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Descriptive Finding

Relationship between vaccination and nutritional status in children: Analysis of recent Demographic and Health Surveys

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Contents

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Abstract

BACKGROUND
A body of evidence suggests that vaccines support the development of the immune system and also improve overall health.

OBJECTIVE
To study the effect of the complete basic vaccination schedule (Bacille Calmette-Guérin, i.e., BCG; measles; polio 3; and Diphtheria, Tetanus toxoids, and Pertussis, i.e., DTP3) on nutritional status of children under 2 years of age.

METHODS
Recent DHS data from 16 countries conducted after 2013 were used. After a bivariate descriptive analysis, a logistic regression analysis was conducted to predict the likelihood of underweight, stunting, and wasting by immunization status. A combined odds ratio was computed and adjusted for background variables.

RESULTS
A significantly higher prevalence of underweight was found among children with incomplete vaccination schedules in seven countries. Similarly, wasting and stunting were frequently observed in under-vaccinated children in four countries. Moreover, logistic regression adjusted for background variables revealed a relation between incomplete vaccination and underweight in Angola, Chad, and Guatemala (95% CI lower bound > 1). Combining data of all countries, underweight (adjusted Odds Ratio, aOR 1.21, 95% CI 1.11–1.31), wasting (aOR 1.18, 95% CI 1.05–1.33), and stunting (aOR 1.07, 95% CI 1.00–1.14) were associated with poor vaccination status. The overall effect was consistent with both sexes except the results for wasting for females and stunting for males, though insignificant.

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CONTRIBUTION

To our knowledge, this is the first paper assessing the relation between vaccination and nutritional status at a multi-country level with a huge dataset. Our analysis suggests a poor nutritional status in children with an incomplete vaccination schedule.

1. Introduction

The importance of immunizations in the decline of infant mortality has been widely recognized (Ozawa et al. 2017). Recent evidence suggests that the effect is not only due to the reduction of vaccine-preventable infections but also due to 'heterologous effects' on other diseases (Flanagan et al. 2013; Higgins et al. 2016; Nicoli and Appay 2017). Vaccines not only prevent specific infections but also prompt the development of the overall immune system (MacGillivray and Kollmann 2014). In particular, live vaccines (such as BCG and measles-containing ones) favor the development of innate and adaptive arms of the immune system (Freyne, Marchant, and Curtis 2015; Kleinnijenhuis et al. 2014; Kleinnijenhuis et al. 2012). This may improve immune responses against vaccines administered at the same moment (Ota et al. 2002) or even later (Libraty et al. 2014; Ritz et al. 2013). However, the most striking effect demonstrated so far is the lower incidence of infections (Rodrigues et al. 2006; Sorup et al. 2014; Valentiner-Branth et al. 2007) and of all-cause mortality (Higgins et al. 2016; Shann 2013) in vaccinated children.

As studies assessing the heterologous effects of vaccines have been conducted in a limited number of countries, we wanted to investigate the effect of complete vaccination on the health and nutrition of children at the multi-country level. Using data from recent Demographic and Health Surveys (DHS), we related the nutritional status of children against their vaccination status.

2. Data and methods

2.1 Data source

Data from the 20 countries where DHS were conducted from 2014 to 2016 were obtained from the DHS Program website (www.dhsprogram.com). Four of them (Afghanistan, Zimbabwe, Colombia, and Egypt) were excluded, as information on immunization and/or nutritional status was not available or not in a comparable form with other countries. DHS are periodic cross-sectional surveys conducted by the

Ministry of Health or Office of Central Bureau of Statistics of each country that collects data focusing on fertility, child mortality, immunization, maternal health, and nutritional status (Corsi et al. 2012). Surveys included in this study had a sample size ranging from 674 to 7,537 children, with response rates of above 96% (Table 1). Trained enumerators collected information after obtaining verbal informed consent. Ethical approvals were obtained from the review board of respective countries.

Table 1: Countries, survey year, total children aged 12–24 months, and total children with immunization and nutrition information

Region	Country	Survey year	Population[1] mid-2017 (millions)	Response rate for household surveys (%)	Total children aged 12–24 months	Children aged 12–24 months with complete immunization and nutritional information
Sub-Saharan Africa	Angola	2015–2016	28.6	99.0	5090	2318
	Chad	2014–2015	14.9	99.0	6185	3674
	Ethiopia	2016	105.0	98.0	3947	3683
	Ghana	2014	28.8	99.0	2204	1091
	Kenya	2014	49.7	97.0	7537	7121
	Lesotho	2014	2.2	98.0	1227	561
	Malawi	2015–2016	18.6	99.0	6491	2038
	Rwanda	2014–2015	12.3	99.0	3136	1503
	Senegal	2016	15.8	98.6	2323	2199
	Tanzania	2015–2016	57.5	98.0	3951	3730
South and Southeast Asia	Bangladesh	2014	164.7	99.0	3197	2964
	Cambodia	2014	15.9	99.0	2828	1831
	Myanmar	2015–2016	53.4	98.0	1634	1470
	Nepal	2016	29.4	99.0	1953	953
Latin America and Caribbean	Guatemala	2014–2015	16.9	99.0	4855	4753
North Africa/West Asia/Europe	Armenia	2015–2016	3.0	96.0	674	612
Total	–	–	–	–	57232	40501

1 https://www.prb.org/pdf17/2017_World_Population.pdf.

2.2 Variables definition and analysis

Undernutrition is measured as stunting (low height for age), wasting (low weight for height), and underweight (low weight for age). Nutritional status is an important measure of overall health, and poor nutrition results in higher mortality and lower

quality of life (Lorem, Schirmer, and Emaus 2017). Stunting is a critical variable to define children's health, as stunting is characterized by several pathologies, and it has consequences on the future growth and potential of individuals (Prendergast and Humphrey 2014). Wasting is more reflective of acute undernutrition primarily due to short-term health issues (Saaka and Galaa 2016).

The primary dependent variables of the study are undernutrition measured as underweight, stunting, and wasting among children between 12 and 24 months of age. Any child below two standard deviations (–2SD) of reference weight for their specific age according to the World Health Organization (WHO) standard is classified as 'underweight.' Any child below –2SD of reference height for their specific age according to the WHO standard is classified as 'stunted.' Any child below –2SD of reference weight for their specific height according to the WHO standard is classified as 'wasted.' Children were analyzed by sex: both sexes combined, males, and females.

The independent variable of the study is immunization status, measured with reference to basic vaccination. Basic vaccination was categorized as 'complete' if all eight basic vaccines (BCG, measles, polio 1-2-3, and DTP 1-2-3) were received by a child.

After a bivariate analysis, a logistic regression to predict the likelihood of undernutrition based on immunization status was conducted. The analysis was then adjusted for age, place of living, sex of the child, wealth quintile, mother's education, breastfeeding, and perceived weight at birth. The odds of underweight, stunting, and wasting as a result of vaccination status were compared between countries.

Bivariate and regression analysis was done using SPSS 17, and pooled analysis [meta-analysis, including test of heterogeneity (Higgins et al. 2003)] was computed using Stata SE 12. The analysis was adjusted for sampling weights and survey design for each country, as recommended by DHS.

3. Results

We analyzed data from 40,501 children between 12 to 24 months of age in 16 countries. As shown in Table S-1, mothers were mostly living in rural areas, literate, and breastfeeding, and around 45% were from poor families. Underweight rates were between 0.6 and 34.2%, stunting rates between 7.8 and 51.7%, and wasting rates between 0.9 and 15.2%. Coverage of BCG, measles, polio (3 doses), and DTP (3 doses) vaccinations were above 90% in 12, 4, 3, and 7 countries respectively. The percentage of children with a complete basic vaccination schedule was between 25.2% (Chad) and 86.5% (Armenia).

Generally, the bivariate analysis showed higher prevalence of underweight children among those with incomplete basic vaccinations, and the difference was statistically significant in Angola, Chad, Ethiopia, Guatemala, Kenya, Myanmar, and Senegal (Table 2). Similarly, stunting was significantly more prevalent in children with incomplete vaccinations in Angola, Bangladesh, Chad, and Guatemala, and wasting in Angola, Chad, Kenya, and Myanmar respectively.

Table 2: Underweight, stunting, and wasting by vaccination status

	Basic vaccination schedule[1]				
	Underweight				
	Complete		Incomplete		
	n Total	n Underw. (%)	n Total	n Underw. (%)	p Value
Angola	689	88 (12.8)	1629	376 (23.1)	<0.001
Armenia	529	4 (0.7)	83	0 (0.0)	0.550
Bangladesh	2537	854 (33.7)	423	159 (37.5)	0.280
Cambodia	1418	315 (22.2)	412	108 (26.2)	0.228
Chad	921	213 (23.1)	2730	1031 (37.8)	<0.001
Ethiopia	1386	298 (21.5)	2297	612 (26.6)	0.019
Ghana	841	119 (14.2)	249	31 (12.3)	0.521
Guatemala	3595	508 (14.1)	1159	205 (17.7)	0.016
Kenya	5189	573 (11.0)	1911	261 (13.7)	0.015
Lesotho	434	50 (11.4)	128	9 (6.9)	0.184
Malawi	1530	152 (9.9)	508	64 (12.7)	0.146
Myanmar	887	147 (16.5)	582	137 (23.5)	0.004
Nepal	750	215 (28.6)	203	68 (33.6)	0.266
Rwanda	632	67 (10.6)	871	91 (10.4)	0.908
Senegal	1533	207 (13.5)	666	118 (17.8)	0.025
Tanzania	2842	398 (14.0)	888	153 (17.3)	0.056

	Basic vaccination schedule[1]				
	Stunting				
	Complete		Incomplete		
	n Total	n Stunt. (%)	n Total	n Stunt. (%)	p Value
Angola	689	259 (37.6)	1629	817 (50.2)	<0.001
Armenia	529	40 (7.6)	83	8 (9.2)	0.650
Bangladesh	2537	969 (38.2)	423	208 (49.2)	0.001
Cambodia	1418	463 (32.7)	412	164 (39.9)	0.052
Chad	921	395 (42.9)	2730	1349 (49.4)	0.012
Ethiopia	1386	589 (42.5)	2297	1059 (46.1)	0.185
Ghana	841	175 (20.8)	249	67 (26.9)	0.109
Guatemala	3595	1821 (50.7)	1159	635 (54.8)	0.045
Kenya	5189	1645 (31.7)	1911	651 (34.0)	0.141
Lesotho	434	156 (35.9)	128	53 (41.5)	0.276
Malawi	1530	614 (40.1)	508	212 (41.7)	0.606
Myanmar	887	267 (30.1)	582	207 (35.5)	0.066
Nepal	750	312 (41.6)	203	80 (39.5)	0.647
Rwanda	632	286 (45.2)	871	403 (46.3)	0.716
Senegal	1533	307 (20.0)	666	160 (24.0)	0.063
Tanzania	2842	1167 (41.1)	888	372 (41.9)	0.722

Table 2: (Continued)

	Basic vaccination schedule[1]				
	Wasting				
	Complete		Incomplete		
	n Total	n Wast. (%)	n Total	n Wast. (%)	p Value
Angola	689	22 (3.2)	1629	111 (6.8)	0.012
Armenia	529	15 (2.7)	83	3 (3.6)	0.701
Bangladesh	2537	357 (14.1)	423	56 (13.3)	0.710
Cambodia	1418	136 (9.6)	412	38 (9.3)	0.876
Chad	921	95 (10.4)	2730	461 (16.9)	<0.001
Ethiopia	1386	144 (10.4)	2297	262 (11.4)	0.501
Ghana	841	51 (6.1)	249	9 (3.5)	0.135
Guatemala	3595	31 (0.9)	1159	12 (1.0)	0.684
Kenya	5189	190 (3.7)	1911	99 (5.2)	0.026
Lesotho	434	16 (3.8)	128	5 (3.6)	0.954
Malawi	1530	39 (2.6)	508	17 (3.4)	0.385
Myanmar	887	52 (5.9)	582	54 (9.3)	0.031
Nepal	750	65 (8.7)	203	26 (13.0)	0.144
Rwanda	632	14 (2.2)	871	21 (2.4)	0.851
Senegal	1533	106 (6.9)	666	62 (9.3)	0.051
Tanzania	2842	108 (3.8)	888	47 (5.3)	0.088

[1] Include: BCG, measles, polio (3 doses), DTP (3 doses).

The effects on underweight were confirmed by the adjusted logistic regression model in Angola, Chad, and Guatemala (Figure 1), where a higher likelihood of underweight in children with the incomplete basic vaccination schedule was observed. Interestingly, these three countries have a different percentage of underweight in children (20%, 34%, and 15% respectively), suggesting that the variability between countries in anthropometric measures does not affect the strength of the association. However, the model did not confirm any of the associations between vaccination schedule and stunting. Interestingly, in Chad and Myanmar, higher probabilities of wasting in children with the incomplete basic vaccination schedule were observed. Notably, the meta-analysis of different countries revealed an association between incomplete vaccination and underweight (aOR 1.21, 95% CI 1.11–1.31) as well as wasting (aOR 1.18, 95% CI 1.05–1.33) but not for the stunting (aOR 1.07, 95% CI 1.00–1.14). Heterogeneity only was statistically significant ($p < 0.05$) for underweight analysis (for both sexes combined).

Figure 1: Adjusted Odd Ratios (aORs) for underweight, stunting, and wasting in children with an incomplete basic vaccination schedule

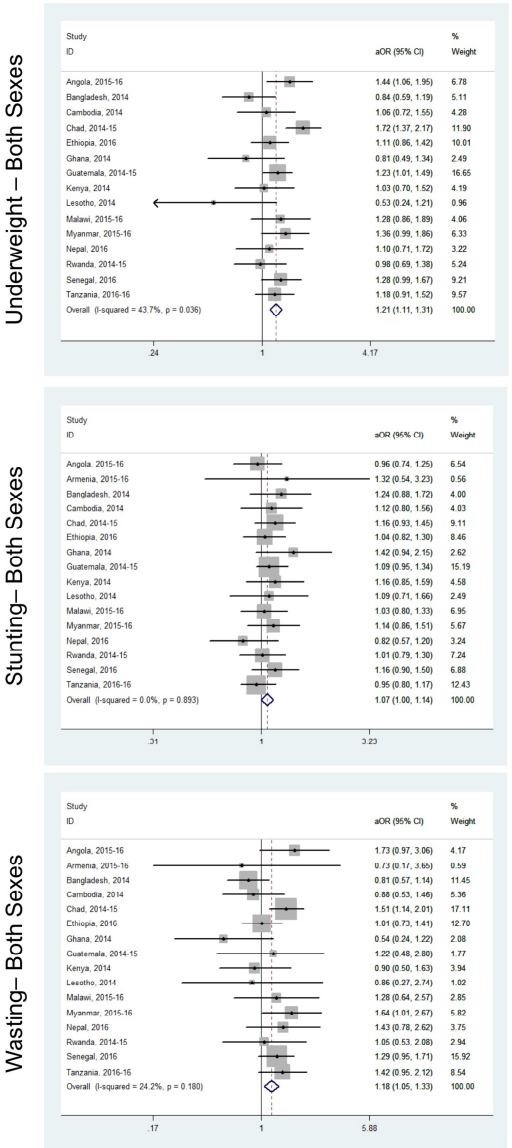
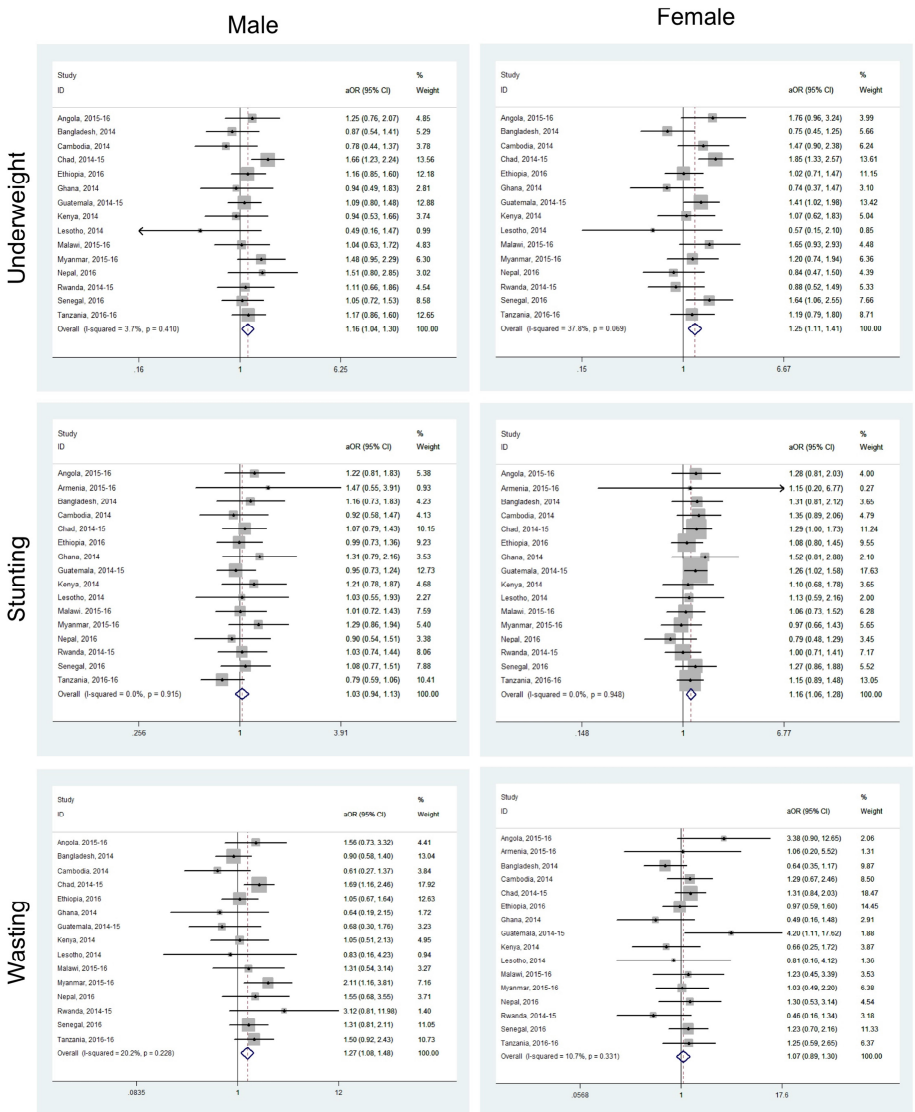


Figure 1: (Continued)



Notes: Adjusted model controls for age, place of living, sex of child, wealth quintile, mother's education, breastfeeding, and perceived weight at birth. Bars represent 95% confidence interval. Results are presented combining both sexes after stratification for sex.

We also analyzed results for sex-specific effects of a complete immunization schedule on nutritional status. In both male and female groups, the meta-analysis revealed an overall higher probability of underweight in children with an incomplete basic vaccination schedule (male aOR 1.16, 95% CI 1.04–1.30; female aOR 1.25, 95% CI 1.11–1.41). However, stunting was associated with an incomplete basic vaccination schedule in females (aOR 1.16, 95% CI 1.06–1.28) but not significant for males (aOR 1.03, 95% CI 0.94–1.13). Wasting was associated with an incomplete basic vaccination schedule only in males (aOR for the meta-analysis 1.27, 95% CI 1.08–1.48).

4. Discussion

In this study, we analyzed the heterologous vaccine effects on overall health as measured by underweight, stunting, and wasting in children, using DHS data from 16 countries representing different continents. As previous studies of non-specific effects of vaccines were usually performed in single countries, we deliberately chose to analyze countries with different characteristics to see if the effect could be generalized or rather associated to country-specific features. Overall, the meta-analysis showed a higher likelihood of poor nutritional status in children with incomplete immunization, as reported previously from India (Anekwe and Kumar 2012). Other reports have shown reduced all-cause mortality (Kristensen, Aaby, and Jensen 2000; McGovern and Canning 2015) as well as reduced morbidity (Otto et al. 2000) and antibiotic use (Wilby and Werry 2012) in fully immunized children, suggesting that immunization not only helps to prevent specific disease of focus but also leads to overall improvements in health.

Interestingly, after stratification for sex, all results showed that incomplete vaccinations led to higher underweight, stunting, and wasting, and the results were statistically significant except for male children for stunting, and female children for wasting. Some sex-specific differences in heterologous effects of vaccines have been postulated, usually in favor of female children (Sankoh et al. 2014). Further studies and different experimental approaches are needed to confirm and better investigate sex-specific associations for wasting and stunting.

One of the limitations of the study is related to the cross-sectional design, with the exposure and outcome being measured simultaneously, thus it is not possible to determine causality, mainly because we cannot assure temporality. In this sense, the presence of reverse causality is possible. In respect to this, we cannot exclude the 'healthy vaccine bias' or, more in general, to the 'healthy user effect.' It has indeed been demonstrated that healthy individuals usually tend to be vaccinated more frequently as well as to undertake other preventive behaviors, and these biases have also

been suggested to affect several vaccine effectiveness studies (Remschmidt, Wichmann, and Harder 2015; Shrank, Patrick, and Brookhart 2011). Despite the fact that we adjusted for a number of variables that may, directly or indirectly, be connected with health, we cannot exclude this hypothesis and, therefore, the interpretation of our results that children with good nutritional status tend to be vaccinated more frequently should be considered while interpreting the data. We could not control the results for some variables that may be related to nutritional status and immunization, such as those related to child morbidity conditions or serum antibody levels, as such data were not collected in DHS. In addition, both the nutritional and vaccination status of children could be an indication of the 'wealth' of the health system in specific countries. However, in our study, the frequency of children with incomplete vaccination status did not significantly correlate with the percentage of undernourished children (data not shown). Thus, our analysis rather supports previous reports indicating that basic vaccinations do not harm children and their health, but complete immunization status shows a positive effect on overall health and nutrition. Since our data cover countries from different continents, we can also conclude that this is not dependent on the geographical location.

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