schedule.

The underimmunization indicator marries immunization coverage and timeliness estimates, making it a useful estimate to comprehensively examine the magnitude of deficiencies in immunization systems.[38] Although 80% of children 12-23 months old were considered as FIC, only 38% of children received all vaccinations without delay. The inclusion of delays drastically reduces the effective population coverage level which is needed to prevent disease outbreaks. For measles vaccine, we found that only 59% of children were immunized by 10 months of age. This estimate is concerning, particularly if these susceptible children are clustered as outbreaks have occurred in populations with less than a 10% susceptible fraction.[40]

This study has several limitations. First, mothers who verbally reported immunization history were excluded from the main analysis. We found higher proportions of children older than 18 months (59%) and lower proportions of households with more than one child under the age of five years old (50%) in those who verbally reported as compared to providing written immunization history, 51%, and 60%, respectively. Older infants are more likely to verbally report because there is more time for the immunization card to be lost.[41] If these mothers were systematically different from those with a MCH booklet and associated with immunization outcomes, our results may be biased.

Secondly, we did not evaluate all possible risk factors for vaccination status. Previous work found that both the quality and frequency of Community Health Worker interactions were significant factors for FIC coverage.[28] Moreover, we had no information on mother's antenatal care seeking behavior and tetanus toxoid immunization[32,43], paternal characteristics including age and education[29], place of delivery[44], and birth order[33] all of which have been significant associated with vaccine coverage and/or timeliness elsewhere. If these variables had been collected and included in analyses, the risk factors and/or their point estimates may differ.

Third, our measure of severe underimmunization may not adequately capture the magnitude of population level underimmunization. To ensure that all children contributed equal person-time to analyses, children were censored at 12 months of age, which limits the number of days measles

vaccination (62 days) can contribute. Future studies would benefit from recording immunization history from children greater than 2 years old to determine if underimmunization persists equally into the second year of life and to allow measles vaccine opportunity to equally contribute to estimates of cumulative days underimmunized.

Furthermore, we included only BCG, the pentavalent series, and measles vaccine in calculations of days underimmunized. Polio and pneumococcal vaccines were omitted because they have the same age-recommended schedule as pentavalent vaccine. Differences in immunization history between these three vaccines are likely due to vaccine stock-outs or errors in the MCH booklet. In our sample, there was 99% congruency in receiving polio1-3 and pentavalent1-3 vaccines (data not shown).

Lastly, concerns our definition of timely and delayed vaccination (i.e. receipt of vaccine within or after four weeks of the scheduled date as performed in other analyses[30,31,45,46]). An alternative analysis may have examined days delayed as a continuous variable where delays accumulate immediately after vaccine is due and not received.[38] This estimate is more sensitive for detecting timeliness but is not easily generalizable to routine reporting systems and the clinical implications and correlates are not yet well understood. Additionally, we did not account for catch-up schedules of previously delayed immunizations, which is particularly important for the pentavalent series. In Kenya, the DVI schedule recommends that pentavalent vaccines be given four weeks apart (e.g. pentavalent3 is due four weeks from the date pentavalent2 was received). If a catch-up schedule was applied to pentavalent3, approximately 92% of children received pentavalent3 on time. We chose the DVI recommend age of vaccination, to calculate pentavalent3 delay because this indicator is easier for vaccine program managers to calculate which makes it more likely to be adopted into routine reporting systems.

In conclusion, the majority of children in western Kenya receive all eight routinely administered vaccine doses, yet a substantial proportion of children are being vaccinated late. Although not often included in reporting of immunization program performance, vaccination timeliness is an important measure, evidenced by delayed pentavalent1 receipt strongly predicting pentavalent and measles drop-

out. Interventions that target this subset of the population offer promise in improving immunization coverage. As global immunization coverage levels have markedly improved over the past decade, but are now stalled[14,47], the paradigm must include not only efforts to vaccinate children but also efforts to ensure that vaccines are given on time.

Conflicts of interest statement: None to declare.

Acknowledgements: We thank the Gem community, KEMRI/CDC project staff, and Danet Opot for programming surveys. This article is published with the approval of the Director of the Kenya Medical Research Institute. The findings and conclusions are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention. Funding was obtained through the Bill & Melinda Gates Foundation

[1] WHO, UNICEF, World Bank. State of the World's Vaccines and Immunization. 3rd Edition. Geneva: World Health Organization, 2009.

[2] Bosch-Capblanch X, Banerjee K, Burton A. Unvaccinated children in years of increasing coverage: how many and who are they? Evidence from 96 low- and middle-income countries. Trop Med Int Health 2012;17(6):697-710.

[3] Canavan ME, Sipsma HL, Kassie GM, Bradley EH. Correlates of complete childhood vaccination in East African countries. PLoS One 2014;9(4):e95709.

[4] Rainey JJ, Watkins M, Ryman TK, Sandhu P, Bo A, Banerjee K. Reasons related to non-vaccination and under-vaccination of children in low and middle income countries: findings from a systematic review of the published literature, 1999-2009. Vaccine 2011;29(46):8215-21.

[5] Wiysonge CS, Uthman OA, Ndumbe PM, Hussey GD. Individual and contextual factors associated with low childhood immunisation coverage in sub-Saharan Africa: a multilevel analysis. PLoS One 2012;7(5):e37905.

[6] Akmatov MK, Mikolajczyk RT. Timeliness of childhood vaccinations in 31 low and middle-income countries. J Epidemiol Community Health 2011.

[7] Clark A, Sanderson C. Timing of children's vaccinations in 45 low-income and middle-income countries: an analysis of survey data. Lancet 2009;373(9674):1543-9.

[8] Briss PA, Rodewald LE, Hinman AR, Shefer AM, Strikas RA, Bernier RR et al. Reviews of evidence regarding interventions to improve vaccination coverage in children, adolescents, and adults. The Task Force on Community Preventive Services. Am J Prev Med 2000;18(1 Suppl):97-140.

[9] Jacobson Vann JC, Szilagyi P. Patient reminder and patient recall systems to improve immunization rates. Cochrane Database Syst Rev 2005;(3)(3):CD003941.

[10] Oyo-Ita A, Nwachukwu CE, Oringanje C, Meremikwu MM. Interventions for improving coverage of child immunization in low- and middle-income countries. Cochrane Database Syst Rev 2011;(7)(7):CD008145.

[11] Shefer A, Briss P, Rodewald L, Bernier R, Strikas R, Yusuf H et al. Improving immunization coverage rates: an evidence-based review of the literature. Epidemiol Rev 1999;21(1):96-142.

[12] Republic of Kenya Ministry of Health. Division of Vaccines and Immunization (DVI) Multi Year Plan 2006-2010. ;2012(May 25).

[13] Global routine vaccination coverage, 2012. Wkly Epidemiol Rec 2013;88(44/45):482-6.

[14] Lim SS, Stein DB, Charrow A, Murray CJ. Tracking progress towards universal childhood immunisation and the impact of global initiatives: a systematic analysis of three-dose diphtheria, tetanus, and pertussis immunisation coverage. Lancet 2008;372(9655):2031-46.

[15] Kenya National Bureau of Statistics (KNBS), ICF Macro. Kenya Demographic and Health Survey 2008-2009. 2010;Calverton, Maryland:KNBS and ICF Macro.

[16] Grant CC, Roberts M, Scragg R, Stewart J, Lennon D, Kivell D et al. Delayed immunisation and risk of pertussis in infants: unmatched case-control study. BMJ 2003;326(7394):852-3.

[17] Kolos V, Menzies R, McIntyre P. Higher pertussis hospitalization rates in indigenous Australian infants, and delayed vaccination. Vaccine 2007;25(4):588-90.

[18] Inskip HM, Hall AJ, Chotard J, Loik F, Whittle H. Hepatitis B vaccine in the Gambian Expanded Programme on Immunization: factors influencing antibody response. Int J Epidemiol 1991;20(3):764-9.

[19] von Kries R, Bohm O, Windfuhr A. Haemophilus influenzae b-vaccination: the urgency for timely vaccination. Eur J Pediatr 1997;156(4):282-7.

[20] Akmatov MK, Kretzschmar M, Kramer A, Mikolajczyk RT. Timeliness of vaccination and its effects on fraction of vaccinated population. Vaccine 2008;26(31):3805-11.

[21] Odhiambo FO, Laserson KF, Sewe M, Hamel MJ, Feikin DR, Adazu K et al. Profile: the KEMRI/CDC Health and Demographic Surveillance System--Western Kenya. Int J Epidemiol 2012;41(4):977-87.

[22] Amek N, Vounatsou P, Obonyo B, Hamel M, Odhiambo F, Slutsker L et al. Using health and demographic surveillance system (HDSS) data to analyze geographical distribution of socio-economic status; an experience from KEMRI/CDC HDSS. Acta Trop 2015;144:24-30.

[23] Republic of Kenya Ministry of Health. Divisions of Vaccinations and Immunization (DVI) Multi year plan 2011-2015.

[24] Gates Foundation's decade of vaccines. Lancet Infect Dis 2010;10(3):139,3099(10)70033-5.

[25] Alonso PL, de Quadros CA, Robert M, Lal AA. Decade of Vaccines. Editorial. Vaccine 2013;31 Suppl 2:B3-4.

[26] Berkley S, Chan M, Elias C, Fauci A, Lake A, Phumaphi J. Decade of Vaccines. Foreword. Vaccine 2013;31 Suppl 2:B1-2.

[27] Calhoun LM, van Eijk AM, Lindblade KA, Odhiambo FO, Wilson ML, Winterbauer E et al. Determinants and coverage of vaccination in children in Western kenya from a 2003 cross-sectional survey. Am J Trop Med Hyg 2014;90(2):234-41.

[28] Kawakatsu Y, Honda S. Individual-, family- and community-level determinants of full vaccination coverage among children aged 12-23 months in western Kenya. Vaccine 2012;30(52):7588-93.

[29] Babirye JN, Engebretsen IM, Makumbi F, Fadnes LT, Wamani H, Tylleskar T et al. Timeliness of childhood vaccinations in Kampala Uganda: a community-based cross-sectional study. PLoS One 2012;7(4):e35432.

[30] Laryea DO, Abbeyquaye Parbie E, Frimpong E. Timeliness of childhood vaccine uptake among children attending a tertiary health service facility-based immunisation clinic in Ghana. BMC Public Health 2014;14:90,2458-14-90.

[31] Le Polain de Waroux O, Schellenberg JR, Manzi F, Mrisho M, Shirima K, Mshinda H et al. Timeliness and completeness of vaccination and risk factors for low and late vaccine uptake in young children living in rural southern Tanzania. Int Health 2013;5(2):139-47.

[32] Vasudevan L, Labrique AB, Mehra S, Wu L, Levine O, Feikin D et al. Maternal determinants of timely vaccination coverage among infants in rural Bangladesh. Vaccine 2014.

[33] Ndiritu M, Cowgill KD, Ismail A, Chiphatsi S, Kamau T, Fegan G et al. Immunization coverage and risk factors for failure to immunize within the Expanded Programme on Immunization in Kenya after introduction of new Haemophilus influenzae type b and hepatitis b virus antigens. BMC Public Health 2006;6:132.

[34] Fiks AG, Alessandrini EA, Luberti AA, Ostapenko S, Zhang X, Silber JH. Identifying factors predicting immunization delay for children followed in an urban primary care network using an electronic health record. Pediatrics 2006;118(6):e1680-6.

[35] Griffin MR, Daugherty J, Reed GW, Standaert SM, Hutchins SS, Hutcheson RH et al. Immunization coverage among infants enrolled in the Tennessee Medicaid program. Arch Pediatr Adolesc Med 1995;149(5):559-64.

[36] Smith PJ, Humiston SG, Parnell T, Vannice KS, Salmon DA. The association between intentional delay of vaccine administration and timely childhood vaccination coverage. Public Health Rep 2010;125(4):534-41.

[37] Williams IT, Milton JD, Farrell JB, Graham NM. Interaction of socioeconomic status and provider practices as predictors of immunization coverage in Virginia children. Pediatrics 1995;96(3 Pt 1):439-46.

[38] Luman ET, Barker LE, Shaw KM, McCauley MM, Buehler JW, Pickering LK. Timeliness of childhood vaccinations in the United States: days undervaccinated and number of vaccines delayed. JAMA 2005;293(10):1204-11.

[39] Moss WJ, Griffin DE. Measles. Lancet 2012;379(9811):153-64.

[40] Gay NJ. The theory of measles elimination: implications for the design of elimination strategies. J Infect Dis 2004;189 Suppl 1:S27-35.

[41] Sheikh SS, Ali SA. Predictors of Vaccination Card Retention in Children 12-59 months old in Karachi, Pakistan. Oman Med J 2014;29(3):190-3.

[42] Ministry of Public Health and Sanitation. Ministry of Public Health and Sanitation Strategic Plan 2008-2012. 2008.

[43] Olusanya BO. Pattern and determinants of BCG immunisation delays in a sub-Saharan African community. Health Res Policy Syst 2010;8:1,4505-8-1.

[44] Fadnes LT, Jackson D, Engebretsen IM, Zembe W, Sanders D, Sommerfelt H et al. Vaccination coverage and timeliness in three South African areas: a prospective study. BMC Public Health 2011;11:404.

[45] Sadoh AE, Eregie CO. Timeliness and completion rate of immunization among Nigerian children attending a clinic-based immunization service. J Health Popul Nutr 2009;27(3):391-5.

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

[47] Brown DW, Burton A, Gacic-Dobo M, Karimov RI, Vandelaer J, Okwo-Bele JM. A mid-term assessment of progress towards the immunization coverage goal of the Global Immunization Vision and Strategy (GIVS). BMC Public Health 2011;11:806,2458-11-806.

Table 1

Table 1. Characteristics of children 12-23 months old with maternal child health booklet (n=1681) and verbal report (n=689)

Characteristic	MCH booklet %	Verbal Report %
Maternal age (years)		
15-24	46.2	50.2
25-29	27.3	25.2
≥ 30	26.5	24.6
Maternal education (years)		
0-8	54.8	55.5
≥ 9	45.2	44.5
Maternal English reading ability		
Easily	55.4	54.1
With difficulty	36.2	38.8
Not at all	8.3	7.1
Marital status		
Monogamous Married/Cohabiting	73.6	68.6
Single/Divorced/Widowed	15.3	19.7
Polygamous Married/ Cohabiting	11.1	11.7
Children < 5 years old in house		
≤ 1	40.3	49.6
> 1	59.7	50.3
Household size (no. of people)		
≤ 4	52.5	57.6
> 4	47.5	42.4
Socioeconomic status[1]		
Bottom 40%	40.0	38.1
Upper 60%	60.0	61.9
Mother's mobile phone ownership		
Owns Phone	54.3	57.8
Has Access/None	45.7	42.2
Distance to clinic (km)		
≤ 2	42.9	36.7
> 2	57.1	63.3
Child's age (months)		
12-18	49.1	40.9
>18-23	50.9	59.1
Child's sex		
Female	47.7	52.8
Male	52.3	47.2

Abbreviations: MCH, maternal and child health

[1]Socioeconomic status derived from multiple correspondence analysis of household possessions

Table 2. Vaccination coverage and delay in children ages 12-23 months old

Vaccine	Recommended Age	Coverage %	When delay starts (days)	Delayed[1] %	Median days delay (IQR) [2]
BCG	Birth (0 d)	98.8	> 28	31.5	23 (10-52)
Polio1	6 weeks (42 d)	99.4	> 70	10.5	21 (6-52)
Polio2	10 weeks (70 d)	97.4	> 98	16.5	23 (8-60)
Polio3	14 weeks (98 d	93.0	> 126	24.2	21 (9-68)
Pentavalent1	6 weeks (42 d)	99.5	> 70	10.2	18 (5-51)
Pentavalent2	10 weeks (70 d)	97.8	> 98	16.1	22 (8-60)
Pentavalent3	14 weeks (98 d)	94.4	> 126	23.8	21 (9-65)
Measles	9 months (275 d)	83.0	> 303	29.0	26 (9-66)
FIC		79.7		54.3	

Abbreviations: d, days; FIC= Fully immunized child and includes BCG, polio1-3, pentavalent1-3, measles vaccines

[1] For individual vaccines, delayed is receiving vaccine greater than 4 weeks from the scheduled date. For fully immunized child (FIC), delayed is receiving all eight vaccines but at least one of the vaccines was received with delay

[2] Days delayed begin counting four weeks after the age-appropriate scheduled date

Table 3

Table 3. Bivariate and multivariate analyses for predictors of non-immunization by vaccine and for fully immunized children (FIC).

	Pentavalent3 Not Received		Measles Not Received		FIC Not Achieved[1]	
Mother's age (yrs)	Crude RR(CI)	MV RR (CI)	Crude RR (CI)	MV RR (CI)	Crude RR (CI)	MV RR (CI)
15-24	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
25-29	1.58 (0.95-2.63)	1.64 (0.96-2.79)	1.08 (0.83-1.42)	1.06 (0.81-1.41)	1.07 (0.84-1.36)	1.05 (0.82-1.34)
≥30	**2.29 (1.43-3.66)**	1.60 (0.95-2.71)	**1.52 (1.19-1.93)**	**1.34 (1.04-1.75)**	**1.43 (1.15-1.78)**	1.21 (0.96-1.53)
Mother's education (yrs)						
0-8	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
≥ 9	**0.51 (0.33-0.79)**	0.77 (0.47-1.26)	**0.61 (0.49-0.77)**	**0.73 (0.57-0.93)**	**0.64 (0.52-0.78)**	**0.79 (0.63-0.99)**
Mother's English reading						
Easily	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	**1.61 (1.05-2.48)**	1.31 (0.82-2.11)	**1.48 (1.18-1.86)**	**1.25 (0.99-1.59)**	**1.45 (1.18-1.78)**	**1.27 (1.03-1.58)**
Not at all	**2.80 (1.61-4.89)**	1.52 (0.81-2.88)	**1.77 (1.26-2.47)**	**1.22 (0.84-1.77)**	**1.87 (1.26-2.50)**	**1.37 (1.00-1.87)**
Marital status						
Monogamous Married	*Ref.*		*Ref.*		*Ref.*	
Single/Divorced/Widowed	0.53 (0.26-1.08)		**0.70 (0.50-0.99)**		0.81 (0.60-1.08)	
Polygamous Married	1.17 (0.67-2.08)		1.06 (0.77-1.46)		1.06 (0.79-1.41)	
Children < 5 y.o. in house						
≤ 1	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
> 1	**1.59 (1.03-2.45)**	1.32 (0.82-2.12)	**1.38 (1.09-1.73)**	1.26 (0.98-1.61)	**1.34 (1.10-1.64)**	1.18 (0.94-1.46)
Household size						
≤ 4 people	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
> 4 people	**1.70 (1.14-2.55)**	1.30 (0.83-2.04)	**1.31 (1.06-1.62)**	1.08 (0.85-1.37)	**1.33 (1.10-1.61)**	1.14 (0.93-1.41)
Socioeconomic status[2]						
Bottom 40%	*Ref.*		*Ref.*		*Ref.*	
Upper 60%	0.79 (0.53-1.17)		0.96 (0.78-1.19)		0.94 (0.77-1.13)	
Mother's mobile phone						
Owns Phone	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Has Access/None	**2.00 (1.33-3.01)**	**1.77 (1.15-2.73)**	**1.35 (1.09-1.67)**	1.22 (0.98-1.52)	**1.37 (1.14-1.66)**	**1.25 (1.03-1.51)**
Distance to clinic (km)						
≤ 2	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
>2	1.01 (0.68-1.51)	0.89 (0.60-1.33)	1.12 (0.90-1.39)	1.08 (0.87-1.33)	1.04 (0.86-1.26)	0.99 (0.83-1.20)
Child's age (months)						
12-18	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
>18-23	0.85 (0.57-1.26)	0.82 (0.55-1.21)	**0.72 (0.58-0.89)**	**0.72 (0.58-0.89)**	**0.78 (0.65-0.95)**	**0.79 (0.66-0.96)**
Child's gender						
Female	*Ref.*		*Ref.*		*Ref.*	
Male	1.47 (0.98-2.20)		1.11 (0.90-1.37)		1.08 (0.89-1.31)	
Pentavalent1 receipt[3]						
On time	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*

Delayed	**6.32 (4.25-9.42)**	**5.20 (3.48-7.77)**	**1.65 (1.25-2.19)**	**1.48 (1.12-1.95)**	**2.08 (1.67-2.61)**	**1.88 (1.51-2.34)**

Abbreviations: CI, confidence interval; FIC, fully immunized child; MV, multi variable; pentavalent1, first dose of pentavalent vaccine; pentavalent3, third dose of pentavalent vaccine; RR, risk ratio

[1]Child that received BCG, Polio1-3, Penta1-3, and Measles. Reference group is children that did not receive all eight vaccines
[2] Socioeconomic status derived from multiple correspondence analysis of household possessions
[3] Delay defined as receiving pentavalent1 four weeks greater than the scheduled date.
Bolded risk ratios and confidence intervals indicate $p<0.05$

Table 4

Table 4. Bivariate and multivariate analyses for predictors of delayed immunization by vaccine

	Pentavalent1 delayed[1]		Pentavalent3 delayed[1]		Measles delayed[1]	
Mother's age (yrs)	Crude RR (CI)	MV RR (CI)	Crude RR (CI)	MV RR (CI)	Crude RR (CI)	MV RR (CI)
15-24	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
25-29	1.33 (0.93-1.90)	1.30 (0.90-1.87)	1.20 (0.96-1.49)	1.20 (0.96-1.49)	1.15 (0.94-1.41)	1.13 (0.92-1.39)
≥30	**1.70 (1.21-2.37)**	**1.57 (1.10-2.23)**	**1.46 (1.19-1.80)**	**1.44 (1.16-1.78)**	**1.38 (1.14-1.68)**	**1.33 (1.09-1.62)**
Mother's education (yrs)						
0-8	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
≥ 9	0.88 (0.66-1.17)	1.05 (0.77-1.44)	**0.73 (0.61-0.87)**	**0.78 (0.64-0.95)**	0.85 (0.72-1.00)	0.94 (0.78-1.12)
Mother's English reading						
Easily	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
With Difficulty	1.30 (0.96-1.76)	1.25 (0.91-1.73)	**1.34 (1.11-1.61)**	1.18 (0.98-1.43)	1.17 (0.97-1.39)	1.10 (0.91-1.32)
Not at all	**1.74 (1.12-2.72)**	1.49 (0.91-2.43)	**1.36 (1.00-1.86)**	1.00 (0.72-1.39)	**1.54 (1.19-1.99)**	1.25 (0.94-1.66)
Marital status						
Monogamous Married	*Ref.*		*Ref.*		*Ref.*	
Single/Divorced/Widowed	0.74 (0.46-1.17)		0.85 (0.66-1.11)		0.87 (0.68-1.12)	
Polygamous Married	**1.49 (1.02-2.17)**		1.15 (0.89-1.50)		1.18 (0.93-1.50)	
Children < 5 y.o. in house						
≤ 1	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
> 1	**1.42 (1.05-1.93)**	1.30 (0.93-1.80)	**1.49 (1.23-1.80)**	**1.43 (1.16-1.75)**	**1.20 (1.01-1.42)**	1.12 (0.93-1.35)
Household size						
≤ 4 people	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
> 4 people	**1.35 (1.01-1.80)**	**1.10 (0.80-1.51)**	**1.27 (1.06-1.51)**	1.01 (0.83-1.22)	**1.23 (1.04-1.45)**	1.10 (0.92-1.33)
Socioeconomic status[2]						
Bottom 40%	*Ref.*		*Ref.*		*Ref.*	
Upper 60%	0.91 (0.69-1.22)		0.94 (0.78-1.12)		1.06 (0.89-1.26)	
Mother's mobile phone						
Owns Phone	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Has Access/None	1.23 (0.93-1.64)	1.20 (0.89-1.60)	**1.23 (1.03-1.46)**	1.18 (0.99-1.41)	1.16 (0.98-1.36)	1.11 (0.94-1.31)
Distance to clinic (km)						
≤ 2	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
>2	1.03 (0.78-1.38)	1.00 (0.75-1.33)	1.14 (0.95-1.37)	1.11 (0.93-1.33)	**1.27 (1.07-1.51)**	**1.26 (1.07-1.49)**
Child's age (months)						
12-18	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*	*Ref.*
>18-23	1.05 (0.79-1.40)	1.06 (0.80-1.41)	**1.32 (1.10-1.58)**	**1.35 (1.13-1.61)**	**1.35 (1.14-1.60)**	**1.36 (1.15-1.61)**
Child's gender						
Female	*Ref.*		*Ref.*		*Ref.*	
Male	1.07 (0.80-1.42)		0.91 (0.77-1.09)		0.92 (0.78-1.09)	

Abbreviations: CI, confidence interval; MV, multi variable; pentavalent1, first dose of pentavalent vaccine; pentavalent3, third dose of pentavalent vaccine; RR, risk ratio

[1] Delayed is vaccination received after four weeks of scheduled date. Reference group is children that received vaccine within four week of scheduled date
[2] Socioeconomic status derived from multiple correspondence analysis of household possessions

Bolded risk ratios and confidence intervals indicate $p<0.05$

Table 5. Days underimmunized in first 12 months of life

	All Vaccines[1]		BCG		Penta1		Penta2		Penta3		Measles	
	N (%)	Median (IQR)	N (%)	Median (IQR)	N (%)	Median (IQR)	N (%)	Median (IQR)	N (%)	Median (IQR)	N (%)	Median (IQR)
All children	1681	16 (0, 66)	1681	0 (0, 9)	1681	0 (0, 0)	1681	0 (0, 0)	1681	0 (0, 5)	1681	0 (0, 48)
Underimmunized children only[2]	1049 (62.4)	62 (21,115)	544 (32.3)	24 (11, 57)	179 (10.7)	20 (5, 59)	302 (18.0)	28 (8, 99)	472 (28.1)	40 (11,157)	690 (41.1)	62 (19, 62)
Total days possible underimmunization	337		337		295		267		239		62	

Abbreviations: IQR, interquartile range

[1] All vaccines include BCG, pentavalent1, pentavalent2, pentavalent3, and measles vaccines. Days underimmunized were not double counted.
[2] Underimmunized children had at least one vaccine delayed or not received

CAPTION: Underimmunized is the number of days a child was unvaccinated for after the age-appropriate scheduled date. Underimmunized days started to accumulate four weeks from the scheduled date

Table 6

Table 6. Bivariate and multivariate analyses for predictors of severe underimmunization

Characteristic	Crude RR (CI)	MV RR (CI)
Mother's age (years)		
15-24	*Ref.*	*Ref.*
25-29	1.36 (0.98-1.89)	1.32 (0.95-1.84)
≥ 30	**2.51 (1.90-3.32)**	**2.17 (1.62-2.91)**
Mother's education (years)		
0-8	*Ref.*	*Ref.*
≥ 9	**0.50 (0.38-0.65)**	**0.67 (0.50-0.90)**
Mother's English reading		
Easily	*Ref.*	*Ref.*
With Difficulty	**1.74 (1.33-2.27)**	**1.38 (1.05-1.82)**
Not at all	**2.99 (2.16-4.15)**	**1.66 (1.16-2.38)**
Marital status		
Monogamous Married	*Ref.*	
Single/Divorced/Widowed	0.78 (0.53-1.13)	
Polygamous Married	1.11 (0.77-1.59)	
Children < 5 years old in house		
≤ 1	*Ref.*	*Ref.*
> 1	**1.39 (1.08-1.80)**	1.20 (0.92-1.58)
Household size		
≤ 4 people	*Ref.*	*Ref*
> 4 people	**1.63 (1.28-2.08)**	1.21 (0.93-1.59)
Socioeconomic status[2]		
Bottom 40%	*Ref.*	
Upper 60%	**0.75 (0.59-0.96)**	
Mother's mobile phone		
Owns Phone	*Ref.*	*Ref.*
Has Access/None	**1.69 (1.32-2.16)**	**1.51 (1.19-1.94)**
Distance to clinic (km)		
≤ 2	*Ref.*	*Ref.*
> 2	1.13 (0.88-1.44)	1.09 (0.86-1.38)
Child's age (months)		
12-18	*Ref.*	*Ref.*
>18-23	1.07 (0.84-1.36)	1.13 (0.90-1.42)
Child's gender		
Female	*Ref.*	
Male	1.05 (0.82-1.33)	

Abbreviation: CI, confidence interval; MV, multi variable; RR, risk ratio

[1] Socioeconomic status derived from multiple correspondence analysis of household possessions

CAPTION: Severely underimmunized children had greater than 90 days underimmunized and were delayed for three of five vaccines (BCG, pentavalent1, pentavalent2, pentavalent3, measles). Comparison group was all other children.