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Evaluation of invalid vaccine doses in 31 countries of the WHO African Region

Manas K. Akmatov[a,b,*], Elizabeth Kimani-Murage[c], Frank Pessler[b], Carlos A. Guzman[d], Gérard Krause[a,e], Lothar Kreienbrock[f], Rafael T. Mikolajczyk[a,e]

[a] Department of Epidemiology, Helmholtz Centre for Infection Research, Braunschweig, Germany
[b] TWINCORE Centre for Experimental and Clinical Infection Research, Hannover, Germany
[c] African Population and Health Research Center, Nairobi, Kenya
[d] Department of Vaccinology and Applied Microbiology, Helmholtz Centre for Infection Research, Braunschweig, Germany
[e] Hannover Medical School, Hannover, Germany
[f] Department of Biometry, Epidemiology and Information Processing, University for Veterinary Medicine, Hanover, Germany

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ABSTRACT

We examined (a) the fraction of and extent to which vaccinations were administered earlier than recommended (age-invalid) or with too short intervals between vaccine doses (interval-invalid) in countries of the World Health Organisation (WHO) African Region and (b) individual- and community-level factors associated with invalid vaccinations using multilevel techniques. Data from the Demographic and Health Surveys conducted in the last 10 years in 31 countries were used. Information about childhood vaccinations was based on vaccination records (n = 134,442). Invalid vaccinations (diphtheria, tetanus, pertussis [DTP1, DTP3] and measles-containing vaccine (MCV)) were defined using the WHO criteria. The median percentages of invalid DTP1, DTP3 and MCV vaccinations across all countries were 12.1% (interquartile range, 9.4–15.2%), 5.7% (5.0–7.6%), and 15.5% (10.0–18.1%), respectively. Of the invalid DTP1 vaccinations, 7.4% and 5.5% were administered at child's age of less than one and two weeks, respectively. In 12 countries, the proportion of invalid DTP3 vaccinations administered with an interval of less than two weeks before the preceding dose varied between 30% and 50%. In 13 countries, the proportion of MCV doses administered at child's age of less than six months varied between 20% and 45%. Community-level variables explained part of the variation in invalid vaccinations. Invalid vaccinations are common in African countries. Timing of childhood vaccinations should be improved to ensure an optimal protection against vaccine-preventable infections and to avoid unnecessary wastage in these economically deprived countries.

1. Introduction

Immunisation services in many African countries still face various problems; among other things there is a lack of trained staff to (correctly) administer vaccinations, and cold chain management is suboptimal [1]. Research showed that many children in African countries receive inappropriately timed vaccinations [2,3]. Most studies examining timeliness of vaccinations were dedicated to delayed vaccinations, i.e. vaccinations administered at older ages than recommended. The latter results in a longer time of susceptibility for infectious diseases [4], thus leaving children vulnerable to vaccine-preventable diseases. Other aspects of timely vaccine administration are (a) premature vaccinations, i.e. vaccinations administered earlier than recommended and (b) vaccinations administered with inappropriately short intervals between vaccine doses. Both may result in a suboptimal vaccine response. The World Health Organisation (WHO) classified those vaccinations as invalid [5]. Some countries (e.g. South Sudan) recommend to repeat them at the appropriate age [6].

The biological impact of invalid vaccinations is not well known. However, there is some indication that premature vaccinations may cause a suboptimal vaccine protection due to interference by maternal antibodies. Recently, the immature immune system of infants was proposed as another possible explanation of a suboptimal protection; for example, independent of maternal measles antibodies, specific humoral immunity was suboptimal in children

* Corresponding author at: TWINCORE Centre for Experimental and Clinical Infection Research, Feodor-Lynen-Str.7, 30625 Hannover, Germany.
Tel.: +49 0511220027 165.
E-mail address: manas.akmatov@twincore.de (M.K. Akmatov).

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vaccinated under six months of age compared to older children [7,8]. The timing of vaccine administration between subsequent vaccine doses also seems to play an important role in determining an optimal vaccine response. Jilg et al. [9] compared different immunisation schedules for hepatitis B vaccination and observed that administering a third dose after a longer interval would result in a better protection against infection. Patriarca et al. [10] also suggested to increase the intervals between oral polio vaccine doses to over 30 days to avoid potential interference with responses to subsequent vaccine doses.

The administrative validity of childhood vaccinations and its risk factors have only been evaluated in a few countries [11,12], mostly in the USA [13–17]. We found only a few studies in the African region which examined this issue [18–23], and none of them examined risk factors for invalid vaccinations. Kahn et al. [20] only showed rural–urban differences in valid vaccinations. A systematic evaluation of administrative validity of childhood vaccinations and its risk factors, including contextual factors and involving several African countries, has not yet been conducted. Thus, the aims of the present study were two-fold: using available data from the Demographic and Health Surveys (DHS) conducted in countries of the WHO African Region we examine (a) the fraction of and extent to which vaccinations were administered earlier than recommended or with too short intervals between vaccine doses and (b) individual- and community-level factors associated with invalid vaccinations.

2. Methods

2.1. Data and sampling

We used the data from the 31 DHS conducted in the last ten years (2003–2013). DHS represent population-based representative household surveys aiming to assess health-related indicators in low- and middle-income countries [24]. The selected DHS were collected at the country level and applied a multistage cluster design [25]. In brief, clusters were selected as primary sampling units in all country regions with the probability proportional to population size. Clusters were administratively defined areas used in the population census and representing more or less homogeneous geographic areas that share common demographic, social and economic characteristics. A number of households were selected randomly in each cluster. In each household, women of reproductive age (15–49 years) were invited to participate. All children below five years of age living in the household were included in the survey (n = 281,115 children). Data were collected during face-to-face interviews. Vaccination data were collected from vaccination cards if available (n = 134,442 children). For these children, detailed data including dates of vaccination of each vaccine dose were available. If cards were not available, respondents were asked to recall all vaccinations the child had received. Information on dates of vaccination was not asked. We only used the subsample of children with available vaccination records for further analysis.

2.2. Outcome variables

Definitions of invalid vaccine doses by country are presented in Table 1. In each country, the national immunisation schedule was used to define invalid vaccine doses. We used the WHO recommendations on invalid vaccine doses [5]; a vaccine dose was defined to be invalid if it met at least one of the following conditions:

(a) a first dose of diphtheria, tetanus and pertussis vaccine (DTP) administered before the recommended age at vaccination, i.e. age-invalid DTP1 vaccine dose (Table 1);
(b) the minimum interval between the second and third DTP doses was less than 28 days in all countries, i.e. interval-invalid DTP3 vaccine dose;
(c) a measles-containing vaccine (MCV) administered before the recommended age at vaccination (<270 days of age in all countries), i.e. age-invalid MCV dose.

2.3. Individual-level variables

Individual-level variables were child's sex, age, birth order and place of delivery (home vs. hospital facility), mother's age and education level, number of children living in the household and the wealth index as an indicator of economic status of the household [26]. The wealth index was divided into quintiles; from the poorest 20% to the richest 20%. Selected individual-level variables were hypothesised to be associated with invalid vaccinations based on previous literature [15,27,28]. In addition, we added a variable "year of survey" to control for possible unmeasured birth cohort effects.

2.4. Community-level variables

Aggregate community-level variables were created at the level of clusters based on the full sample of 281,115 children. We included the following community-level variables:

a. Community health-seeking behaviour: percentage of respondents in the community who gave birth at home.
b. Community illiteracy: percentage of respondents in the community with no formal education.
c. Community women unemployment level: percentage of adult female respondents in the community currently not working.
d. Community poverty: percentage of children in the community below 20% of the wealth index.
e. Percentage of children in the community with missing vaccination records.
f. Residence: rural vs. urban.

All variables, except residence, were divided into three equal groups and categorised as low (lowest tertile), medium (middle tertile) and high (highest tertile). The variable "residence" with the categories "rural" and "urban" was already provided in the data sets.

2.5. Statistical analysis

First, we displayed the fraction of age-invalid DTP1 and MCV and interval-invalid DTP3 vaccinations by country. For age-invalid DTP1 and MCV vaccinations, we used a subsample of children with complete data on date of birth, including the day of birth (n = 86,915). The age at vaccination of each dose was calculated in days. In the analysis at the country level, sample weights already provided in the data sets were used to obtain country-representative estimates [29]. Furthermore, to analyse individual- and community-level factors associated with the interval-invalid DTP3 and age-invalid MCV vaccinations we applied multilevel multivariable logistic regression (two separate models). We constructed a three-level model with children at the individual level (level 1) nested within clusters (level 2) nested within countries (level 3). Initially, we examined whether there was variation in invalid vaccinations due to community and country effects. This was done in models with no explanatory variables (empty models), and median odds ratios (MOR) were calculated as measures of unexplained community and country heterogeneity. "As the median value of the odds ratio between the area at highest risk and the area at lowest risk when randomly picking out two areas the MOR can be conceptualised

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Table 1
Recommended age at vaccination according to the national immunisation schedules by country and definitions of invalid vaccine doses[a].

	Burkina Faso, Tanzania	Benin, Burundi, Cameroon, Chad, Congo Democratic Republic, Côte d'Ivoire, Ethiopia, Gabon, Ghana, Guinea, Kenya, Lesotho, Liberia, Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Swaziland, Uganda, Zambia	Congo	Zimbabwe
Recommended age at DTP1 vaccination	4 weeks	6 weeks	8 weeks	12 weeks
Age-invalid DTP1 vaccination	<28 days	<42 days	<56 days	<84 days
Recommended age at DTP2 vaccination	8 weeks	10 weeks	12 weeks	16 weeks
Interval-invalid DTP2 vaccination	<28 days	<28 days	<28 days	<28 days
Recommended age at DTP3 vaccination	12 weeks	14 weeks	16 weeks	20 weeks
Interval-invalid DTP3 vaccination	<28 days	<28 days	<28 days	<28 days
Recommended age at measles vaccination	9 months	9 months	9 months	9 months
Age-invalid MCV vaccination	<270 days	<270 days	<270 days	<270 days

[a] Information on recommended ages at vaccination was based on the WHO reports on vaccine-preventable diseases in the respective years.

as the increased risk that (in median) would have if moving to another area with a higher risk" from an area with a lower risk [30]. MOR are directly comparable with odds ratios (OR) for individual- and community-level variables. Furthermore, we added into the models individual- and community-level variables and calculated adjusted ORs (AOR) and 95% confidence intervals (CI) as measures of association between outcome variables and independent variables. Variables on the country level were not added into the models, because it was not the aim of the study. The analysis was done with the statistical programme SAS for Windows, version 9.2.

2.6. Ethical approval

The analysis of this study was based on existing survey data collected by the DHS (The DHS Programme, www.dhsprogram.com). All surveys included in the analysis were approved by the Institutional Review Board of ICF International in Calverton, MD, USA. Study participants provided informed consent before participation. Survey data were provided by ICF International, Inc.

3. Results

3.1. Sample

We assessed the availability of vaccination records in a pooled sample. About 70% of the children had vaccination records; however, the records were not available for some of them at the day of the interview due to unknown reasons (Table 2). For the remaining 16% of children, the respondents reported that they never had vaccination record cards, 6% no longer had them, and 9% of children died before the interview and vaccination records were not available for them. The older the child was, the less likely was he/she to have a vaccination record (Table 2). If vaccination records were available, complete dates of vaccinations were available in the majority of cases.

Selected socio-demographic characteristics by country are presented in Table 3. Median sample size across all countries was 7810 (interquartile range [IQR]: 5632–11,713). There were minor differences across countries in terms of children's gender and mothers' age. The proportion of children with vaccination records ranged from ~20% in Chad, Democratic Republic of the Congo and Nigeria to ~90% in Sao Tome and Principe. The proportion of children living in rural areas varied between 40% (Congo and Gabon) and 90% (Malawi). The mean community percentage of home births varied between 10% in the Congo and 75% in Ethiopia.

3.2. Invalid vaccine doses

There was a considerable variation in invalid vaccinations across countries (Fig. 1). There were countries where the proportion of invalid vaccinations was high for all three vaccinations (e.g. Democratic Rep. of Congo, Nigeria, and Sierra Leone), whereas in some countries the proportion of all three invalid vaccinations was low (e.g. Lesotho, Sao Tome and Principe, and Tanzania). The median percentage of age-invalid MCV, age-invalid DTP1 and interval-invalid DTP3 vaccinations across countries was 15.5% (IQR, 10.0–18.1%), 12.1% (IQR, 9.4–15.2%) and 5.7% (IQR, 5.0–7.6), respectively. Of the DTP1 vaccinations classified as administratively invalid, 7.4% and 5.5% were administered at child's age of less than one and two weeks, respectively (Fig. 2A). Of the interval-invalid DTP3 vaccinations about 25% were given with an interval of less than two weeks (Fig. 2b). In 12 countries, the proportion of interval-invalid DTP3 doses administered with an interval of less than two weeks before the preceding dose varied between 30% and 50% (Table 1 in the appendix). Of the age-invalid MCV doses, 18% were given at the age of less than six months (Fig. 2c). In 13 countries, the proportion of MCV doses administered at the age of less than six months varied between 20% and 45% (Table 1 in appendix).

3.3. Individual- and community-level factors of invalid vaccinations

Random intercept models with no explanatory variables showed that part of the variance in invalid vaccinations was explained by community and country effects. For example, the MORs for community level area were 1.64 for interval-invalid DTP3 vaccination and 1.65 for age-invalid MCV vaccination. In other words, children were more likely to have invalid vaccinations if they moved to a community with a higher risk of invalid vaccinations. The MOR for country was 1.48 (interval-invalid DTP3) and 1.70 (age-invalid MCV). Univariable logistic regression analysis showed that the risk of interval-invalid DTP3 vaccination was higher among children of younger mothers, those whose mothers were not working, and children from poorer families (Table 4). The effect of mother's age and mother's working status disappeared in multilevel multivariable logistic regression analysis. At the community level, children living in rural areas were more likely to have interval-invalid DTP3 vaccination.

Univariable logistic regression analysis showed a decrease in the proportion of age-invalid MCV vaccination over the survey years (Table 5). Furthermore, socio-economic variables such as mother's education, mother's working status and economic status of the family were associated with age-invalid MCV vaccinations. In multilevel multivariable analysis only the effect of mother's education and the economic status of the family remained significant. At the community level, the risk of age-invalid MCV vaccinations was higher among children living in rural areas and in communities with high unemployment rates.

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Table 2
Availability of vaccination records, pooled sample (%).

Availability of vaccination records	Child's age at interview (years)					Total
	0	1	2	3	4	
Vaccination records were seen	60.7	57.2	47.0	38.6	34.3	47.8
Vaccination records were not seen	11.6	18.1	23.5	27.6	29.5	21.9
Child has no vaccination records at all	20.4	12.7	13.7	15.1	15.1	15.5
Child has no longer vaccination records	2.0	4.3	6.4	7.9	9.2	5.9
Vaccination records were not available[a]	5.3	7.7	9.5	10.7	11.8	8.9
Total number of children	59,504	56,084	55,519	56,197	53,811	281,115

[a] These are children who died before the interview

4. Discussion

Using recent data from the population-based representative DHS surveys in 31 countries of the WHO African Region, we provide the first analysis of invalid vaccine doses based on a sample size of this magnitude. We found that a substantial proportion of children in this region were vaccinated earlier than recommended or received vaccine doses spaced inappropriately close to each other. The highest proportion of invalid vaccinations was observed for measles vaccination, followed by DTP1 and DTP3. Six countries (Cameroon, Chad, Congo Democratic Rep., Ethiopia, Mali, and Niger) had the highest proportion of age-invalid MCV vaccination (between 20% and 30%). Administration of childhood vaccinations a few days earlier than recommended may not be a noteworthy problem; however, we observed that a substantial proportion of children were vaccinated too early or with too short intervals between vaccine doses. For example, of those children who received an age-invalid MCV, every fifth child received it at the age of less than six months. Of those children who received an interval-invalid DTP3 vaccine dose, every fourth received it with an interval of less than two weeks. These considerable deviations from vaccination recommendation may lead to a suboptimal protection against vaccine-preventable diseases. In addition, some African countries recommend to repeat invalid vaccine doses which may result in an avoidable wastage of financial resources.

To our knowledge, a systematic evaluation of invalid vaccine doses in the African Region has never been conducted. A few relatively small studies in Kenya [22], Nigeria [19], South Africa [18] and Uganda [21,23] reported somewhat different estimates of invalid vaccinations than our study did and are not comparable because they used different definitions of invalid vaccinations. We followed the WHO criteria to define invalid vaccine doses that allowed

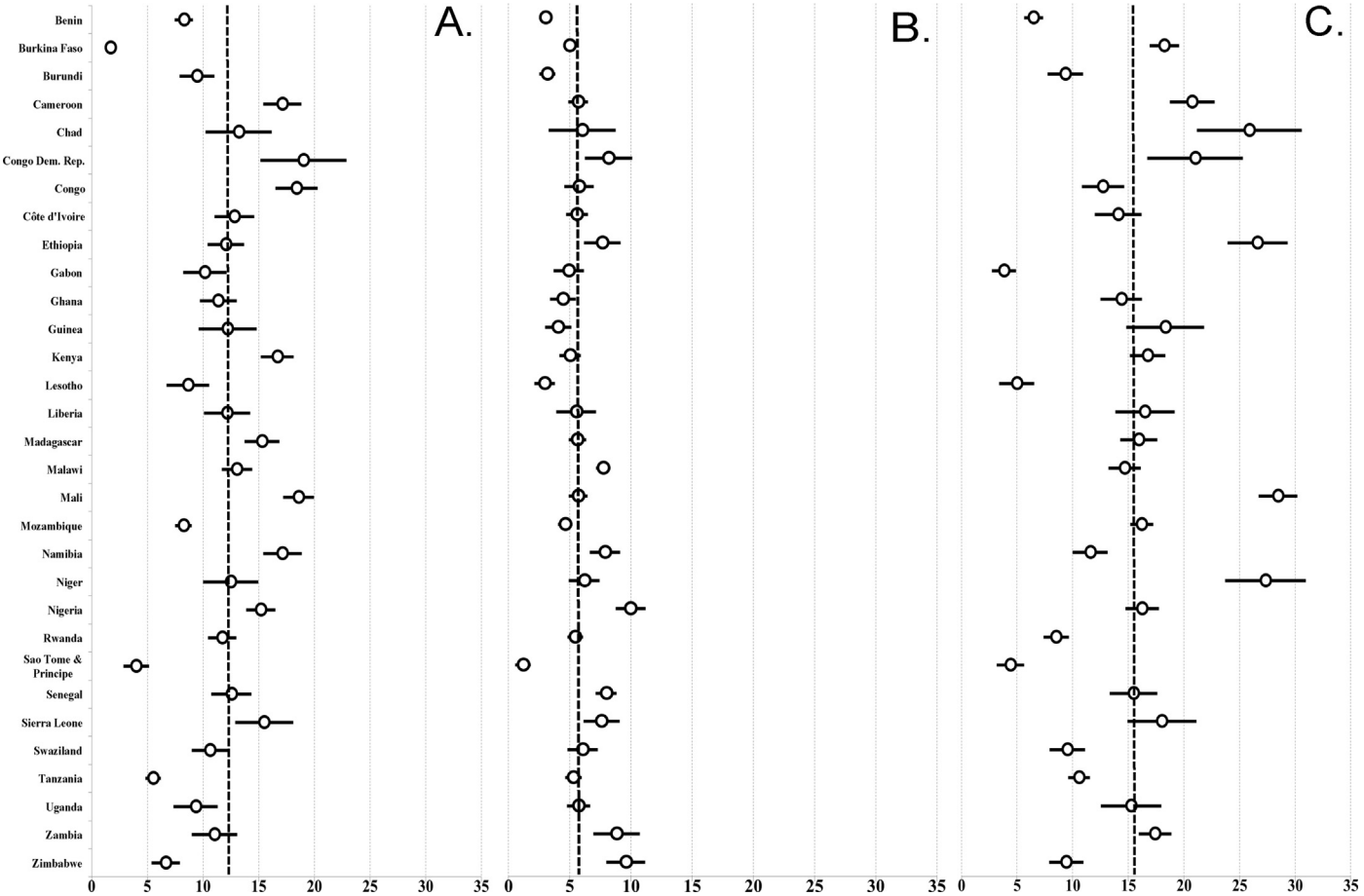

Fig. 1. Proportion of invalid vaccinations by country (%). (A) Age-invalid DTP1 vaccination; (B) interval-invalid DTP3 vaccination; (C) age-invalid MCV vaccination. Whiskers indicate 95% confidence intervals. A dash line represents the median value across all countries.

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Table 3
Selected characteristics of the samples by country.

Country	Year of survey	Total number of children	Total number of clusters	Mean number of children per cluster	Proportion of children with available vaccination records (%)	Proportion of female children (%)	Respondent's age, mean (SD)	Proportion of children living in rural areas (%)	Mean community percentage of home birth (%)	Mean community percentage of respondents with no formal education (%)
Benin	2006	16,075	750	21.4	54.0	49.6	29.2	64.5	17.0	70.2
Burkina Faso	2010	15,044	573	26.3	70.0	49.2	29.3	78.4	26.2	78.4
Burundi	2010	7742	376	20.6	53.9	49.2	30.2	82.4	33.9	47.4
Cameroon	2011	11,732	578	20.3	50.4	50.4	27.9	60.0	28.1	17.9
Chad	2004	5635	196	28.8	19.8	49.6	28.0	55.6	72.6	71.5
Congo Democratic Rep.	2007	8992	300	30.0	19.6	50.2	29.1	60.2	26.2	23.4
Congo	2005	4835	225	21.5	56.1	48.8	28.1	40.5	10.1	6.2
Côte d'Ivoire	2011–12	7776	351	22.2	67.5	49.5	28.8	66.8	36.9	62.7
Ethiopia	2011	11,654	596	19.6	23.7	48.6	29.0	83.0	75.1	60.3
Gabon	2012	6067	334	18.2	65.6	50.1	28.3	38.8	15.1	5.9
Ghana	2008	2992	408	7.3	74.5	49.0	30.1	66.6	37.0	29.1
Guinea	2005	6364	295	21.6	42.0	48.6	29.6	78.5	64.4	83.6
Kenya	2008–09	6079	398	15.3	62.0	48.5	28.2	75.9	46.4	14.5
Lesotho	2009	3999	399	10.0	71.2	49.7	27.7	83.2	37.8	2.0
Liberia	2007	5799	298	19.5	30.8	48.4	29.1	64.9	60.0	47.4
Madagascar	2008–09	12,448	594	21.0	49.3	48.8	28.4	82.2	59.2	25.2
Malawi	2010	19,967	849	23.5	73.3	50.0	28.4	90.5	23.3	15.5
Mali	2006	14,238	407	35.0	46.6	49.5	28.5	70.5	52.3	82.6
Mozambique	2011	11,102	610	18.2	75.2	49.5	28.4	67.5	32.7	29.8
Namibia	2006–07	5168	495	10.4	64.6	48.6	28.9	61.8	17.2	10.3
Niger	2006	9193	342	26.9	40.2	48.8	29.0	71.6	70.1	81.4
Nigeria	2008	28,647	886	32.3	20.2	49.0	29.3	73.4	55.7	37.7
Rwanda	2010	9002	492	18.3	75.7	49.1	30.6	86.4	28.6	18.1
Sao Tome and Principe	2008–09	1931	104	18.6	88.8	49.0	29.2	60.2	20.8	6.1
Senegal	2010–11	12,326	391	31.5	53.9	48.6	28.9	70.4	30.4	70.3
Sierra Leone	2008	5631	352	16.0	48.7	49.6	28.8	65.9	69.2	69.5
Swaziland	2006–07	2812	274	10.3	75.3	49.7	27.6	74.3	21.2	8.5
Tanzania	2010	8023	475	16.9	75.5	50.0	29.5	81.2	43.4	22.1
Uganda	2011	7878	404	19.5	51.8	49.9	28.6	78.7	36.7	16.3
Zambia	2007	6401	319	20.1	68.5	50.3	28.4	67.6	47.6	12.4
Zimbabwe	2010–11	5563	406	13.7	61.7	49.5	27.5	71.0	27.8	1.4
Median (IQR)	–	7810 (5632–11,713)	–	–	56.1 (47.7–70.6)	49.5 (48.8–49.7)	28.8 (28.3–29.2)	70.5 (64.7–78.6)	36.7 (26.2–54.0)	25.2 (13.5–62.1)

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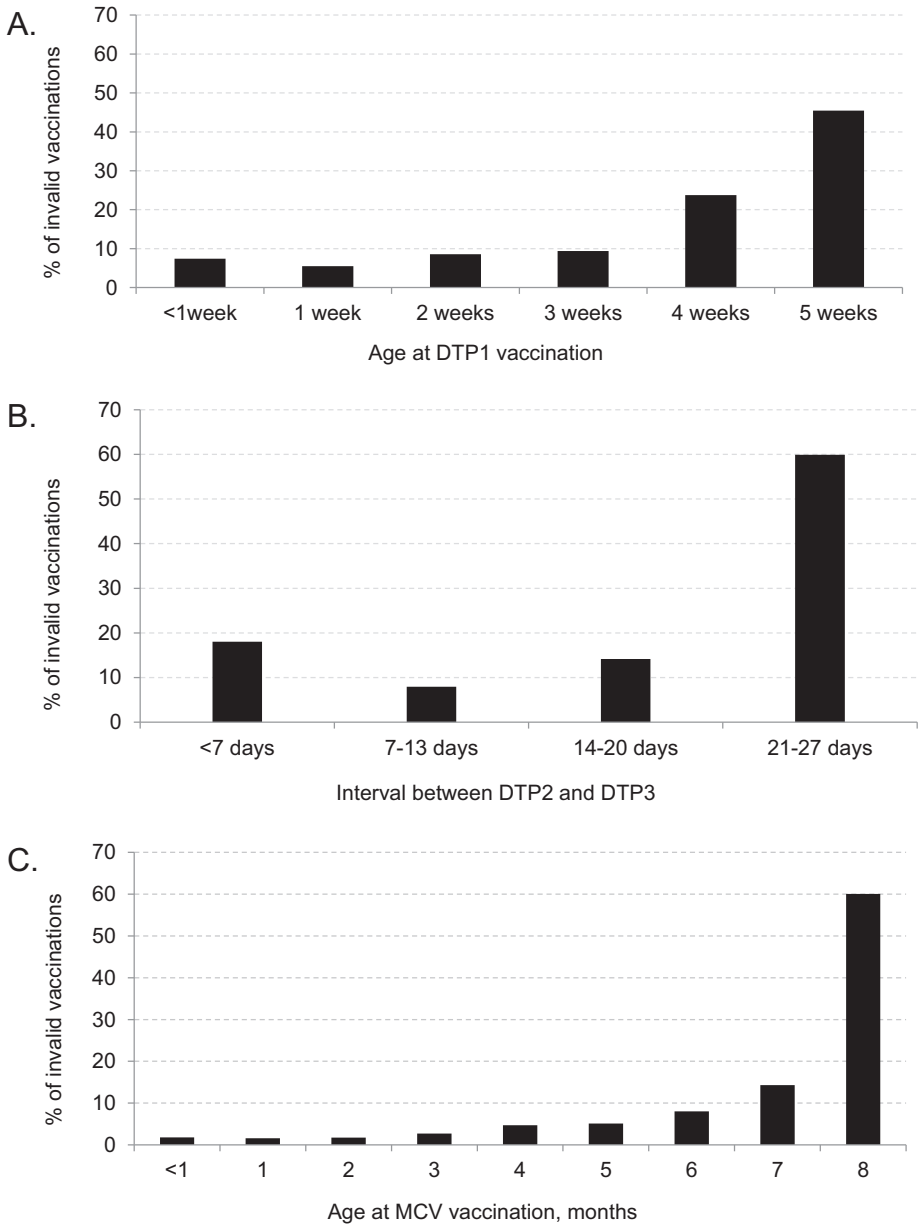

Fig. 2. Extent of invalid vaccinations, pooled sample. (A) Age-invalid DTP1 vaccination (Burkina Faso, Congo, Tanzania and Zimbabwe were excluded because they had different recommendations on age at vaccination); (B) interval-invalid DTP3 vaccination; (C) age-invalid MCV vaccination.

cross-country comparison in our study. The lack of a systematic evaluation may in part be explained by methodological obstacles. First, vaccine recommendations differ across countries in terms of recommended ages. For example, many African countries recommend the first dose of a DTP vaccine at the age of six weeks, whereas in several countries the age at vaccination is four, eight or 12 weeks. Second, there are country differences in immunisation schedules with regard to recommended units (e.g. weeks or months in the case of DTP vaccination) which in turn hamper a cross-country comparative analysis. For instance, four weeks does not necessarily mean one month, since the former implies 28 days, while the latter may imply 30 or 31 days. We considered a month to have 28 days to allow cross-country comparison of the findings regarding DTP vaccination. Third, the quality of routine vaccination data in African countries is suboptimal [1] and varies considerably across countries. We used data from the DHS, which applied standardised instruments (e.g. similar sampling strategies and standardised questionnaires) and are known to provide reliable statistics compared to officially reported data. In particular, DHS data regarding childhood vaccinations were used to validate officially reported national vaccination data [31].

Using multilevel techniques we investigated the simultaneous effect of individual- and community-associated factors on invalid vaccinations. At the individual level, children living in households with a poor economic status were more likely to have both interval-interval DTP3 and age-invalid MCV vaccinations. In addition, children of mothers with no formal education were more likely to have age-invalid MCV vaccination. Socioeconomic differences have been observed in other vaccination-related outcomes, such as missing or delayed vaccination [2,32] and may be explained by inadequate utilisation of health-care services. Poor knowledge of immunisation schedule among mothers with lower socioeconomic status may also explain these differences. Since the correct administration of vaccinations is to a greater extent the responsibility of health care facilities, we expected factors relating to community health to play an important role in determining invalid

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Table 4
Risk factors for interval-invalid DTP3 vaccination.

	N of invalid vaccinations	Empty model	Single-level simple OR (95% CI)	Multilevel adjusted OR (95% CI)
Fixed effects				
Control variable				
Survey year (change per year)			1.01 (0.99–1.03)	0.97 (0.91–1.03)
Individual-level variables				
Child's gender				
Female	2118		Reference	Reference
Male	2104		0.98 (0.92–1.04)	0.99 (0.93–1.07)
Child's age in years				
2	1150		1.14 (1.03–1.25)	1.09 (0.98–1.21)
3	905		1.04 (0.93–1.15)	1.02 (0.92–1.14)
4	778		1.05 (0.94–1.17)	1.06 (0.95–1.18)
5	646		Reference	Reference
Child's birth order				
1	893		Reference	Reference
2	806		0.97 (0.86–1.02)	1.01 (0.85–1.20)
3	695		1.00 (0.90–1.10)	1.01 (0.88–1.15)
4+	1828		0.94 (0.86–1.02)	1.00 (0.88–1.12)
Child's place of delivery				
Hospital	2602		Reference	Reference
Home	1563		1.06 (0.99–1.13)	1.00 (0.91–1.09)
Respondent's age				
<20 years	254		1.29 (1.09–1.53)	1.09 (0.85–1.40)
20–29 years	2190		1.13 (1.00–1.27)	0.99 (0.84–1.18)
30–39 years	1434		1.08 (0.96–1.22)	0.99 (0.86–1.15)
40–49 years	344		Reference	Reference
Respondent's education				
No education	1815		0.92 (0.68–1.23)	1.10 (0.75–1.61)
Primary	1782		0.95 (0.70–1.27)	1.02 (0.70–1.48)
Secondary	577		0.85 (0.63–1.15)	0.88 (0.61–1.28)
Higher	48		Reference	Reference
Respondent's current working status				
Working	2593		Reference	Reference
Not working	1617		1.10 (1.03–1.17)	0.99 (0.91–1.08)
Number of children in the family (change per one child)			0.99 (0.97–1.00)	0.97 (0.94–1.01)
Economic status of the household				
Poorest	1097		1.38 (1.23–1.53)	1.21 (1.03–1.42)
Poor	932		1.37 (1.22–1.53)	1.14 (0.98–1.33)
Medium	901		1.30 (1.16–1.46)	1.13 (0.98–1.31)
Rich	795		1.25 (1.11–1.40)	1.10 (0.95–1.27)
Richest	497		Reference	Reference
Community-level variables				
Place of residence				
Urban	826		Reference	Reference
Rural	3396		1.32 (1.22–1.42)	1.23 (1.09–1.39)
Community poverty				
Low				Reference
Medium				0.95 (0.86–1.06)
High				0.93 (0.78–1.12)
Community unemployment				
Low				Reference
Medium				1.07 (0.96–1.18)
High				1.07 (0.93–1.22)
Community home delivery				
Low				Reference
Medium				0.95 (0.86–1.05)
High				1.00 (0.87–1.14)
Percentage of children in the community with missing vaccination records				
Low				Reference
Medium				1.02 (0.93–1.12)
High				1.04 (0.73–1.49)
Random effects				
Variance				
Community	NA	0.27 (0.22–0.33)	NA	0.29 (0.23–0.36)
Country	NA	0.17 (0.10–0.35)	NA	0.20 (0.12–0.42)
Median odds ratio (MOR)				
Community	NA	1.64	NA	1.68
Country	NA	1.48	NA	1.53

NA – not applicable.

vaccinations. Research in some African countries showed the effect of community associated factors on health-related outcomes, health-seeking behaviour and utilisation of primary preventive measures, including vaccination uptake [27,32]. We observed that community-level factors explained a considerable fraction of the variation in invalid vaccinations. The effect of some community-level factors was even higher than that of some individual-level factors, suggesting that the former should be considered when

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Table 5
Risk factors for age-invalid MCV vaccination.

	N of invalid vaccinations	Empty model	Single-level simple OR (95% CI)	Multilevel adjusted OR (95% CI)
Fixed effects				
Control variable				
Survey year (change per year)			0.94 (0.93–0.95)	0.96 (0.89–1.03)
Individual-level variables				
Child's gender				
Female	3084		Reference	Reference
Male	3121		0.99 (0.94–1.04)	0.99 (0.93–1.05)
Child's age in years				
2	1783		1.08 (0.99–1.18)	1.04 (0.95–1.14)
3	1468		1.02 (0.94–1.11)	0.99 (0.91–1.09)
4	1202		0.99 (0.90–1.08)	0.98 (0.89–1.08)
5	1059		Reference	Reference
Child's birth order				
1	1290		Reference	Reference
2	1137		0.93 (0.86–1.02)	0.87 (0.75–1.01)
3	994		0.97 (0.88–1.06)	0.90 (0.80–1.01)
4+	2784		1.00 (0.93–1.07)	0.90 (0.81–1.00)
Child's place of delivery				
Hospital	3542		Reference	Reference
Home	2600		1.22 (1.15–1.29)	1.02 (0.94–1.10)
Respondent's age				
<20 years	327		1.34 (1.15–1.56)	0.95 (0.76–1.17)
20–29 years	3195		1.11 (1.01–1.23)	1.02 (0.89–1.18)
30–39 years	2145		1.05 (0.94–1.16)	1.03 (0.91–1.17)
40–49 years	538		Reference	Reference
Respondent's education				
No education	2886		1.68 (1.27–2.22)	1.49 (1.06–2.09)
Primary	2410		1.30 (0.98–1.71)	1.39 (0.99–1.94)
Secondary	852		1.12 (0.84–1.49)	1.27 (0.91–1.77)
Higher	57		Reference	Reference
Respondent's current working status				
Working	3643		Reference	Reference
Not working	2547		1.16 (1.10–1.23)	1.03 (0.95–1.11)
Number of children in the family (change per one child)			1.01 (0.99–1.02)	1.00 (0.97–1.03)
Economic status of the household				
Poorest	1536		1.22 (1.12–1.34)	1.25 (1.09–1.44)
Poor	1368		1.29 (1.17–1.42)	1.33 (1.16–1.52)
Medium	1359		1.27 (1.15–1.39)	1.27 (1.12–1.45)
Rich	1148		1.12 (1.02–1.24)	1.17 (1.04–1.32)
Richest	794		Reference	Reference
Community-level variables				
Place of residence				
Urban	826		Reference	Reference
Rural	3396		1.19 (1.12–1.27)	1.14 (1.03–1.27)
Community poverty				
Low				Reference
Medium				1.02 (0.93–1.12)
High				1.04 (0.89–1.22)
Community unemployment				
Low				Reference
Medium				1.02 (0.93–1.12)
High				1.15 (1.02–1.29)
Community home delivery				
Low				Reference
Medium				1.00 (0.91–1.10)
High				0.97 (0.86–1.09)
Percentage of children in the community with missing vaccination records				
Low				Reference
Medium				1.05 (0.97–1.14)
High				1.18 (0.88–1.59)
Random effects				
Variance				
Community	NA	0.28 (0.24–0.33)	NA	0.27 (0.22–0.33)
Country	NA	0.31 (0.20–0.59)	NA	0.28 (0.17–0.54)
Median odds ratio (MOR)				
Community	NA	1.65	NA	1.64
Country	NA	1.70	NA	1.65

NA – not applicable.

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planning immunisation services. In particular, living in rural areas and in communities with high unemployment rates was a risk factor for invalid vaccinations.

4.1. Strengths and limitations

To the best of our knowledge, this is the first study which featured a systematic evaluation of invalid vaccinations in African countries and examined their risk factors at the individual and community levels. Our study provided both country-specific and summary estimates for 31 of the 46 countries of the WHO African Region with recently available data. While the former are particularly important for local policy makers for evaluating immunisation services and designing intervention programmes, the latter can be used to monitor the regional situation. Our findings provide additional insights into the performance of immunisation services in these countries. A widely used indicator of performance of immunisation services is the coverage with three doses of DTP among children between 12 and 23 months of age (i.e. up-to-date coverage at 23 months). However, this indicator does not take into consideration the timeliness of vaccinations. For instance, it is not known whether a child received a vaccine dose too early or too late.

The main limitation of the present study is the substantial variation in the availability of vaccination cards across countries. About 22% of the children had no vaccination cards and a missing vaccination card per se may be associated with poor vaccination uptake [33]. Therefore, children without vaccination records may be more likely to have invalid vaccinations and our analysis may have underestimated the true frequency of invalid vaccinations. Furthermore, our analysis was limited to variables available in the datasets. Variables indicating vaccine shortage, cold-chain issues or personnel shortage have not been collected in the DHS surveys.

4.2. Conclusions

Invalid vaccinations are common in countries of the WHO African Region indicating that immunisation services in this part of the world should be improved. This is important as the economic implication of repeating invalid vaccinations may be huge, particularly for low-income countries. Factors at the community level explained a considerable part of the variation in invalid vaccinations. This indicates that not only individual training of health care providers administering vaccines but also general organisation of health care services e.g. with respect to accessibility could be a field for improvement in order to ensure an optimal protection against vaccine-preventable diseases.

Author's contribution

MKA conceived and oversaw the study, performed the statistical analyses and wrote the first draft of the manuscript. He had access to all data and takes the responsibility for their integrity. EKM, GK, FP and CAG participated in data interpretation and writing of the manuscript. LK contributed to data analysis. RTM contributed to data analysis and writing the manuscript. All authors have reviewed and approved the submitted version of the manuscript.

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Conflict of interest statement: We declare that we do not have conflicts of interest relating to this study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2014.10.089.

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