

**The actual order in which vaccines are given in the EPI:
analysis of data from 102 national surveys.**

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1 Introduction

Aaby and a variety of co-workers have suggested that there are adverse effects of DTP vaccine on the overall health of young children, but that these are moderated if DTP is followed by a dose of BCG or measles vaccine¹. A number of more specific hypotheses have been proposed, with one recent formulation as follows:

1. BCG vaccine reduces mortality from infections other than tuberculosis until an inactivated vaccine is given.
2. Measles vaccine reduces mortality from infections other than measles until an inactivated vaccine is given; this effect may be stronger if the child still has maternal antibody when receiving measles vaccine.
3. Whole-cell diphtheria-tetanus-pertussis vaccine (DTP) increases mortality from infections other than diphtheria, tetanus and pertussis until a live vaccine is given; this effect is stronger in females than in males.
4. Live and killed vaccines may interact to produce good or bad non-specific effects when given simultaneously or when the sequence is changed, and the effects may be modified by vitamin A.

At its meeting in November 2011, the SAGE requested a review of the evidence relating to these hypotheses. This paper reviews evidence from nationally representative survey data on the extent to which different vaccines are given out of order or on the same day.

Objectives

This analysis uses existing nationally representative survey data for a preliminary examination of the following questions:

1. What % of children were given a first dose of DTP with or before BCG?
2. What % of children were given a last dose of DTP with or after MCV?
3. For how many child weeks before age 24 months was DTP the last vaccine given?
4. What % of children were given live (BCG or MCV¹) and killed (DTP) vaccines on the same day?
5. What % of children were given MCV and vitamin A on the same day?

2 Data

The data used were from the Demographic Health Surveys (DHS) rounds 5 and 6, and the Multiple Indicator Cluster Surveys (MICS) round 3. Background information about each survey, and on the completeness of the survey data, are given in Table 1 and Appendix Tables 1.0 to 1.8. Table 1 provides a summary in the form of median values overall and for each WHO Choice/burden-of-

¹ The first dose of measles vaccine.

disease sub-region. Tables A1.0 to A1.7 provide more detail and data for each survey grouped by WHO Region. Table A1.8 shows differences for countries surveyed more than once.

From Table 1 it can be seen that largest numbers of surveys were in Africa. In the Eastern Mediterranean, South East Asian and Western Pacific Regions there were relatively few. Median vaccination periods covered by the surveys were from 2004 to 2007 overall, but the studies in the high adult mortality countries in Africa (sub-region E) tended to be more recent (2006-2009). The median number of children in each survey aged between 24 and 59 months at the time of interview was 3,401.

The DHS series includes a question to mothers on how many of their children have died. In Tables 1 and A1.1 to 1.7, mortality rates estimated from the survey data are compared to the UNPOP infant mortality estimates. It can be seen that for surveys in some regions the DHS-based rates are a little lower than the UNPOP estimates, but in general they are broadly similar.

Table 1: Preliminary examination of the data

		Median values for the group of countries										
WHO sub-Region	Surveys available	Children in survey aged 24m +	Year of vaccination earliest latest BCG MCV		Infant mortality			Infant mortality UNPOP	Died before interview DHS	% of MCV given after age 24m	% of vaccinated children that have age median	
Overall	102	3,401	2004	2007	7%	7%	6%	6%	5%	3%	24-35m	73%
											24-59m	68%
AFR D	22	4,076	2003	2007	9%	9%	9%	9%	7%	3%	24-35m	59%
											24-59m	50%
AFR E	27	4,165	2006	2009	9%	9%	8%	8%	6%	2%	24-35m	71%
											24-59m	65%
AMR	16	3,871	2003	2007	4%	3%	3%	3%	3%	6%	24-35m	78%
											24-59m	75%
EMR	8	6,094	2003	2006	4%	4%	3%	3%	2%	0%	24-35m	53%
											24-59m	50%
EUR	11	1,297	2001	2005	3%	2%	2%	2%	2%	2%	24-35m	94%
											24-59m	94%
SEAR	11	5,132	2004	2007	5%	3%	2%	4%	3%	1%	24-35m	85%
											24-59m	82%
WPR	7	2,248	2003	2006	7%	6%	5%	7%	5%	4%	24-35m	74%
											24-59m	68%

In both DHS and MICS surveys, exact dates of vaccination are copied from vaccination cards if they are available; otherwise the mother is asked whether or not their child has had each vaccination. To determine the order of vaccine administration, only data from children with dates for all the relevant vaccines can be used. The proportion with data from cards ranged from over 90% in surveys in the EURO B & C sub-regions down to about 50% in the AFR D and EMR B & D sub-regions, and in some surveys the percentage of vaccinations with dates was very low indeed (eg Georgia 4%, Pakistan 12%, Nepal 13%, Mauritania 15%). Only surveys with at least 20% of vaccines with dates were included in the rest of the tables. Data from surveys with between 20% and 40% were included in the tables but excluded from calculation of the 'overall' figures at the top of each table. Also in

countries with more than one survey, only the most recent data were included in the summary figures. These inclusion criteria also required of any country-specific figures mentioned in the text. For all the children aged 24-59m at interview in included studies, dates from cards were available for 67% of vaccinations (median across included surveys), ie 33% of reports were based on mother's recall or an undated record.

There were 102 surveys in all. Of these 92 were included in the tables, and 56 were used for calculating summary statistics: 14 from the AFR D sub-region, 14 from AFR E, 11 from AMR B & D, 3 from EMR B & D, 7 from EUR B & C, 3 from SEAR B & D, and 4 from WPR B.

From Table A1.8 it can be seen that in the 17 countries with two or more eligible surveys, in the more recent years the % of doses of MCV given after age 24m have tended to be lower, and the % of data from vaccination cards rather than mother's recall have tended to be higher.

3 Analysis

The survey data were taken from interviews with mothers about children that were less than 5 years old. To achieve the same length of follow-up for each child, the analysis was restricted to vaccinations in the first 24 months of life. This meant that: i) children aged less than 24m at the time of the mother's interview were excluded (about 40% of the children surveyed); and ii) any vaccinations given after age 24m were ignored. Typically the percentage of the first doses of the measles vaccine given after age 24 months (and so not taken into account in these analyses) was around 3%. This proportion was generally higher in the Americas Region (6%) and much higher in some specific surveys, the highest being Guinea-Bissau 2002-6 (14%)².

The following results were reported for first DTP before, with or after BCG; last BCG before with or after MCV; child-weeks with DTP as the most recent vaccine ('DTP weeks'); and for vaccines given on the same day:

- *for each survey*: % overall, for boys v girls, for urban v rural, and by wealth quintile.
- *overall and for each sub-region*: medians, upper quartiles and deciles overall, and medians for boys v girls, for urban v rural, and by wealth quintile.

'DTP weeks' were calculated for each child as the number of weeks before age 24m for which any dose of DTP was the most recent vaccine received. Thus if doses were complete and in order, this was from the date of DTP1 to the date of MCV. If eg BCG was given between DTP1 and DTP2, the total DTP weeks were from date of DTP1 to BCG plus date of DTP2 to MCV. If the child was given DTP but no MCV, usually the total DTP weeks would be from date of first DTP to age 24m, but an out-of-

² These were some higher figures than this in some of the surveys excluded because of missing vaccine dates

order dose of BCG would reduce this. If a child had BCG and a dose of DTP on the same day, no DTP weeks were accrued until after the first subsequent dose of DTP.

It was found that both the numbers of DTP weeks and the completeness of recording of vaccination dates were related to the numbers and combinations of vaccines received. In particular, children who had had all five vaccines were more likely than the others to have complete sets of dates, and of the children with complete dates, those who had had all five vaccines tended to have lower values for DTP weeks than children who had missed MCV. Thus simply using the data from children with complete dates would have given a biased estimate of DTP weeks. For children with incomplete dates, the combinations of vaccines that they had received were used to impute values for DTP weeks using the distributions for children with the same combinations of vaccines but known dates.

In calculating summary figures such as medians, no attempt was made to weight different survey results by eg population size, or to interpolate for missing countries. Thus the summary figures in the tables, overall and for surveys in each region, should not be interpreted as global and regional estimates.

When specific surveys are mentioned in the text, the relevant ranges of vaccine years are given, defined as follows: at least 90% of doses of BCG were given during or after the start of the range, and at least 90% of the doses of BCG were given before the end of it.

Details of the calculations are given in footnotes to the tables.

4 Results

What % of children were given a first dose of DTP before or with BCG?

Overall, for about 99% of children there were data on whether they had had BCG and DTP or not. Of these, about 5% of children had received neither, 2% had had BCG but no DTP, and 1% DTP but no BCG. In these children the question of order did not arise. This was most common in the AFR D sub-region (Table A2.1a col 2+ col 3 +col 4 = 18%), especially in the poorest groups (30%: Table A2.1b), although there is substantial within-region variation, with high levels in eg Niger 2001-5 (59%) but much lower levels in Gambia 2001-4, Ghana 2004-7 and Senegal 2006-9 (5 to 7%). There were also high levels in Lao PDR (48%). In EUR B & D by contrast, the corresponding figure was less than 1%.

Two countries (Suriname 2002-5 and Trinidad & Tobago 2002-5) did not include BCG in their survey. Also the percentage of children recorded as having DTP but not BCG was unusually high in Jordan 2003-6 (19%),

Table 2 shows the percentages of children who received their first dose of DTP before BCG. The overall figure was 2%. In most countries the figure was less than 5%, but it was more common in specific countries such as Jordan 2003-6 (17%), Zambia 2003-6 (12%) and Haiti 2007-12 (11%).

Table 2: Percentage of children with their first dose of DTP before BCG

Median values for surveys in each group of countries; data for children aged 24-59m

<i>Region</i>	<i>Median</i>	<i>Upper quartile</i>	<i>Boys</i>	<i>Girls</i>	<i>Urban</i>	<i>Rural</i>	<i>Wealth quintile</i>	
							<i>top</i>	<i>bottom</i>
Overall	2%	4%	2%	2%	1%	3%	1%	2%
AFR D	3%	4%	3%	3%	2%	4%	1%	4%
AFR E	1%	5%	1%	1%	1%	1%	1%	1%
AMR	3%	4%	2%	3%	2%	4%	1%	5%
EMR	5%		6%	5%	6%	4%	4%	3%
EUR	2%	3%	2%	2%	1%	3%	1%	1%
SEAR	1%		0%	1%	1%	1%	1%	1%
WPR	2%	2%	2%	2%	1%	2%	2%	2%

Table 3 shows the percentage of children who had BCG and their first dose of DTP on the same day. The overall figure was 5%, but in general it was much common in the poorest quintile (13%) than the richest (4%), and much more common than this in some countries. Bangladesh 2003-6 was an outlier at over 60%, but figures of 20% or more were seen in eg Guinea-Bissau 2002-6, Madagascar 2004-7, Malawi 2006-9, Jamaica 2001-4 and Lao PDR 2002-5. In the countries with 2 or more surveys, the proportions of children with first doses of DPT given before or on the same day as BCG tended to be smaller in the more recent data (Table 2.8), even though the proportions of children receiving at least one dose of DPT had increased.

Table 3: Percentage of children with BCG and their first dose of DTP on the same day

Median values for surveys in each group of countries; data for children aged 24-59m

<i>Region</i>	<i>Median</i>	<i>upper quartile</i>	<i>Boys</i>	<i>Girls</i>	<i>Urban</i>	<i>Rural</i>	<i>Wealth quintile</i>	
							<i>top</i>	<i>bottom</i>
Overall	5%	15%	5%	6%	4%	7%	3%	9%
AFR D	9%	17%	10%	9%	6%	11%	4%	15%
AFR E	7%	20%	6%	7%	3%	9%	3%	10%
AMR	4%	8%	4%	4%	3%	7%	1%	7%
EMR	5%		5%	5%	4%	5%	1%	4%
EUR	1%	1%	1%	1%	0%	1%	0%	1%
SEAR	6%		6%	6%	4%	7%	3%	9%
WPR	10%	14%	10%	9%	6%	11%	4%	16%

What % of children were given their last dose of DTP with or after MCV?

Overall 6% of children had had at least one dose of DPT but no MCV (Appendix Table 2, which also shows the percentages of children who had missing data for DTP or MCV, the % who had neither or only one of these vaccines).

Table 4 shows that overall about 4% of children had their last dose of DTP after the MCV³. Table 5 shows that about 2% had both doses of vaccine on the same day. The potential problems were greatest in the AFR D sub-region (4% and 5% respectively) and WPR B (5% and 5%), but again the summary figures conceal a good deal of country-to-country variation. At least one country in each region had high percentages, examples being Gambia (16% , 7%), Guinea-Bissau (14%, 12%), Sierra-Leone (4%,8%), Uganda 2007-10 (3%, 10%) and Lao PDR 2002-5 (7%, 13%).

Table 4: Percentage of children who had their last dose of DTP after MCV

Median values for surveys in each group of countries; data for children aged 24-59m

<i>Region</i>	<i>Median</i>	<i>Upper quartile</i>	<i>Boys</i>	<i>Girls</i>	<i>Urban</i>	<i>Rural</i>	<i>Wealth quintile</i>	
							<i>top</i>	<i>bottom</i>
Overall	4%	6%	3%	4%	3%	3%	2%	3%
AFR D	4%	6%	4%	4%	3%	3%	4%	4%
AFR E	2%	4%	2%	2%	1%	2%	1%	3%
AMR	5%	9%	4%	5%	3%	5%	3%	6%
EMR	1%		1%	1%	1%	1%	0%	1%
EUR	3%	4%	2%	3%	4%	2%	4%	2%
SEAR	3%		3%	2%	1%	3%	0%	4%
WPR	5%	6%	4%	5%	3%	5%	4%	5%

In the countries with more than one survey, the proportions of children with last doses of DPT given after or on the same day as MCV again tended to be smaller in the more recent data (Appendix Table 2.8).

Table 5: Percentage of children who had MCV and their last dose of DTP on the same day

Median values for surveys in each group of countries; data for children aged 24-59m

<i>Region</i>	<i>Median</i>	<i>upper quartile</i>	<i>Boys</i>	<i>Girls</i>	<i>Urban</i>	<i>Rural</i>	<i>Wealth quintile</i>	
							<i>top</i>	<i>bottom</i>
Overall	2%	6%	2%	3%	1%	3%	1%	4%
AFR D	5%	7%	5%	5%	4%	6%	2%	7%
AFR E	3%	5%	3%	3%	2%	3%	1%	4%
AMR	2%	4%	2%	2%	2%	2%	1%	2%
EMR	1%		1%	1%	1%	1%	1%	1%
EUR	1%	1%	1%	0%	0%	1%	0%	0%
SEAR	1%		1%	1%	1%	1%	1%	1%
WPR	5%	8%	5%	6%	1%	6%	1%	8%

³ or first dose of MCV if there was more than one. Data on MCV2 were not routinely collected in these surveys.

For how many child weeks before age 24 months was DTP the last vaccine given?

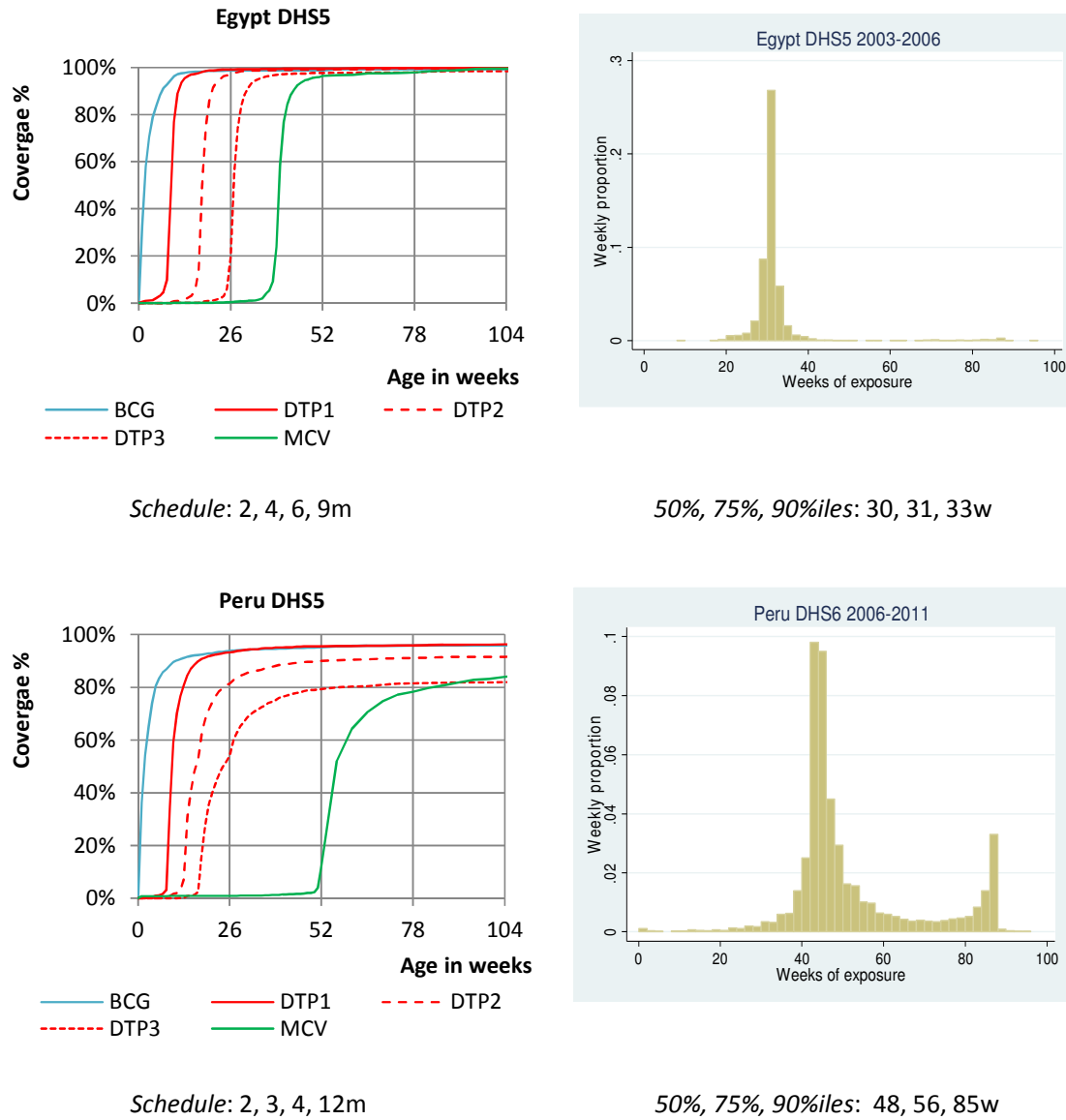
Table 6 and section 5 of Appendix Table 2 (cols 17-20) give the estimated median, upper quartile and 90th percentile values of total ‘DTP weeks’ Appendix Table 2 also gives the number of cases that the estimates are based on. Overall around 50% of children spent 35 weeks or more of their lives with DTP as their most recent dose of vaccine. However for about 10% of children the number of DTP weeks was 78 or more. Results for AFR D and E, and WPR B were close to the overall, but the figures were higher for surveys in AMR (45 and 80 weeks), and lower in EMR (31 and 39 weeks) and SEAR (32 and 45 weeks). At least part of the explanation lies in the different schedules used in different regions. For much of the period concerned, the scheduled ages were [6w, 10w, 14, 9m] in AFR but [2m, 4m, 6m 12m] in AMR, with mixtures elsewhere, so the scheduled gap between DTP1 and MCV was largest in AMR.

Table 6: DTP weeks before age 24 months

Region	Median values for surveys in each group of countries.								
	Median	upper quartile	upper decile	Boys	Girls	Urban	Rural	Wealth top	Wealth bottom
Overall	35	46	78	35	35	35	35	34	36
AFR D	34	51	85	34	34	34	34	34	35
AFR E	34	40	76	34	34	34	34	34	35
AMR	45	55	80	45	45	45	45	45	45
EMR	31	34	39	31	31	31	31	31	30
EUR	44	46	57	43	44	44	44	43	43
SEAR	32	36	45	32	32	32	32	33	32
WPR	35	57	83	37	34	34	36	34	35

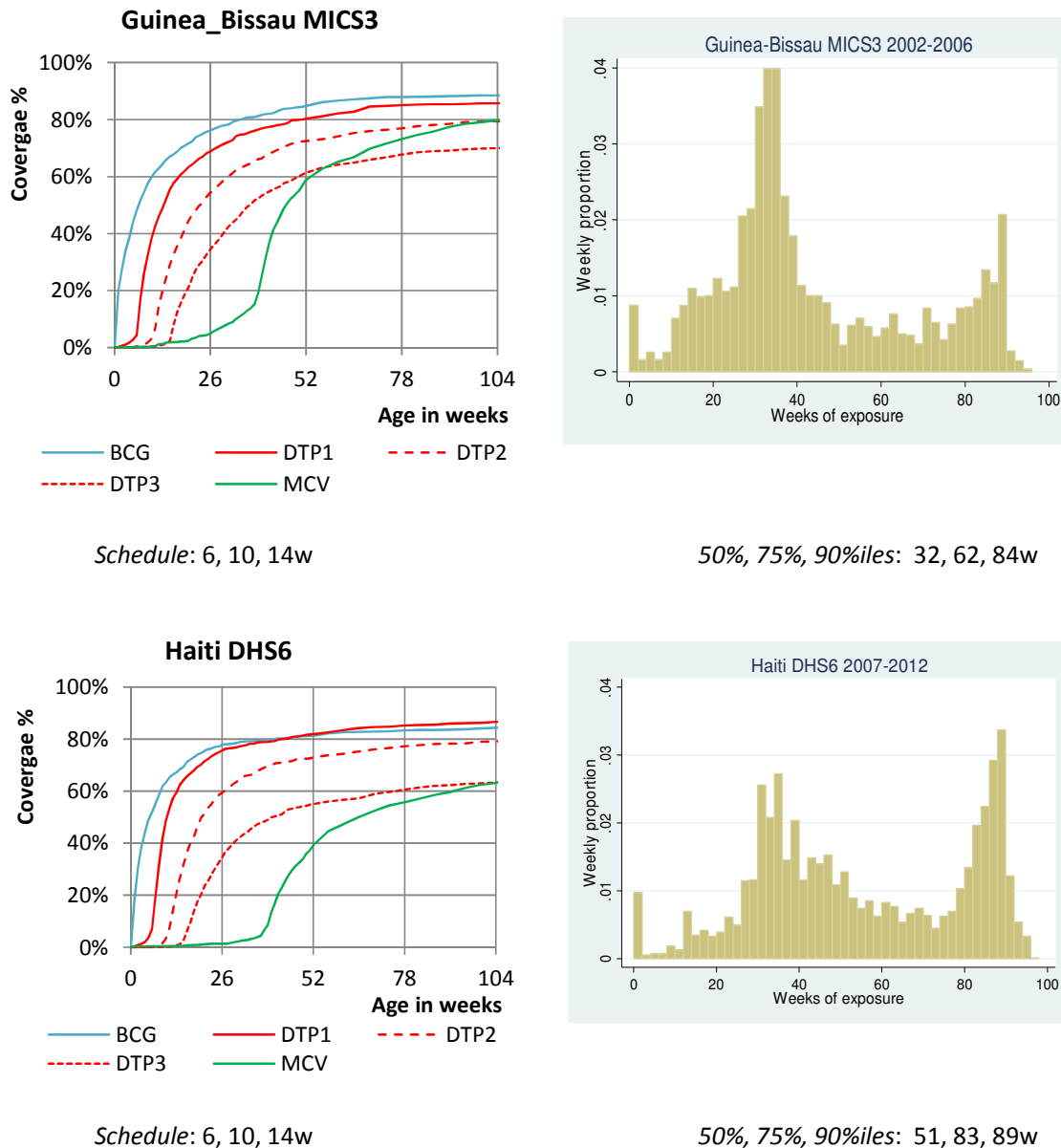
This relationship between DTP weeks and the schedule is shown in Figure 1, with data from Egypt and Peru. In each case there is a diagram on the left showing age-specific coverage for BCG, DTP1-3 and MCV, and the vaccine schedule underneath; and on the right there is a histogram showing the probability distribution of DTP weeks, with the 50th, 75th and 90th percentiles underneath. Egypt 2003-6 is an example of a country with high coverage for all five vaccine doses, with most given on time or close to it. The histogram for DTP weeks has a single sharp peak at around 30 weeks, close to the scheduled difference between DTP1 and MCV. Vaccination in Peru is slightly less prompt, particularly for DTP3, and also there is a marked difference in coverage between DTP1 and MCV. The histogram has one main peak which is later than in Egypt (at around 48 weeks, reflecting the longer gap between DTP1 and MCV in the schedule) and more spread out (reflecting the somewhat less timely programme). It also has a secondary peak at around 90 weeks. This is the result of children having had DTP but not MCV, and reflects the length of time between DTP1 in the schedule and the end of the follow-up period at age 24 months.

Figure 1: Vaccine coverage and DTP weeks: Egypt and Peru



Similar diagrams for Guinea-Bissau 2002-6 and Haiti 2007-12 are shown in Figure 2. The histograms for DTP weeks extend towards zero, indicating some children with small gaps between DPT1 and MCV, and both have the second peak at the right characteristic of lower coverage for MCV than for DTP. Both countries have relatively low coverage for scheduled vaccinations, and in the DHS and MICS reports on these two surveys it was mentioned that in both countries there had been vaccination campaigns during the period covered by the data.

Figure 2: Vaccine coverage and DTP weeks: Guinea-Bissau and Haiti



What % of children are given different vaccines on the same day?

The results of this analysis are given in Table 7, with results for each survey in Appendix Table 3. These tables cover some of the same ground as earlier sections but in a different way and with more detail. For each pair of vaccines or vaccine plus vitamin A, the denominator is the number of children who had both, and the numerator is the number of children who had both on the same day. Also instead of the first and last doses of DTP, figures are given for DTP1, DTP2 and DTP3 specifically.

For pairs of vaccines, BCG with DPT1 was far the most common combination; overall, about 6% of children who had had both were given them on the same day. The corresponding figures were 1% for DTP2 and MCV, and 2% for DTP3 with MCV. In general the figures for combinations were higher in surveys in the AFR and WPR regions and lower in surveys in the EMR and EUR regions. Overall, DTP1 with BCG was far more common in rural than in urban areas (8% vs 4%), and in the poorest wealth quintile than in the richest (9% vs 3%). This gradient was seen in all regions except EUR, where the combination was rare. In the countries with two or more surveys, the overall figure for DTP1 given on the same day as BCG fell from around 11% in the earlier surveys to 6% in more recent ones.

The question on vitamin A was not asked in a number of surveys, and this is shown as blanks in the relevant sections of Appendix Table 3. The summary figures are based only on the surveys that included the question. Eleven percent of children had vitamin A and MCV on the same day, and 1% had vitamin A with DTP3.

Table 7: For vaccines and vitamin A, % of children who had both given them on the same day.

Median values for surveys in each group of countries.

<i>Region</i>	<i>BCG +</i>	<i>BCG+</i>	<i>DTP1+</i>	<i>DTP2 +</i>	<i>DTP3+</i>	<i>BCG +</i>	<i>DTP3+</i>	<i>MCV+</i>
	<i>DTP1</i>	<i>DTP2</i>	<i>MCV</i>	<i>MCV</i>	<i>MCV</i>	<i>vitA</i>	<i>vitA</i>	<i>vitA</i>
Overall	6%	0%	0%	1%	2%	0%	1%	11%
AFR D	9%	1%	1%	1%	3%	1%	1%	13%
AFR E	7%	0%	0%	0%	2%	0%	1%	21%
AMR	6%	0%	0%	1%	2%	0%	2%	5%
EMR	5%	1%	0%	0%	1%	0%	0%	1%
EUR	1%	0%	0%	0%	1%	0%	0%	0%
SEAR	6%	0%	0%	0%	1%	0%	0%	38%
WPR	10%	1%	1%	2%	4%	7%	1%	6%

5 Discussion

From the evidence of these surveys, giving vaccines out of order or on the same day has been quite a common occurrence in some countries, but very rare in others. As a generalisation, these phenomena were more common in Africa, particularly in sub-region D, and less common in the European and East Mediterranean regions. However every region has countries where they are seen to a significant extent. Numbers of ‘DTP weeks’ are highly variable, but partly dependent on the local schedule and how well it is adhered to.

How robust is this evidence? The data are from well-established surveys, designed to be nationally representative. The broad similarity of the survey-based and the UNPOP estimates of infant mortality is reassuring although it appears that in some surveys either respondents are relatively healthy or very young deaths are under-reported. Also it is not safe to generalise from these surveys to whole regions,

particularly those with few surveys to go on. The countries that are included may well not be representative, because the focus of both survey series is on poorer and higher-mortality countries. On the other hand their high mortality makes them the countries of greatest public health interest.

In some surveys the proportion of children for whom the vaccination card, and hence data on vaccination order, are unavailable is clearly a matter for concern when interpreting these results. An arbitrary threshold of at least 40% of vaccinated children with cards was chosen as the basis for including surveys in the calculation of summary medians and comments in the text, but results are given for all surveys with over 20%, so that readers with knowledge of particular countries can use their own judgement. In a sensitivity analysis with the threshold at 60% there were 32 surveys left (11 from AFR). The % of children with their first dose of DTP before BCG, with their last DTP after MCV, and with their last DTP on the same day as MCV were the same as in the baseline analysis but the % with their first DTP on the same day as BCG dropped from 5% to 4%, and the median number of DTP weeks went up from 35 weeks to 36. With the threshold set at 70% there were only 17 surveys were left (3 from AFR). The method used for imputation was simple, and while giving less bias than assuming that children without vaccine dates would have had the same distribution of DTP weeks as children with dates, it will not have eliminated bias entirely.

Use of this kind of survey data involves a trade-off between excluding large numbers of children and truncating the length of follow-up. In this case the focus on children aged 24-59 months at the time of their mother's interview involved discarding data on about 40% of the subjects, but also excluding any vaccinations given after age 24m. Extension of the follow-up period to say 36m would have involved sacrificing another 20% of the data. Also this would have meant limiting the analysis to data from older children, and the proportion of children with vaccination cards available drops off with age. Thus recording of age at vaccination would have been more complete (72% rather than 67%) if the analysis had been restricted to children aged 24-35m at mothers' interview, but at the expense of sample size. The effect of excluding vaccinations after age 24m will be to overestimate the proportion of children for whom DTP is the last dose, but arguably a final dose of MCV after age 24m would be too late to provide protection against any adverse effects of DTP during the period of highest risk of mortality. Encouragingly, the survey data are becoming more complete.

How do these results compare with other community-based studies? In an analysis of surveillance data from 1986 to 2001 for the Matlab area of Bangladesh², children were given BCG on the same date as DTP1, DTP2 and DTP3 in 55%, 10% and 5% of cases respectively. The very high total of 70% is above the estimate of 63% found in the DHS data covering vaccinations in 2007-10, but the DHS study was rather later. In a community-based 3-monthly surveillance study of children born between 1987 and 1989 in 45 contiguous villages in India³, of the 2015 children who had had both DTP1 and BCG, in 27% the two vaccines were given together and in 32% BCG was given after DTP1. The corresponding figures in the DHS data for 2001-05 were 15% and 29%. Of 893 who had

been given DTP and MCV, 9% had them at the same time and 5% had DTP after MCV (DHS: 1% and 23%).

In a report by Welaga et al⁴ on data from trial of vitamin A supplementation in Ghana in 1989-91, on enrolment to the placebo group, 76% of the children with vaccination cards had had BCG with DTP, and 86% had had a dose of DTP either with or after MCV (14% and 17% respectively in the DHS data for 2004-07). In a community-based cohort study in Malawi by Aaby et al⁵ of children born in 1995-97, 22 (about 4%) children were given DTP and MCV on the same day (DHS 2006-09: 2%, MICS 2002-05: 5%). The actual number for whom DTP3 was the last given was not reported, but appears from a figure to be about 16%. This compares with 6% in DHS for 2006-09 and 10% in MICS for 2002-05. In surveillance data for 1998 and 2000 from one area in the Gambia⁶ with a population of about 17,000, 6% of children had had DTP after, or at the same time as, measles vaccine (MICS 2001-04: 30%).

Two more recent reports on this question from Guinea-Bissau give contrasting results. In data gathered between 2003 and 2009 from biannual surveillance of randomly selected villages⁷, in 5806 children given BCG by age 12m, 54% had received DTP before or with the BCG (MICS 2002-6: 33%). Among those given MCV by age 12m, 28% had received DTP with or after MCV (MICS 2002-6: also 28%). But the most recent data (2008-9) are from a health and demographic surveillance system covering a population of about 78,000. Of the children with vaccination cards, about 5% had BCG with or after DTP1, and about 4% had DTP with or after MCV⁸.

Most of these studies are in specific areas of the countries concerned, and quite substantial local variations around a national figure can be expected. However one point that does stand out is that much of the published data on out-of-order vaccination are from around twenty years ago or more. Some of the national surveys were also done some ago, but at least part of any apparent discrepancies between the results of national surveys and of more focussed studies can be attributed to the passage of time. It does appear that out-of-order, and same-day vaccinations are on the decline. As Ouédraogo et al point out, 'correct sequencing of childhood vaccinations has significantly improved in recent years in West Africa', and the limited information on trends from the survey data suggest that has also been happening elsewhere.

6 References

- 1 Aaby P, Benn C, Nielsen J, Lisse IM, Rodrigues A, Ravn H. Testing the hypothesis that diphtheria-tetanus-pertussis vaccine has negative non-specific and sex-differential effects on child survival in high-mortality countries. *BMJ Open*. 2012;2:e000707.
- 2 Breiman RF, Streatfield PK, Phelan M, Shifa N, Rashid M, Yunus M. Effect of infant immunisation on childhood mortality in rural Bangladesh: analysis of health and demographic surveillance data. *Lancet* 2004; 364: 2204-11.
- 3 Hirve S, Bavdekar A, Juvekar S, Benn CS, Nielsen J, Aaby P. Non-specific and sex-differential effects of vaccinations on child survival in rural western India. *Vaccine* 2012.
- 4 Welaga, P, Nielsen J, Adjuik M et al. (2012), Non-specific effects of diphtheria-tetanus-pertussis and measles vaccinations? An analysis of surveillance data from Navrongo, Ghana. *Trop Med & Int Hlth*, 17: 1492–1505.
- 5 Aaby P, Vessari H, Nielsen J et al. Sex differential effects of routine immunizations and childhood survival in rural Malawi. *Pediatr Infect Dis J* 2006; 25: 721-727.
- 6 Aaby P, Jensen H, Walraven G. Age-specific changes in the female-male mortality ratio related to the pattern of vaccinations: an observational study from rural Gambia. *Vaccine* 2006;24: 4701–08.
- 7 Hornshøj L, Benn CS, Fernandes M, et al. Vaccination coverage and out-of-sequence vaccinations in rural Guinea-Bissau: an observational cohort study. *BMJ Open* 2012;2:e001509.
- 8 Ouédraogo N, Kagoné M, Sié A, H. Becher H, Müller O. Timeliness and Out-of-Sequence Vaccination among Young Children in Burkina Faso –Analysis of Health and Demographic Surveillance System (HDSS). *Data Int J Trop Dis Hlth* 2013; 3: 45-56.