Timely completion of childhood vaccination and its predictors in Burkina Faso

Jean-Louis Koulidiati[1], Rémi Kaboré[2], Eric I Nebié[3;4], Annick Sidibé[5], Julia Lohmann[1,6], Stephan Brenner[1], Hermann Badolo[7], Saidou Hamadou[8], Nobila Ouédraogo[9], Manuela De Allegri[1]

[1] Heidelberg Institute of Global Health, University Hospital Heidelberg and Faculty of Medicine, Heidelberg, Germany
[2] Institut de Santé Publique d'Epidémiologie et du Développement (ISPED), Université de Bordeaux, France
[3] Centre de recherche en santé de Nouna (CRSN) ; Nouna Burkina Faso
[4] Swiss Tropical and Public Health Institute, University of Basel, Switzerland
[5] Ministère de la santé, Direction de la prévention par la vaccination, Ouagadougou, Burkina Faso
[6] Department of Global Health and Development, London School of Hygiene & Tropical Medicine, London, UK
[7] Centre MURAZ, Bobo-Dioulasso, Burkina Faso.
[8] The World Bank, Washington DC, USA
[9] German Cancer Research Center, Heidelberg, Germany

Abstract

Background: Despite important progress in global vaccination coverage, many countries are still facing preventable disease outbreaks. Timely vaccination is important in getting adequate protection against disease. In light of the paucity of relevant literature, this study investigated the timely completion of childhood routine immunization and identified factors associated with timely vaccination in Burkina Faso.

Methods: We extracted data on child vaccination and other child characteristics from a household survey conducted across 24 districts in 2017. We extracted data on health system characteristics from a parallel facility survey. We applied a Kaplan-Meier time-to-event analysis to estimate timely vaccination coverage defined as the proportion of children that received a given vaccine in the period between three days before and 28 days after the recommended age. We used a Cox proportional hazard model with mixed effects to identify factors associated with timely vaccination.

Results: In total, 3,138 children aged between 16 and 36 months who could present an immunization booklet were included in the study.The main finding is the existence of an important gap showing that timely vaccination coverage was lower than vaccination coverage. More specifically,this gap ranged from 16% for BCG to 43% for Penta 3. In addition, region and distance between the household and the nearest health facility were the main factors associated with timely full vaccination coverage and specifically for Penta3, MCV1 and MCV2.

Conclusions: This study highlights that timely vaccination coverage remains substantially lower than vaccination coverage. Timeliness of vaccination should therefore be considered as a metric to assess the status of immunization in a country. Geographical accessibility continues to represent a major barrier to timely vaccination, calling for specific interventions on both supply-side (e.g. outreach activities) and demand-side (e.g. vouchers or community-based interventions for vaccination) to counteract its negative effect.

Introduction

Vaccination is largely recognized as one of the most cost-effective interventions public health can rely on [1, 2]. Since 1974, vaccination coverage has increased significantly through the implementation of the World Health Organization (WHO) Expanded Program on Immunization (EPI) in many low-and-middle-income countries (LMICs) [3]. For instance, the global coverage of the first dose of measles containing vaccine (MCV1) increased from 73% to 86% between 1990 and 2018 in infants younger than 12 months, resulting in a substantial decline in global measles deaths [4, 5]. Similar to MCV1, coverage of the third dose of diphtheria and tetanus toxoids and pertussis-containing vaccine (DTP3) increased globally from 79% in 2007 to 85% in 2017 [6].

However, while important progress has been made at a global level, many sub-Saharan African (SSA) countries are still facing preventable disease outbreaks [7-9]. For instance, in Burkina Faso, the largest measles outbreak occurred in 2009 with 54,111 measles cases and 367 measles deaths reported [7]. More recently, the country experienced two measles outbreaks in 2018 [10] and 2020, [11] despite an apparent increase in measles vaccination coverage.

Timely vaccination is important in getting adequate protection against disease [12, 13]. Therefore, as timing is a key to effectiveness, timely vaccination coverage can be understood as a measure of effective vaccination coverage [14]. As some studies have showed, high vaccination coverage rates do not necessarily imply timely vaccination [15], and could even hide delays in vaccination timing, which carry important health consequences [16, 17]. Hence, there is a growing interest in measuring vaccination timeliness in LMICs. The need to determine timely vaccination coverage is crucial, as delayed immunization remains a strong risk factor for disease [15, 18, 19]. A recent systematic review on vaccination timeliness and delays in LMICs identified only 67 studies, including 29 studies in the WHO Africa region, having been conducted between 2007-2017 [18]. This review found that Bacille Calmette-Guérin vaccine (BCG), DTP, measles and polio vaccines were the most frequently investigated, whereas newer vaccines, such as rotavirus and pneumococcal conjugate vaccine (PCV), were less likely to be included in existing analyses. Furthermore, the review revealed that while many factors had been used to explain the timeliness of vaccination, some potentially important factors, such as geographical accessibility, have not yet been sufficiently explored.

Specific to Burkina Faso, we note a few studies having examined timely vaccination and its determinants. All of these studies, however, have a limited geographical focus and/or report on the old vaccination schedule, prior to the introduction of two new vaccines, rotavirus and PCV. For instance, in the North-West of Burkina Faso, Kagoné et al describing the timeliness of vaccination found that 80% of fully immunized children received all the vaccines in the recommended sequence [20]. Ouedraogo et al. in the same region in Burkina Faso, observed that timely vaccination coverage among U5YO children ranged from 68% for BCG to 33% for MCV1 [21]. Another study found that timely adherence to vaccination schedule of children between 12-23 months, was about 70% for BCG vaccination, but only 48% for Penta3 and 46% for measles. In addition, mothers' education, socio-economic status, season of birth, and area of residence were significantly associated with failure of timely adherence to the complete vaccination schedule [19].

To narrow existing knowledge gaps on vaccination timeliness, our study aimed first to investigate the timely completion of childhood routine immunization in Burkina Faso, including new vaccines such as rotavirus and PCV, and second to identify both demand-side and supply-side factors associated with timely vaccination.

METHODS

Study settings

Burkina Faso is a landlocked country located in West Africa. This low-income country [22] covers an area of 274,200 km2 with a population of 18.4 million inhabitants, of which about 18% are under five years old (U5YO). In 2016, the under-five mortality rate and the neonatal mortality rate were 85 and 26 per 1,000 live births respectively [23].

To reduce child mortality and morbidity, Burkina Faso has adopted the Expanded Program of Immunization since 1979 and has progressively increased the number of vaccines [24]. Between late 2013 and early 2014, the Ministry of Health (MoH) introduced two new vaccines (rotavirus vaccine and pneumococcal conjugate vaccine) and a second dose of measles vaccine in the national vaccination schedule, which recommends as follows in Table 1.

(Insert Table 1)

Study design and data sources

Our analysis relied on two cross-sectional data sources, a household survey and facility survey conducted in 2017 as part of a larger study aimed at evaluating the impact of the performance-based financing (PBF) program implemented in the country between 2014 and 2018. Both the household and the facility survey were conducted in 24 districts distributed across six out of 13 regions of the country. We used data independently of the PBF intervention and with the sole intention of investigating levels and factors associated with timely vaccination; we did not aim to draw any link to the PBF program.

Study population and data collection

Details of sampling have been described elsewhere [25]. In brief, the facility survey was carried out in a total of 537 primary level health facilities distributed across the 24 districts included in the PBF impact evaluation, as either intervention or control. The household survey was carried out in the catchment area of the 537 abovementioned facilities. Households were selected using a two-stage sampling technique. First, one village was randomly selected within the catchment area of each selected facility. Second, 15 households were randomly selected from a listing of all households with at least one woman with a history of pregnancy up to 24 months prior to the interview date. Within households, we recorded and aimed at interviewing all household members.

For this study specifically, our study sample is based on those children, not on the woman who served as entry point into the household. In total, 7,898 households were included in the survey. Out of a total of 14,228 U5YO children surveyed, our study used data from the 3,138 children aged between 16 and 36 months who could present an immunization booklet (verified by the research assistant). Figure 1 illustrates the steps followed to identify the sample for our analysis. We set the lower-bound at 16 months to identify the earliest timepoint by which full vaccination coverage should be expected (i.e. all recommended vaccinations are to be completed by 15 months of age according to the national vaccination schedule). We set the upper-bound at 36 months to account for the fact that two new vaccines and the second dose of measles were introduced between the end of 2013 and early 2014 respectively. Since the survey took place between April and June 2017, we defined the upper-bound for full vaccination coverage at 36 months of age (i.e. all children born between June 2014 and June 2017, before the changes in the national vaccination schedule). We used this age span to capture children likely to have received all relevant vaccines in a timely manner as described by the national vaccination schedule. In line with many previous studies [19, 26], we restricted the sample to children who could present an immunization booklet, in order to limit bias from parental recall.

The household survey questionnaire collected information on household socio-demographic and economic profiles as well as on the health status and the health service utilization patterns of the single household members. Specific to our research question, information on a child's vaccination coverage and timing was extracted from their immunization booklet. The facility survey included both an infrastructure assessment tool and a provider survey, so that we had access to a broad range of information, such as service volume and staff knowledge on the vaccination schedule.

Outcomes and their measurement

Table 2 reports on all the variables used for our analysis.

Outcome variables

Our primary outcome variable (1) was defined as timely full vaccination coverage, i.e. we assessed whether a child had received all vaccinations within the prescribed time period established by national guidelines [27]. To determine timely vaccination coverage, we used the birthdate and the date of vaccination based on the child immunization booklets. Hence, we defined timely full vaccination coverage as the proportion of children that received all doses prescribed in the national vaccination schedule in the period between three days before and 28 days after the recommended age [19, 26]. Those who received vaccinations too early or too late were considered as untimely vaccinated. In the absence of a clear indication of non-timely vaccination, we relied on this threshold based on previous studies in Burkina Faso [19].

Based on the same definition of timeliness, our secondary outcome variables were: 2) timely BCG vaccination coverage; (3) timely Penta3 vaccination coverage; (4) timely MCV1; and (5) timely MCV2 vaccination coverage. These vaccines allowed the assessment of the immunization program's performance [18]. The third dose of pentavalent coverage is very often used as the main performance indicator in immunization programs [28], since it reflects an immunization system's ability to revaccinate a child on multiple occasions. As measles is a target of global efforts for vaccine-preventable disease eradication, measles vaccination coverage requires specific attention [29].

Explanatory variables

To determine the factors associated with the timeliness of vaccination, we selected explanatory variables based on the relevant literature (Table 2). Reflecting the use of two data sets, a household and a facility-based survey, we grouped explanatory variables into demand and supply-side factors as follows:

<u>Demand-side factors</u>

Variables related to children's characteristics such as age, sex, season of birth, household head's religion.

Variables related to mother or caretaker characteristics: age, literacy, and marital status.

Variables related to household characteristics: area of residence, region, distance between household and nearest primary care facility measured as a straight-line distance using GPS coordinates. Household socio-economic status (SES) measured as a wealth index computed on the basis of household assets using standard Multiple Correspondence Analysis [30]. This variable was grouped into tertiles (1st tertile (poorest), 2nd tertile (middle) and 3rd tertile (least poor).

<u>Supply-side factors</u>

These variables are related to the health system and reflect the score of health workers knowledge of the vaccination schedule and service volume (number of patients) in the month prior to the survey date. Although our study did not assess the impact of PBF in any way, we included a variable representing whether a child lived in a district with or without PBF.

(Insert Table 2)

Analytical Approach

To estimate cumulative vaccination coverage at any given age, we applied the Kaplan-Meier time-to-event analysis, a non-parametric method used to analyze time-to-event data while accounting for censoring [41]. In our analysis, the event of interest was the reception of the vaccine, while censoring occurred when the observation period (from birth to the date of the vaccination card inspection) ended with a child not yet having received the expected vaccination. Birthdate and the date of vaccination were used to calculate the age at vaccination in days (time axis for Kaplan-Meier and Cox model). For each interval, the survival function S(age) was defined as the ratio of children not vaccinated by the end of an age interval to children not vaccinated at the beginning of this interval. For each vaccine in the national vaccination schedule, we estimated the cumulative event function at time t, defined as the probability that the event had happened by time t. At any given age, the cumulative event function was measured as 1−S(age).

Finally, to determine the factors associated with timely vaccination, we applied a Cox regression model with mixed effects [42], taking into account the hierarchical structure of the data. The Schönfeld residuals method was used to test for proportional hazards. Only the variables associated with a p-value of 0.20 in univariate analysis, not correlated with each other and satisfying the model assumptions were considered. Accounting for clustering at the facility level, we incorporated random effects in the Cox model. We performed a distinct model for the primary outcome as well as for each of the secondary ones.

Statistical analysis was performed using SAS software, version 9.3 (SAS Institute Inc, Cary, NC, USA).

Ethical considerations

This study obtained clearance from both the Burkina Faso National Ethics Committee (protocol number 2013-7-06) and the Ethics Committee of the Medical Faculty at Heidelberg University (protocol number S-272/2013). Written informed consent was obtained from all study participants.

RESULTS

Sample characteristics

Table 3 describes the characteristics of 3,138 children included in the study. Fifty-five percent of these children were less than 24 months old, and half (50.7%) of them were female. Fifty-two percent were born during the dry season and most children (60%) lived less than 5 km from a health facility. The children had between one and three siblings in 49% of cases. Mothers' or caretakers' characteristics show that most of them were illiterate (80%), married or living with a partner (98%) and were between 25 and 35 years old (57%). Only 17% of mothers or caretakers were pregnant at the time of the interview.

(Insert table 3)

Coverage and timely vaccination coverage

Figure 2 presents vaccination coverage and timely vaccination coverage for each specific vaccines and full vaccination (i.e.´all the vaccines). We found that vaccination coverage was ranged between 98% for BCG and 52,8% for MCV2. Also, we observed high rates (> 80%) of vaccination coverage for all the vaccines except MCV2. However, the proportion of fully immunized children (i.e. children who received all the 17 doses of vaccines) was 36.6%.

As showed in Figure 2, the highest rates of timely vaccination coverage were observed with vaccines recommended at birth (with 81.7% and 81.3% for Polio 0 and BCG respectively) whereas the lowest rates were observed with vaccines given in late infancy (20.3% for MCV2). In addition, the timely full vaccination coverage was very low (5.8%)

Comparing coverage and timely vaccination coverage, we found important gaps. More specifically, this gap ranged from 16.3% for BCG to 43% for Penta3.

(Insert Figure 2)

Cumulative vaccination coverage based on Kaplan Meier method

Figure 3 presents Kaplan–Meier plots (inverse and cumulative) describing the time course of completion of BCG, Penta3, MCV1 and MCV2. All Kaplan Meier plots of all the vaccines of the national vaccination schedule can be found in a supplementary file (Figure S1). We observed that across vaccines the proportion of "untimely too early" was negligible. Most untimely cases were delayed vaccinations (Supplementary Figure S2). Approximately 25 % of children completed BCG vaccine at the recommended age (at birth) while it took 28 days for more than 80% of the children to complete it. For Penta 3 vaccine (recommended at 16 weeks or 112 days), 50% of children were vaccinated at 140 days (20 weeks) of age. For measles vaccine, around 60% of children received the MCV1 around 10 months, and around 30% of them received the second dose MCV2 around 16 months.

(Insert Figure 3)

Factors associated with timely vaccination

Full vaccination

Region and the distance between the household and the nearest health facility were factors associated with timely full vaccination coverage. Children living more than 5 km from the health facility (aHR 0.67 95% CI [0.46 - 0.99]) were less likely to be timely fully vaccinated than those living 5 km or less from the health facility. Also, children in "Centre-Nord" (aHR 0.71 95% CI [0.40 - 1.28]) "Nord" (aHR 0.50 95% CI [0.28 - 0.91]) and "Sud-Ouest" (aHR 0.46 95% CI [0.16 - 1.35]) regions were less likely to be timely fully vaccinated than children in other study regions.

BCG vaccination

BCG vaccination was more likely to be untimely in rural than in urban settings (aHR 1.44 95% CI [1.14 - 1.81]). Children living in the Boucle du Mouhoun region were less likely to receive the BCG vaccine untimely compared with the other study regions. In addition, facility service volume was positively associated with BCG timely vaccination (aHR 1.24 95% CI [1.10 - 1.40]).

Penta3 vaccination

The season of birth was associated with timely Penta3 vaccination. Children born in the rainy season (aHR 1.28 95% CI [1.15 - 1.43]) were more likely to be timely vaccinated than those born in the dry season. Also, the least poor children (aHR 95% CI [1.06 - 1.40]) were more likely to have correctly timed vaccination with Penta3 than the poorest children. Penta3 vaccination was more likely to be untimely when the distance between the household and the nearest health facility was more than 5 km (aHR 0.69 95% CI [0.60 - 0.80]). Children from "Centre-Est" (aHR 1.77 95% CI [1.37 - 2.29]), and "Centre-Ouest" (aHR 1.65 95% CI [1.33 - 2.05]) regions had significantly more chance of being timely vaccinated (Table 4).

Measles vaccination

Living far (≥5km) from the health facility were negatively associated with timely MCV 1 vaccination (aHR 0.87 95% CI [0.77 - 0.98]). Children living in the "Centre-Nord" (aHR 0.75 95% CI [0.62 - 0.91]) and "Nord" (aHR 0.75 95% CI[0.62 - 0.90]) regions were less likely to have correctly timed vaccination with MCV1 than in the Boucle du Mouhoun region. (Table 4).

With regards to MCV2 vaccination, the least poor children (aHR 1.38 95% CI [1.11 - 1.72]) were more likely to have correctly timed vaccination with Penta3 than the poorest children. MCV2 vaccination was more likely to be untimely for children living more than 5km from the health facility (aHR 0.68 95% CI [0.54 - 0.85]). Children living in the Boucle du Mouhoun region were more likely to receive the MCV2 vaccine timely compared with the other study regions (Table 4).

(Insert table 4)

DISCUSSION

Aiming to explore levels and factors associated with timely vaccination, our study makes an important contribution to the relevant literature. In most LMICs, including Burkina Faso, vaccination coverage is still the main immunization performance indicator [27]. This stands in contrast to the fact that the global health community increasingly recognizes the need to assess the performance of health interventions in relation to effective coverage, i.e. outcome-adjusted coverage, rather than crude coverage [14]. With specific reference to vaccination, timely vaccination coverage has been proposed as a useful proxy of effective coverage, given that measuring immune responses resulting from vaccination, i.e. the gold standard of vaccination effective coverage measures, appears unfeasible from a policy perspective.

The first finding of relevance is the existence of an important gap between vaccination coverage and timely vaccination coverage. For instance, this gap ranged from 16% for BCG to 43% for Penta 3. A previous study in rural Burkina Faso also observed this same large gap between 27% (BCG) and 45% (Penta 3) [19]. The overall rate of timely vaccination was low, increasing the risk of vaccine preventable diseases (VPDs) for children. The delays in vaccination detected in our study are aligned with what was detected in prior research in SSA countries including Burkina Faso [19,21,31,35]. Nonetheless, they are worrisome, since they could lead to the occurrence of outbreaks of VPDs, as a large proportion of children still received incomplete and untimely vaccination. Also in line with prior literature[31], we observed that this gap increased as children get older. Many reasons could explain this situation. First, in Burkina Faso, post-natal consultations (PNC), which occur in the 42 days after delivery, are an opportunity for health workers to check children's vaccination status and to administer timely the recommended vaccines within this early stage of life. After this PNC period, children are less frequently seen at health facilities. Thus, to reduce missed opportunities for vaccination, (MOV), health workers are expected to engage in outreach activities. These activities, however, are likely to be insufficient, due to logistics (transport, cold chain etc.) or staff challenges [27]. Therefore, in addition to outreach activities, combining other programs with vaccination could reduce MOV and further improve vaccination coverage and timeliness. For instance, in Ghana, a measles vaccination campaign was linked with a distribution of insecticide-treated bed nets for malaria prevention [43], leading to higher coverage rates for both interventions.

Another explanation might be that some mothers or caretakers simply do not recall their children's date of vaccination visit, especially when there is a long time between two recommended vaccinations (e.g., there are 5 months between Penta 3 and MCV1, and 6 months between the first and the second dose of measles vaccine). Therefore, there is a need to move towards a digital-based system for immunization [44] to help parents to recall the appointments. In developing countries like Burkina where mobile phones are common, automated messages or phone calls could be used to remind mothers or caretakers about their children's upcoming vaccination visits [45]. With the increasing complexity of the Burkina Faso immunization schedule due to the introduction of new vaccines, mobile-based approaches for immunization programs could remarkably improve not only vaccination coverage, but also timely vaccination coverage [46].

Looking more closely at the factors associated with timely vaccination, we find hardly any statistical association between exposures and outcomes of interest. This can be related to the limits of a quantitative approach and more specifically to the constrained number of explanatory variables at our disposal. Some potentially relevant variables such as the place of birth or birth order were not available in the dataset. Thus, additional qualitative research is needed to better explore factors such as vaccine hesitancy, which is not tangible but could affect timely vaccination. Nonetheless, we found that the further a child lived from a health facility, the less likely the child received timely full vaccination and specifically Penta3 and measles (MCV1 and MCV2) vaccines. These findings corroborate previous evidence from LMICs including Burkina Faso [19, 35, 47]. Although vaccination for children under five is free of charge in Burkina Faso, the opportunity cost (e.g., transportation, loss of income, etc.) might be high for people living far from the health facility. For instance, in rural Mozambique, the travel costs for people living 5km or further from the nearest health facility could represent 2.5 % of their annual income [47]. Hence, improving both the coverage and the timeliness of vaccination goes through the reduction of inequalities in terms of geographical access. Many strategies addressing both the demand and the supply-side barriers of geographical accessibility could be implemented. For instance, community-based interventions for vaccination, vouchers or integrated outreach services could be implemented to handle transport associated costs and means [48]. Therefore, in Burkina Faso, immunization programs could prioritize such strategies to tackle issues related to geographical accessibility.

We also identified important regional differences in timely vaccination coverage. This is not a surprising finding because important differences between regions (ranged from 96% to 57%) have previously been observed in relation to vaccination coverage [49]. These differences are likely to have exacerbated, as many regions of the country (including four out of the six study regions: Boucle du Mouhoun, Centre-Est regions and Centre-Nord and Nord regions which are the most affected) face instability, largely due to terrorist attacks starting in 2015. The instability in these regions is likely to continue to affect the provision of vaccination services to the populations. While some health facilities were simply closed, others reduced their activities (e.g. outreach activities for vaccination were not carried out) [49]. Therefore, vaccination coverage progressively decreased in these regions and could further affect timely vaccination coverage.

Moreover, we noticed that different factors explained variation in timely vaccination across different vaccines. While factors associated with timely vaccination for vaccines to be administered further away from birth, such Penta3, MCV1 and MCV2, largely reflected demand-side barriers to access (e.g., distance, season of birth, SES), factors associated with timely vaccination for the one vaccine to be administered at birth, i.e. BCG, largely reflected supply-side readiness (e.g., service volume). In addition, we postulate that restrictive vial opening policies could have affected more firmly timely BCG vaccination than other vaccines [50]. For instance, in Burkina Faso, the vial opening policy imposes that a BCG vaccine vial (which containing 20 doses) must be used within six hours of opening while a Pentavalent vaccine vial (containing 10 doses) must be used within 28 days of opening, if kept under specific conditions [49]. As such, in light also of the limited tolerance for vaccine waste at time of the study, delays in BCG vaccination might have resulted from health workers having to gather the maximum of children before opening a BCG vaccine vial. Recent policy development to increase tolerance for vaccine waste may result in better outcomes for BCG timely vaccination.

Methodological considerations

Our study has strengths and limitations that are noteworthy. Given the absence of a recent Demographic Health Survey (DHS) or Living Conditions Monitoring Survey (LCMS) as well as of a nation-wide Service Provision Assessment (SPA) or Service Availability and Readiness Assessment (SARA), the data we used (from the PBF impact program) represent the most recent comprehensive facility and household survey data, representative of at least one third of the country,available for analysis of child and maternal indicators in Burkina Faso.We do recognize that using a recent history of pregnancy as sampling criterion entails that our sample likely included younger and more actively reproductive households than the population at large. Nonetheless, this potential sampling limitation does not affect the validity or credibility of our findings, given our target population of choice, children below 36 months, are also to be found in this younger and more actively reproductive households. Another limitation is that only vaccination data based on child immunization booklets were considered. We excluded from the study population children who could not show their immunization booklets. We cannot exclude that these children could be at higher risk of not being vaccinated or not being timely vaccinated. As such, our estimates represent a conservative higher-bound estimate, suggesting that the true timely vaccination value may be even lower than the figure detected in our sample. Also, immunization booklets can be prone to data recording errors or incompleteness, which could affect the vaccination delays. As Burkina Faso does not yet have a functional Immunization Information system (IIS), which serves as an objective and accurate source of vaccination data [18], the immunization booklet remains a reliable, but not fully error-proof source. Moreover, the age restrictions we applied to our sample might have introduced an additional constraint, leading to an underestimation of the prevalence of immunization delays by excluding older children. Finally, we relied on an arbitrary threshold of three days before and 28 days after the recommended schedule, making it difficult to compare our findings with those emerging in settings with different vaccination schedules. Nonetheless, we trust that having been applied before, this threshold has good internal validity when considering the context of Burkina Faso.

Conclusion

Our study has highlighted how in Burkina Faso timely vaccination coverage remains lower than vaccination coverage, suggesting that reliance on crude vaccination coverage is likely to overestimate the real protection afforded by the population. It follows that timely vaccination should be adopted as a preferred performance indicator for immunization programs. Moreover, the gap observed between crude and timely vaccination coverage exposes the population to an increased infant morbidity and mortality risk from vaccine-preventable diseases. Given a context of widespread political and social insecurity and the new challenges imposed by the COVID-19 pandemic, this gap has probably widened even further than what was detected in 2017. Geographical accessibility continues to represent an important obstacle to timely vaccination, deserving of policy makers' attention. Intensified outreach campaigns, accompanied by advancements in the use of digital solutions and effective demand-side interventions, such as vouchers or community-based interventions for vaccination, can increase timely vaccination coverage.

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TABLES

Table 1. Burkina Faso national vaccination schedule

Contact	Vaccines	Recommended age
1	BCG; Polio0	At birth
2	Penta1, PCV1, Rota1, Polio1	8 weeks
3	Penta2, PCV2, Rota2, Polio2	12 weeks
4	Penta3, PCV3, Rota3, Polio 3; IPV	16 weeks
5	MCV1; Yellow Fever	9 months
6	MCV2, MenA	15 months

Two new vaccines (PCV and Rota) and the second dose of measles (MCV2) were introduced between the end of 2013 and early 2014 respectively. MenA and IPV vaccine was introduced in March 2017 and July 2018 respectively.

Table 2 Definition of variables and their measurements

Outcome variables		
Variables	**Definition**	**Measurement**
1- Full vaccination coverage	Completion of the total vaccination schedule (i.e. receiving 17 doses)[a]	0= Untimely 1= Timely received all the doses
2- BCG coverage	Vaccination of the BCG dose	0= Untimely 1= Timely received the BCG vaccine
3- Penta3 coverage	Vaccination of the third dose of pentavalent vaccine.	0= Untimely 1= Timely received the Penta3 vaccine
4- First dose of measles (MCV1) coverage	Vaccination of the first dose of measles	0= Untimely 1= Timely received the MCV1
5- Second dose of measles (MCV2) coverage	Vaccination of the second dose of measles	0= Untimely 1= Timely received the MCV2
Explanatory variables		
Variables	**Measurement**	**Literature sources (when relevant)**
1- Child sex	0=Female, 1=Male	Mbengue, et al. 2017 [31]; Mvula, et al.2016 [32]
2- Season of birth	0=Dry (November-May), 1=Rainy (June-October)	Schoeps et al. 2013[19]
3- Region	1=Boucle du Mouhoun ; 2= Centre-Est ; 3= Centre-Nord ; 4= Centre-Ouest ; 5= Nord ; 6= Sud-Ouest	Suárez-Castaneda et al. 2014 [33]
4- Area of residence	0=Urban, 1=Rural	Akmatov et al. 2008 [25]; Schoeps et al. 2013[19]
5- Distance between child's household and health facility	0= "≤5km", 1= "> 5km"	Calhoun et al. 2014 [34]; Le Polain de Waroux et al. 2013 [35].
6- Household socio-economic status	1= 1st tertile (Poorest); 2= 2nd tertile; 3= 3rd tertile (Least poor)	Mutua et al. 2016 [36]; Mbengue, et al. 2017 [31]
7- Age of caretaker/mother	< 25 years; [25-35]; >35 years	Babirye et al 2012 [37]; Fisker et al. 2014 [38]
8- Literacy of caretaker/mother	0=Illiterate; 1= Literate;	Fadnes et al. 2011 [15]; Schoeps et al 2013[19]
9- Marital status of caretaker/mother	0=Not married; 1=Married or living with a partner	Babirye et al 2012 [29]; Chiabi et al. 2017 [38]
10- Religion	1= Muslim 2=Catholic 3=Protestant 4= Animist/others	Chiabi et al. 2017[39]; Gram et al. 2014 [40]
11- Study group	0= Non PBF; 1= PBF[c]	
12- Score of health workers knowledge of the vaccination schedule[d]	0= <6 1= 6	
13- Number of patients at the month prior to the survey	0= <431[b] 1= ≥431	

[a]We excluded the Meningitidis A vaccine (MenA) and Inactivated Polio Vaccine (IPV) from the analysis because these vaccines were introduced in March 2017 (only two months before the data collection) and July 2028 (more than one year after the data collection) respectively..

[b]This cut-off represents the median of the number of patients the month prior to the study

[c] Performance-based financing program

[d] All the clinical staff available on the day of the interviewer team visit was interviewed to assess their knowledge of the national vaccination schedule. The interviewer asked them the recommended ages of the six visits needed to complete the national vaccination schedule. Each true answer represents 1 point, otherwise 0. Hence the maximum score was 6.

Table 3: Description of sample characteristics

Variables	Frequency (n)	Percentage (%)
Child age		
Less than 24 months	1751	56
More than 24 months	1387	44
Child sex		
Female	1591	51
Male	1547	49
Season of birth		
Dry	1657	53
Rainy	1481	47
Study group		
PBF	2466	79
Non PBF	672	21
Distance between child's household and health facility		
≤ 5 km	1858	59
> 5 km	1280	41
Mother/Caretaker age		
< 25 years	1249	40
25-35 years	1380	44
>35 *years*	509	16
Mother/caretaker literacy (ability to read and write in any language)		
Illiterate	2524	80
Literate	614	20
Mother/Caretaker marital status		
Not married	54	2
Married or living with a partner	3084	98
Socio-economic status		
Poorest (1st tertile)	1035	33
2nd tertile	1036	33
Least poor (3rd tertile)	1067	34
Score of health workers knowledge of the vaccination schedule (score max =6)		
< 6	2613	83
6	494	16
Missing	31	1
Number of patients		
≤ 431	1520	48
>431	1502	48
Missing	116	4
Area of residence		
Rural	2930	93.5
Urban	191	6
Missing	17	0.5
Religion		
Animist/Traditional	267	8
Catholic	606	19
Muslim	1966	63
Protestant	179	6
Missing	120	4
Region		
Sud-Ouest	633	20
Boucle du Mouhoun	379	12
Centre-Est	639	20
Centre-Nord	559	18
Centre-Ouest	752	24
Nord	176	6

Table 4 Factors associated with timely vaccination (Multivariable Cox analysis)

	All vaccines			BCG			Penta3			MCV1			MCV2		
	N= 2869	aHR[a]	95% (CI)[b]	N=2748	aHR	95% CI	N=2869	aHR	95% CI	N=2869	aHR	95% CI	N=2869	aHR	95% C
Child sex															
Female	1448	1		1378	1		1448	1		1448	1		1448	1	
Male	1421	0.96	[0.71- 1.31]	1370	1.03	[0.94 - 1.12]	1421	1.08	[0.97 -1.21]	1421	1.03	[0.93 - 1.14]	1421	1.08	[0.92 - 1.
Season of birth															
Dry	1519	1		1449	1		1519	1		1519	1		1519	1	
Rainy	1350	1.14	[0.84 - 1.56]	1299	1.07	[0.98 - 1.17]	1350	1.28	[1.15 - 1.43]	1350	0.91	[0.82 - 1.01]	1350	0.99	[0.84 - 1.
Mother/Caretaker age															
< 25	1099	1		1051	1		1099	1		1099	1		1099	1	
[25-35]	1300	1.45	[1.02 - 2.06]	1250	1.03	[0.93 - 1.13]	1300	1.04	[0.92 - 1.17]	1300	1.05	[0.93 -1.18]	1300	1.13	[0.94 - 1.
>35	470	1.14	[0.70 - 1.86]	447	1.11	[0.97 - 1.26]	470	1.03	[0.88 - 1.21]	470	1.08	[0.92 - 1.26]	470	1.02	[0.78 - 1.
Distance between child's household and health facility															
≤ 5 km	1692	1		1619	1		1692	1		1692	1		1692	1	
> 5 km	1177	0.67	[0.46 - 0.99]	1129	0.97	[0.87 - 1.09]	1177	0.69	[0.60 - 0.80]	1177	0.87	[0.77 - 0.98]	1177	0.68	[0.54 - 0.
Mother/caretaker literacy															
Illiterate	2303	1		2207	1		2303	1		2303	1		2303	1	
Literate	366	1.16	[0.78 -1.72]	541	1.09	[0.97 - 1.22]	566	1.09	[0.95 - 1.26]	566	0.96	[0.84 - 1.10]	566	1.09	[0.88 - 1.
Mother/Caretaker marital status															
Not married	47	1		47	1		47	1		47	1		47	1	
Married or living with a partner	2822	2.77	[0.38 -20.48]	2701	1.36	[0.96 - 1.93]	2822	1.15	[0.74 - 1.79]	2822	1.40	[0.90 - 2.19]	2822	1.86	[0.85 - 4.
Socio-economic status															
1st tertile (poorest)	925	1		882	1		925	1		925	1		925	1	
2nd tertile	941	1.22	[0.81 -1.83]	901	1.08	[0.97 - 1.20]	941	1.15	[1.00 - 1.33]	941	1.09	[0.96 - 1.24]	941	1.26	[1.02 - 1.
3rd tertile (least poor)	1003	1.30	[0.87 - 1.94]	965	1.03	[0.92 - 1.15]	1003	1.22	[1.06 - 1.40]	1003	1.07	[0.94 - 1.22]	1003	1.38	[1.11 - 1.
Area of residence															
Rural	2709	1		2596	1		2709	1		2709	1		2709	1	
Urban	160	1.56	[0.76 - 3.22]	152	1.44	[1.14 - 1.81]	160	0.92	[0.68 - 1.25]	160	1.12	[0.87 - 1.45]	160	1.16	[0.74 - 1.

Study group															
PBF	2252	1		2156	1		2252	1		2252	1		2252	1	
Non PBF	617	1.19	[0.76 - 1.86]	592	1.12	[0.98 - 1.28]	617	0.94	[0.79 - 1.11]	617	0.91	[0.78 - 1.05]	617	1.10	[0.85 - 1.4
Region															
Boucle du Mouhoun	588	1		570	1		588	1		588	1		588	1	
Centre-est	342	1.46	[0.77 - 2.76]	329	1.64	[1.33 - 2.02]	342	1.77	[1.37 - 2.29]	342	1.02	[0.82 - 1.28]	342	0.74	[0.50 - 1.
Centre-nord	563	0.71	[0.40 - 1.28]	534	1.51	[1.27 - 1.80]	563	1.17	[0.94 - 1.46]	563	0.75	[0.62 - 0.91]	563	0.47	[0.33 - 0.
Centre-ouest	526	1.19	[0.69 - 2.05]	499	1.64	[1.37 - 1.96]	526	1.65	[1.33 - 2.05]	526	1.02	[0.85 - 1.23]	526	0.70	[0.51 - 0.9
Nord	693	0.50	[0.28 - 0.91]	664	1.14	[0.96 - 1.36]	693	0.91	[0.72 - 1.13]	693	0.75	[0.62 - 0.90]	693	0.45	[0.32 - 0.
Sud-ouest	157	0.46	[0.16 - 1.35]	152	1.49	[1.15 -1.93]	157	1.15	[0.82 - 1.62]	157	0.74	[0.55 - 1.01]	157	0.51	[0.29 - 0.
Religion															
Muslim	1860	1		1778	1		1860	1		1860	1		1860	1	
Animist / traditional	252	1.12	[0.58 - 2.15]	243	1.20	[0.99 - 1.44]	252	1.18	[0.93 - 1.49]	252	0.94	[0.75 - 1.17]	252	0.78	[0.53 - 1.
Catholic	583	0.71	[0.45 - 1.12]	558	1.01	[0.89 - 1.14]	583	1.02	[0.87 - 1.19]	583	0.94	[0.81 - 1.09]	583	0.87	[0.68 - 1.
Protestant	174	1.24	[0.67 - 2.30]	169	0.92	[0.75 - 1.12]	174	1.06	[0.83 - 1.35]	174	1.06	[0.85 - 1.33]	174	1.14	[0.80 - 1.
Score of health workers knowledge of the vaccination schedule															
< 6	2401	1		2304	1		2401	1		2401	1		2401	1	
6	468	1.21	[0.75 - 1.97]	444	0.96	[0.83 - 1.12]	468	1.15	[0.95 - 1.39]	468	0.95	[0.81 - 1.12]	468	1.13	[0.85 - 1.
Number of patients															
≤ 431	1469	1		1409	1		1469	1		1469	1		1469	1	
>431	1400	0.85	[0.56 - 1.29]	1339	1.24	[1.10 - 1.40]	1400	0.93	[0.80 - 1.08]	1400	0.93	[0.81 - 1.06]	1400	0.92	[0.73 - 1.

[a]adjusted Hazard Ratio

[b]95% Confidence Interval

Figures

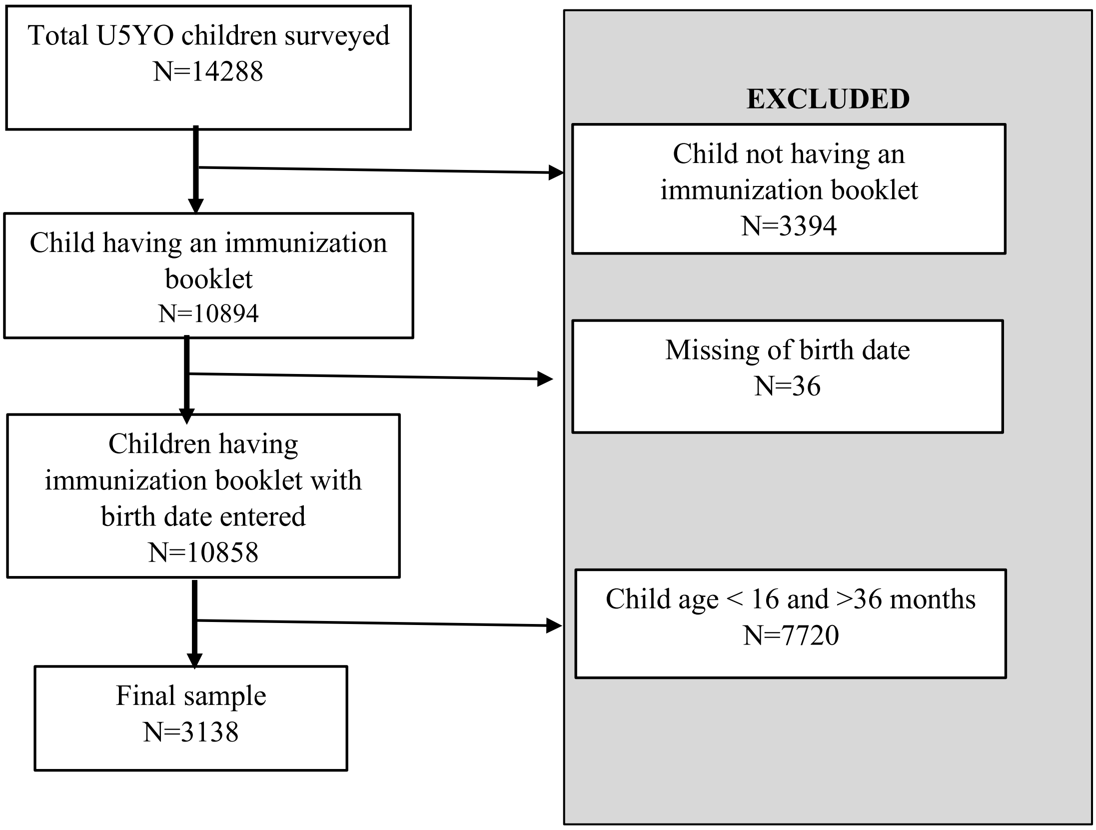


Figure 1: Flow of study population

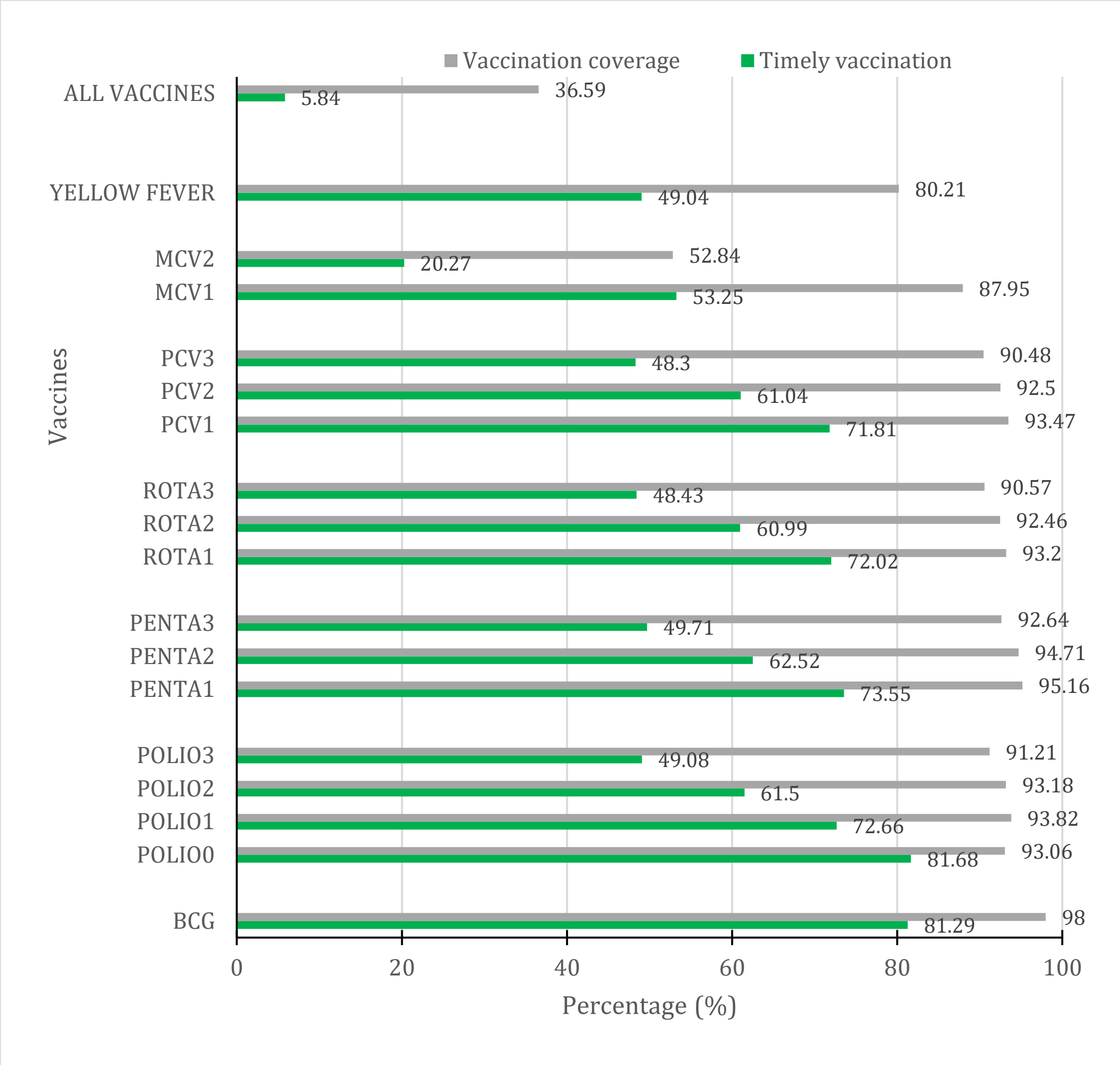


Figure 2: Vaccination coverage and timeliness of vaccination coverage for each vaccine

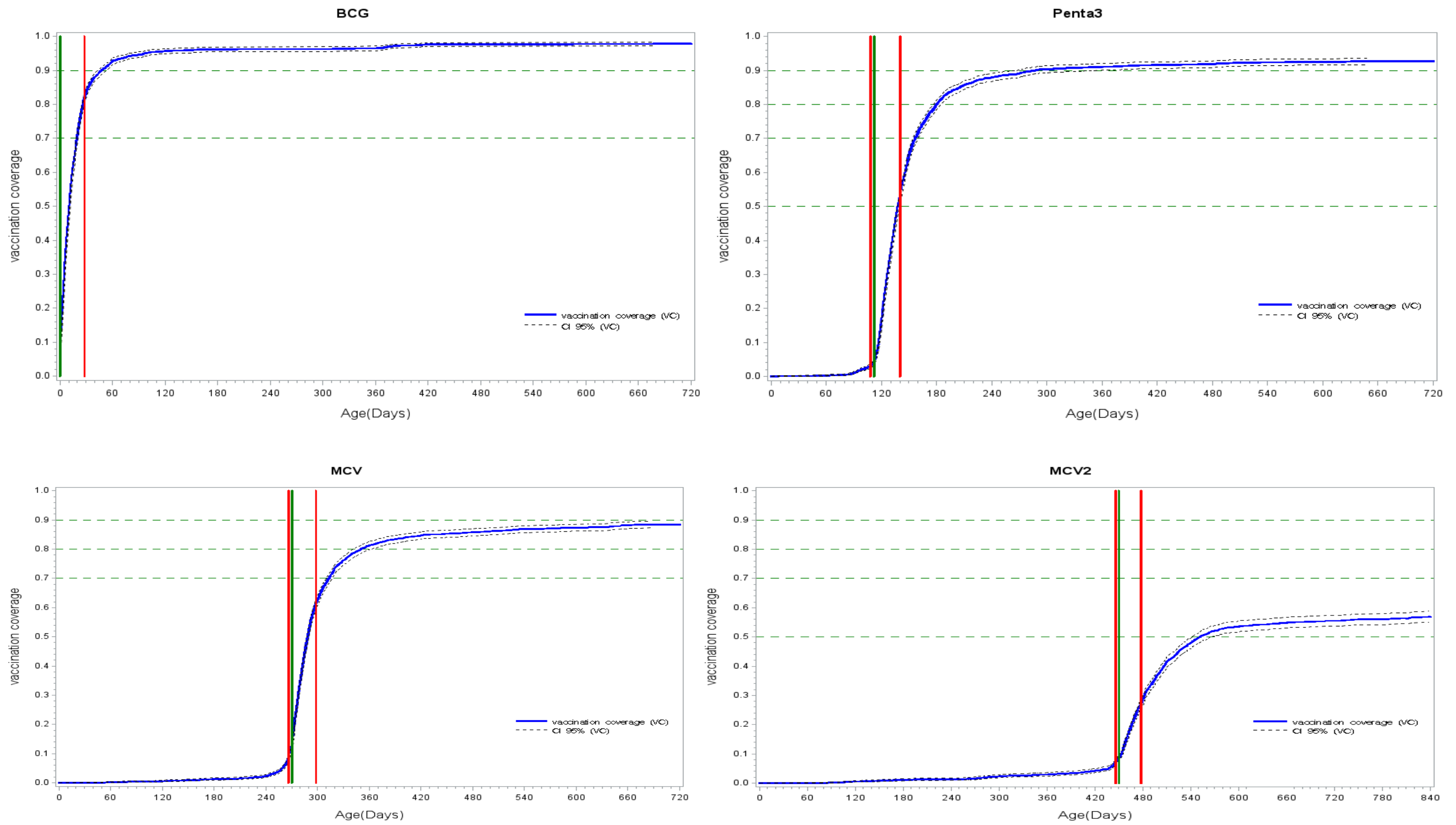
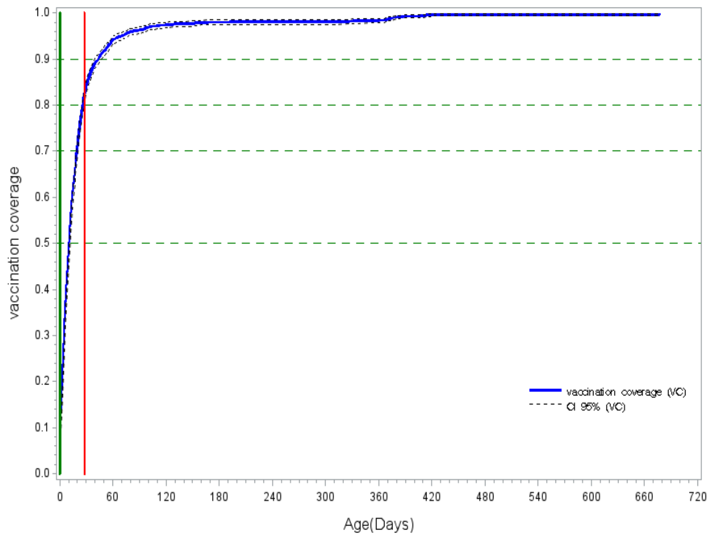


Figure 3: Cumulative coverage (1-Kaplan Meier) for BCG, Penta3 and Measles (1st and 2nd dose) vaccines.

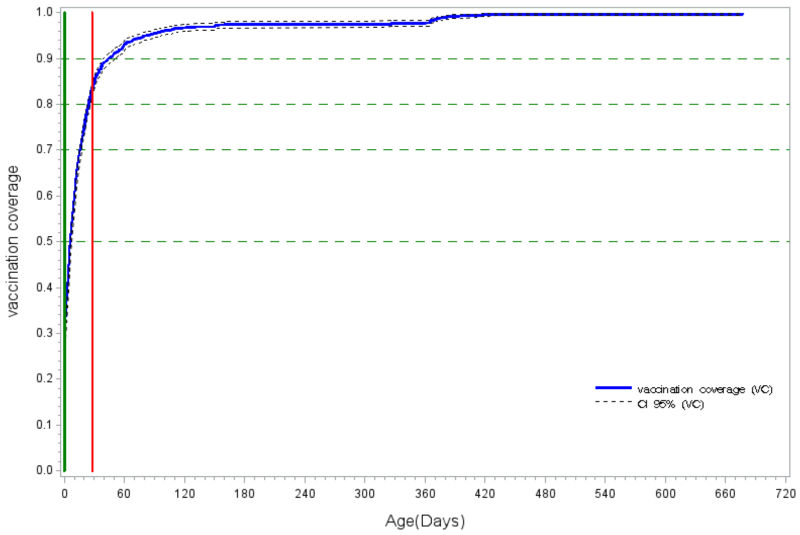
The vertical green line indicates the recommended age and the red lines indicate the outer ranges for the recommended age. The horizontal green dotted lines represent coverage at 50, 70, 80 and 90 %.

Supplementary files

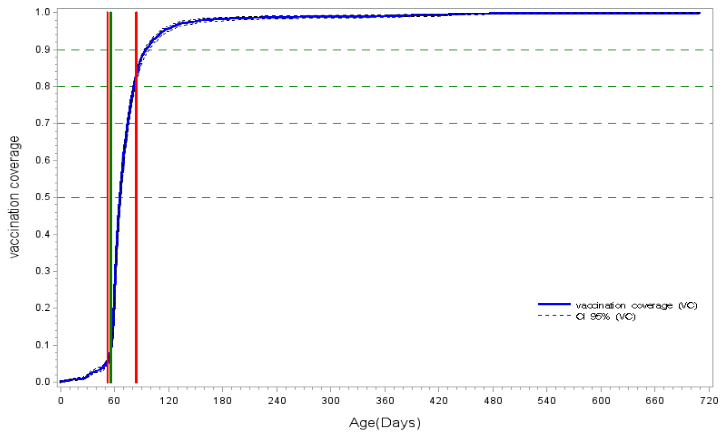
BCG



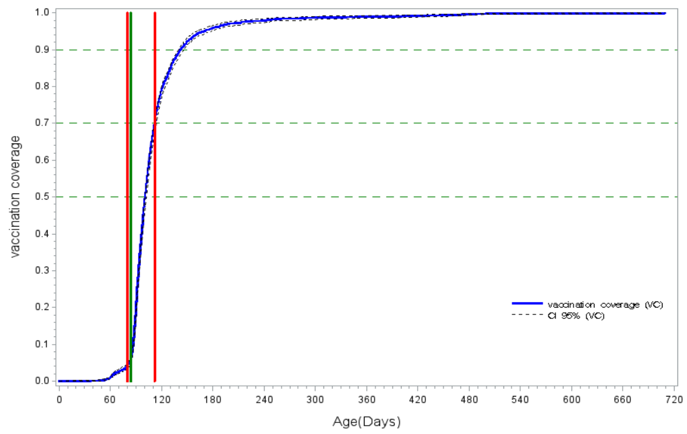
Polio0



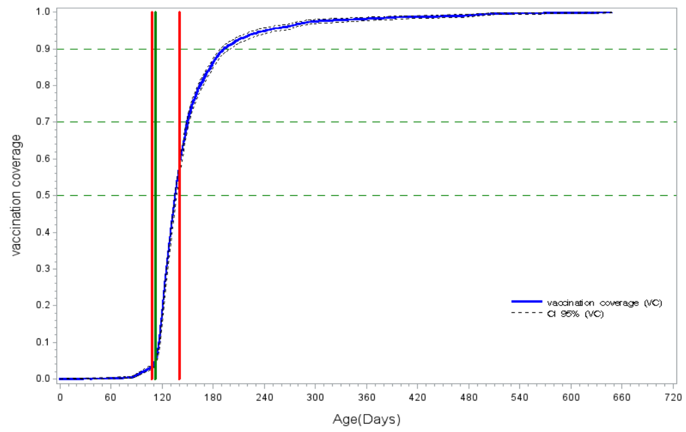
Polio1

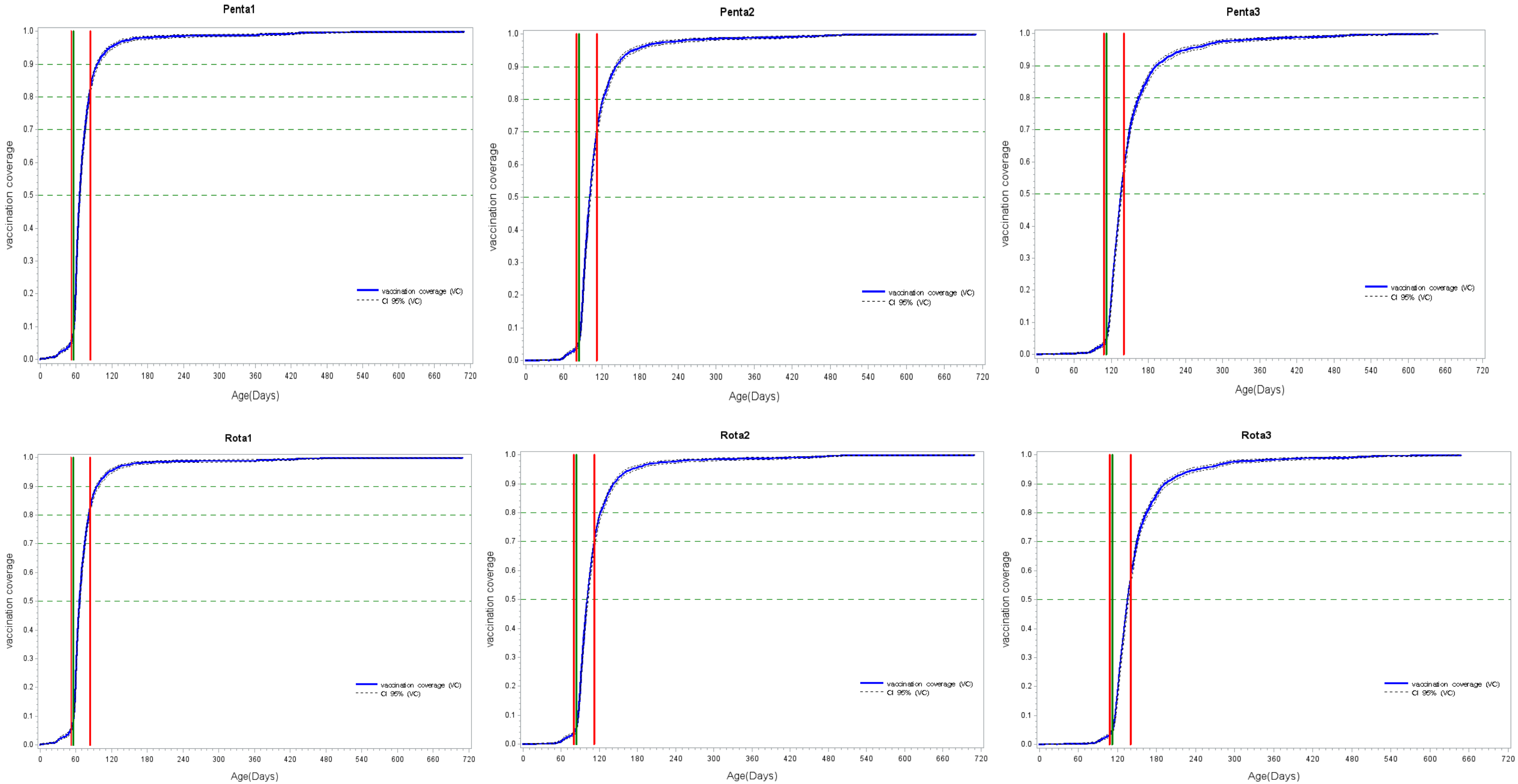


Polio2

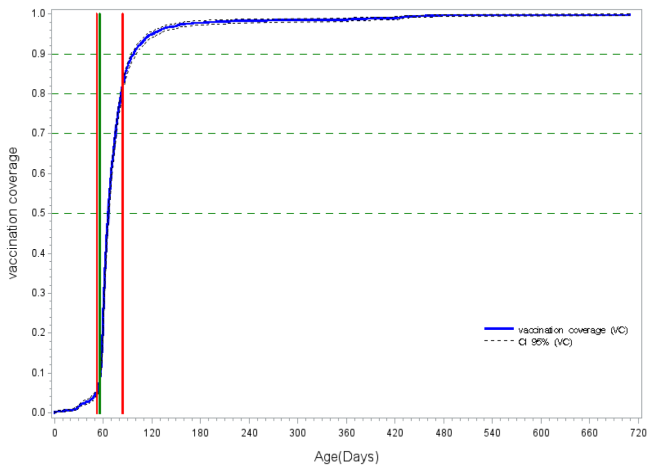


Polio3

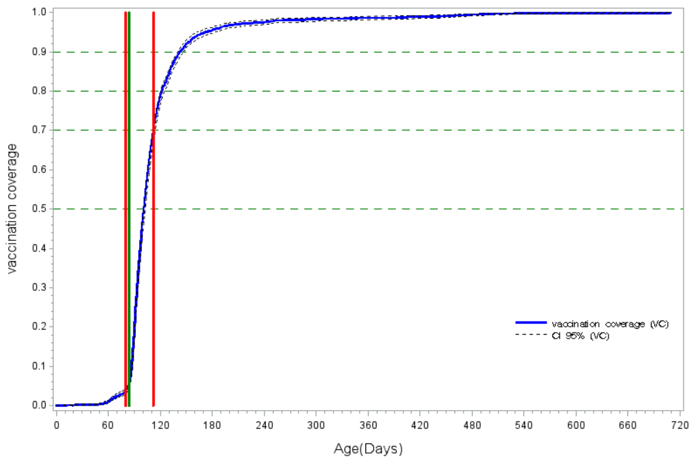



Penta1
Penta2
Penta3
Rota1
Rota2
Rota3
vaccination coverage
Age(Days)
vaccination coverage (VC)
CI 95% (VC)

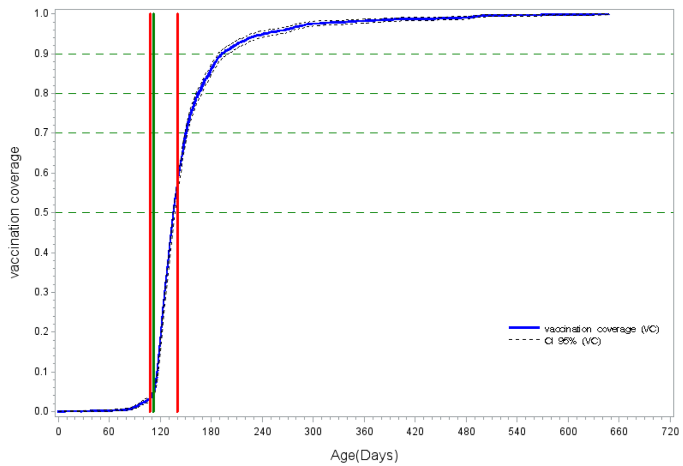
PCV1



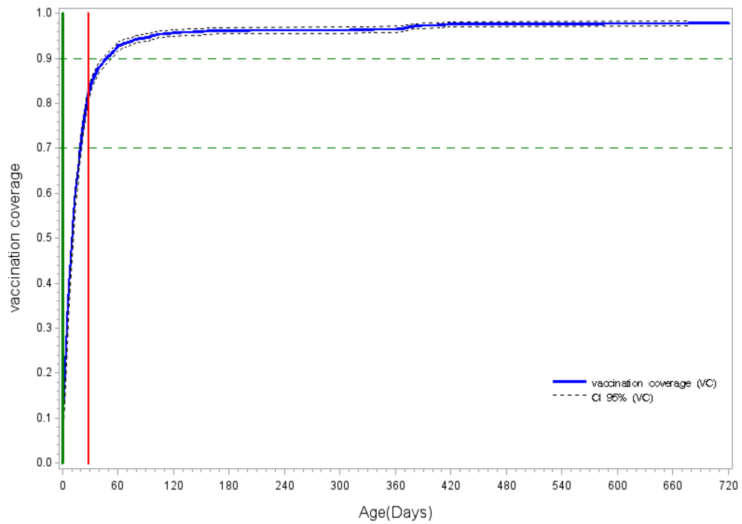
PCV2



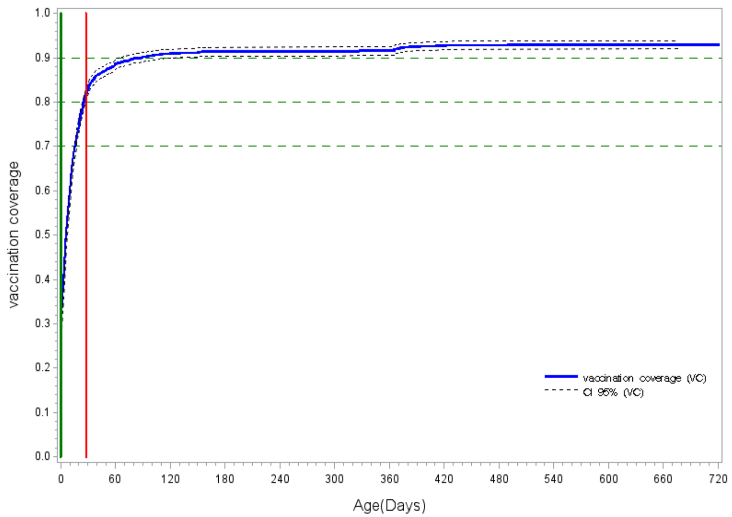
PVC3



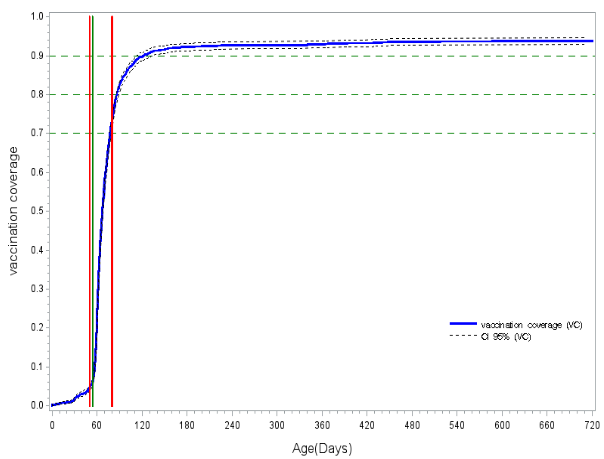
BCG

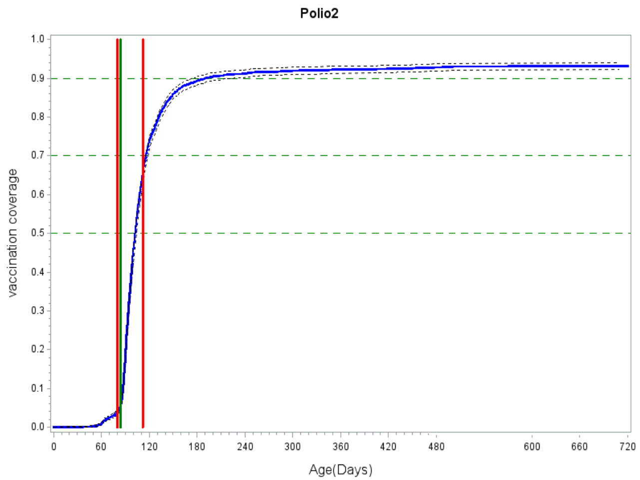


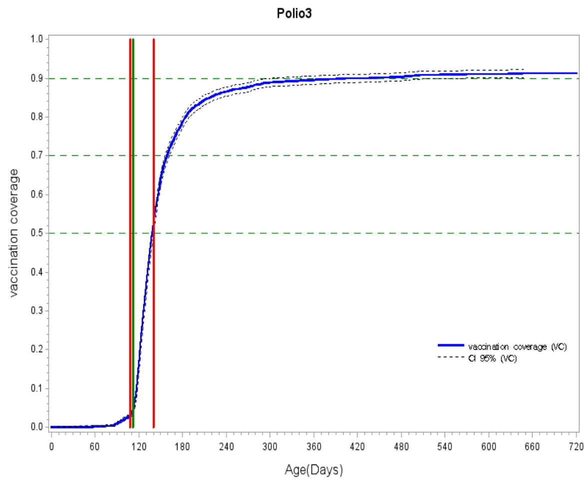
Polio0

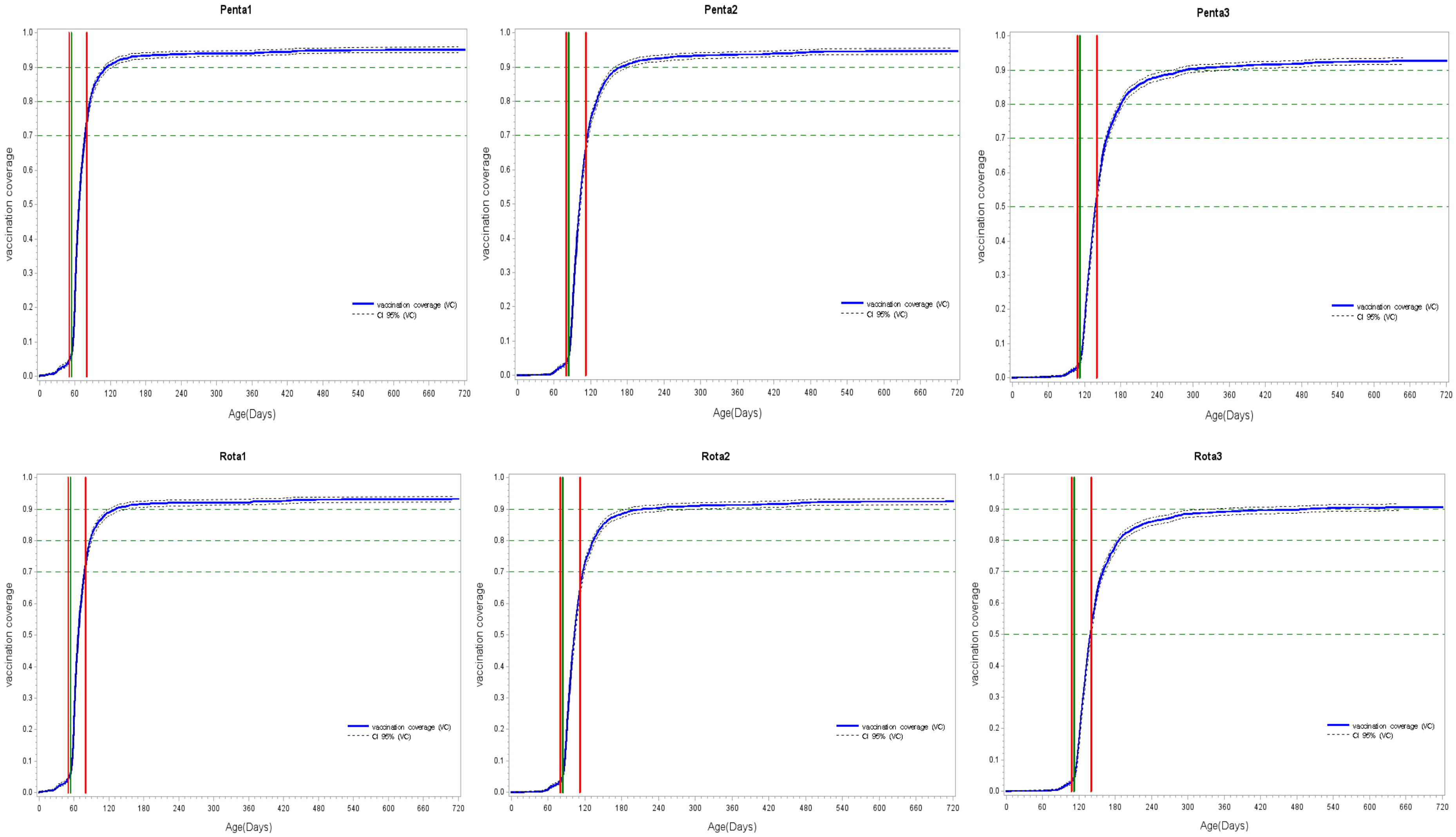


Polio1




Polio2
vaccination coverage
Age(Days)


Polio3
vaccination coverage
Age(Days)
vaccination coverage (VC)
CI 95% (VC)


Penta1
Penta2
Penta3
Rota1
Rota2
Rota3
vaccination coverage
Age(Days)
vaccination coverage (VC)
CI 95% (VC)

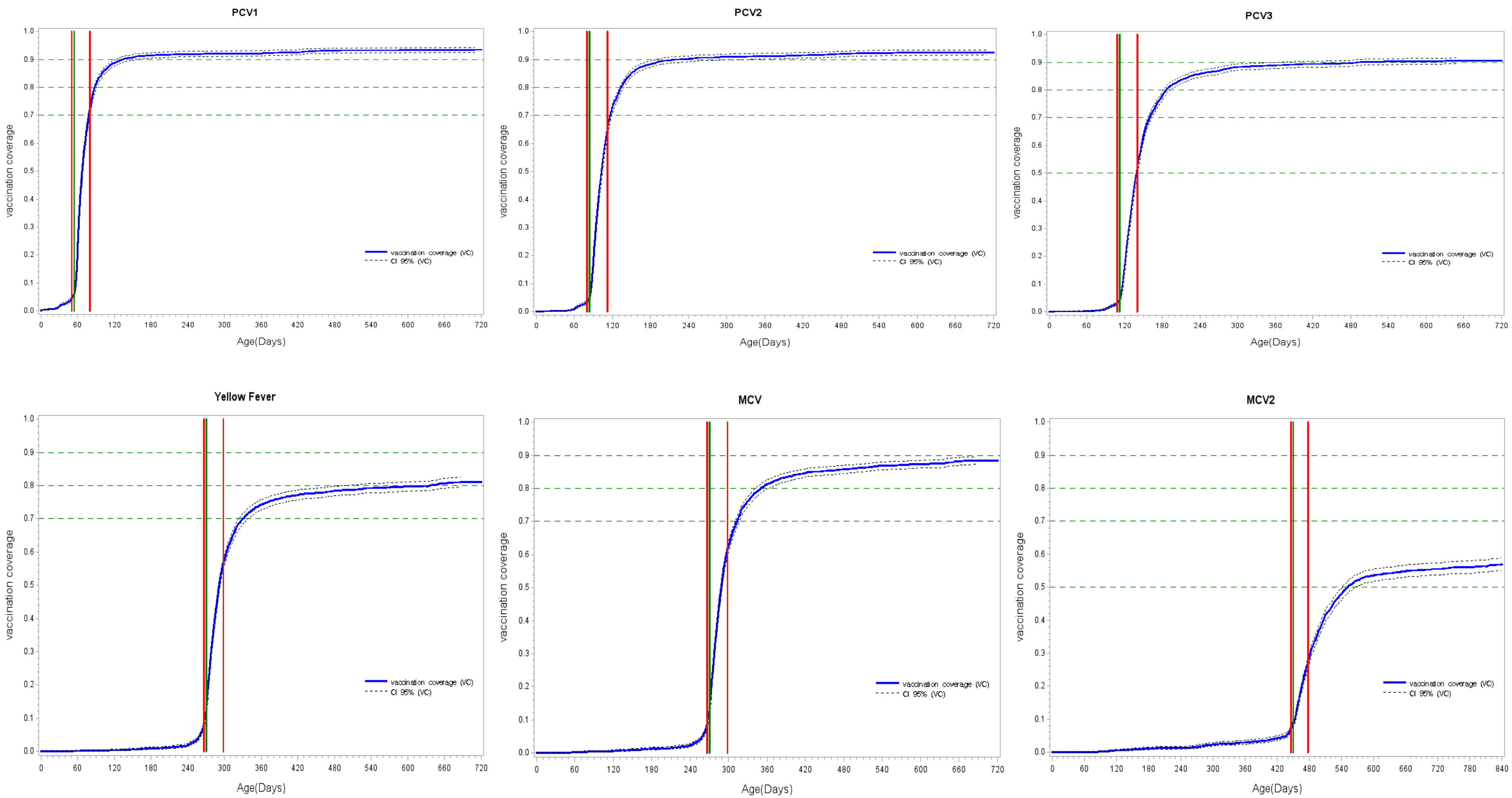


Figure S1: Cumulative coverage (1-Kaplan Meier) for each vaccine of the national vaccination schedule.

The vertical green line indicates the recommended age and red lines indicate the outer ranges for the recommended age. The horizontal green dotted lines represent coverage at 50, 70, 80 and 90 %.

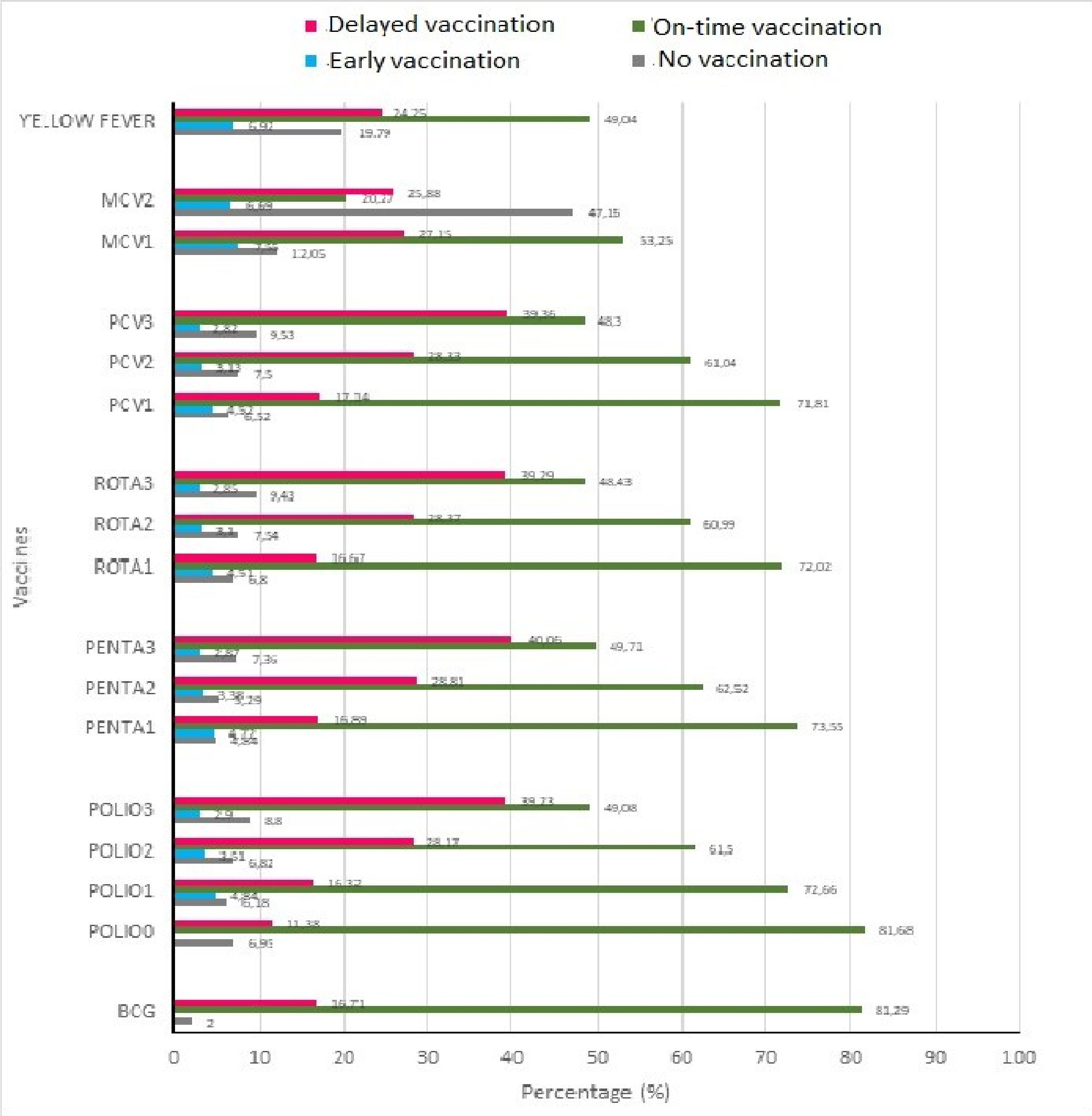


Figure S2: Timeliness of vaccination for specific vaccines among children