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Is Colombia reaching the goals on infant immunization coverage? A quantitative survey from 80 municipalities



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ABSTRACT

Objectives: This study aimed to evaluate the coverage of the Colombian Expanded Program on Immunization among children less than 6 years old, to evaluate the timeliness of immunization, to assess the coverage of newly introduced vaccines, and to identify factors associated with lack of immunization. *Methods:* We conducted a cross-sectional survey in 80 municipalities of Colombia, using a two-stage cluster random sampling. We attempted to contact all children less than 6 years old living in the sampled blocks, and asked their caregivers to provide immunization record cards. We also collected basic sociode-mographic information.

Results: We reached 81% of the attempted household contacts, identifying 18,232 children; of them, 14,805 (83%) had an immunization record card. Coverage for traditional vaccines was above 90%: BCG (tuberculosis) 95.7% (95%CI: 95.1–96.4), pentavalent vaccine 93.3% (92.4–94.3), MMR (measles, mumps, rubella) initial dose 94.5% (93.5–95.6); but it was lower for recently introduced vaccines: rotavirus 80% (77.8–82.1), influenza 48.4% (45.9–50.8). Results for timely vaccination were not equally successful: pentavalent vaccine 44.2% (41.4–47.1), MMR initial dose 71.2% (68.9–73.4). Mother's education was significantly associated with higher immunization odds. Older age, a greater number of siblings, low socioeconomic status, and not having health insurance were significantly associated with lower immunization odds. There was significant heterogeneity in immunization rates by municipality across the country.

Conclusions: Although absolute immunization coverage for traditional vaccines met the goal of 90% for the 80 municipalities combined, disparities in coverage across municipalities, delayed immunization, and decline of coverage with age, are common problems in Colombia that may result in reduced protection. Newly introduced vaccines require additional efforts to reach the goal. These results highlight the association of health inequities with low immunization coverage and delayed immunization. Identification of vulnerable populations and their missed opportunities for vaccination may help to improve the reach of immunization programs.

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1. Introduction

Child immunization is one of the most cost-effective public health interventions available [1], but continuous evaluation and

monitoring of immunization programs are necessary to keep successful control of communicable diseases [2]. A key performance indicator of immunization programs is the coverage level, i.e. the proportion of children of a target age receiving a vaccine or set of vaccines. The World Health Organization (WHO) has set the goal to reach a 90% coverage for all vaccines in national immunization programs by 2020 [2]. The WHO has been collecting and publishing data on this indicator by country at least since 1980 [3]; thus, in a global setting, national coverages may be readily available for comparisons across groups and along time. National coverage rates in the Americas region are among the highest in the world, but this



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summary measure may hide sub-national disparities. In 2012, about 50% of the municipalities in Latin America and the Caribbean were below 95% coverage, and 23% were below 80% [4], thus creating pockets of low coverage that represent a risk for reemergence of vaccine-preventable diseases.

As middle-income countries strengthen their immunization programs, the national coverage may meet the goal proposed by the WHO, especially for vaccines that have been in use for decades [5]. However, three key problems may be missed when using an evaluation approach centered on national coverage: (1) the importance of timely vaccination may be overlooked; (2) national averages may hide within-country heterogeneities in immunization coverage; and (3) coverage may be lower for newly introduced vaccines.

Colombia reports a high national coverage [6], but those three issues are a concern. First, in spite of the paucity of data regarding timely vaccination, at least two Colombian studies [7,8] have identified delayed vaccination as a potential barrier for the success of immunization programs. Second, Colombia is a very heterogeneous country comprising 1102 municipalities (i.e., districts), the political and administrative subdivisions ultimately responsible for implementing, administering and evaluating the immunization program at the local level. Since their cultural, social and economic characteristics are very diverse, pronounced inequalities in immunization rates across municipalities are expected. In addition, it is estimated that 76% of the total population lived in urban areas as of 2012, and nearly 50% lived in the 10 major cities [9]. As a consequence, an average national immunization rate may be easily driven by the major urban centers, which are likely to have better coverage than other territories. Third, three vaccines have been added to the Colombian Expanded Program on Immunization (CEPI): seasonal influenza (added in 2007), oral rotavirus vaccine (2009), and conjugate pneumococcal vaccine (2010). However, adherence to this new expanded immunization schedule has not been thoroughly evaluated.

Following these considerations, the aims of the present study were: (1) to evaluate the differences between the *absolute* immunization coverage and *timely* immunization coverage in children less than 6 years old in a sample of municipalities in Colombia in 2012; (2) to evaluate the heterogeneity in immunization rates across municipalities; (3) to evaluate the coverage of the vaccines recently added to the CEPI; and (4) to identify the sociodemographic factors associated with lack of vaccination and late administration of vaccines among children less than 6 years in Colombia in 2012.

Improved understanding of the factors associated with immunization coverage and timely vaccination will help to implement appropriate interventions, or redirect the program efforts to secure the coverage of population groups with non-modifiable vulnerabilities.

2. Materials and methods

2.1. Study design and setting

Between June and December 2012, we conducted a crosssectional survey of children less than 6 years of age residing in 80 municipalities of Colombia. These municipalities were selected by the Colombian Ministry of Health (CMH) in a non-probabilistic manner to cover the spectrum of the cultural, geographical and demographic heterogeneity of the country; thus, the municipalities were distributed across the five geographical regions of Colombia (the Andean region, the Amazon basin, the Caribbean coast, the Pacific coast, and the Eastern plains), the spectrum of urbanicity, including large urban centers as well as predominantly rural areas, and the range of administrative coverage reports, including municipalities with high (>95%) and low (<70%) coverage reports from the previous year. Within those municipalities, which can be deemed as strata, we used a two-stage cluster sampling strategy, with census block groups as primary sampling units, and the blocks within them as secondary units. At both stages, the sampling units were selected using probabilities of inclusion proportional to the size of the total population living in each unit, as described by Särndal et al. [10]. Once a block was selected in the sample, all the households in that block were surveyed to identify all children in the targeted age interval. The sampling frame and population sizes were supplied by the Colombian National Administrative Department of Statistics (i.e. the *cartographic statistical frame* referenced in the Methodological Summary Sheet of the Colombian census of 2005 [11]).

2.2. Participants

Children under 6 years of age residing in the selected blocks were considered eligible for the survey if: (1) there was at least one adult in the household during the interview, (2) the adult consented to serve as informant for the survey, and (3) the informant reported that the visited household was the primary place of residence of the child. When it was not possible to locate an informant at the first attempt, we did up to two additional visits to maximize the chance of including all eligible children.

2.3. Data sources and data collection

The CEPI uses immunization record cards to keep track of the immunization history of all children in the country. Each time a vaccine is administered, it is recorded on the immunization card, which is kept by the child's caregivers. In this survey, the informant at each household was asked to provide immunization record cards for all eligible children living in the residence. When record cards were not available, this was annotated along with the reason reported for not having it. Information regarding immunization status and dates was directly taken from the immunization record cards. In addition, the informants were asked to respond a questionnaire collecting socio-demographic information about the household, the respondent, and the child.

All field procedures adhered to international guidelines on ethical conduct of research [12], and were approved by the institutional review board at the National University of Colombia School of Medicine.

2.4. Variables and measures

Vaccines included in the CEPI as of 2012 were BCG (tuberculosis), hepatitis B at birth, oral polio, pentavalent (DTP, *Haemophilus influenzae* type b, Hepatitis B), oral rotavirus, pneumococcal conjugate, seasonal influenza virus, MMR, DTP booster doses, and yellow fever. Several of these are administered simultaneously according to a schedule based on child's age. For the purpose of this paper we focused on two main subsets of vaccines: (1) an indicator subset of the basic schedule (BCG, pentavalent, MMR, DTP), selected to reflect the different ages at which vaccines should be administered, and (2) the subset of those vaccines more recently introduced to the CEPI (rotavirus, pneumococcal conjugate, and influenza virus).

For each subset, we evaluated *absolute* and *timely* coverages. *Absolute coverage* was defined as the proportion of children having the number of doses of each vaccine required for their age, even if attained through the use of a catch-up schedule. *Timely coverage* was defined as the proportion of children receiving every single dose within the time frame specified in the immunization schedule and guidelines published by the CMH [13]. For example, if a child

who was 9 months old at the time of the survey had a BCG vaccine administered at birth, and 3 doses of the pentavalent vaccine administered at 5, 7, and 9 months old, then the child was considered completely vaccinated according to the absolute coverage indicator, but was not counted as timely vaccinated since the immunization schedule specifies that pentavalent vaccine should be administered at 2, 4 and 6 months old. Details about the acceptable Colombian immunization timeframe are provided later in this paper. Children still lacking at least one dose of a vaccine that they should have already received according to their age by the date of interview were deemed as *incompletely immunized*.

We also collected information about socioeconomic position (SEP), defined according to Colombian law [14] as an ordinal variable with 6 strata, where 1 is the more deprived category and 6 is the wealthiest; this measure is assigned by municipal governments to geographically defined groups of households and is linked to the cost of utilities, but also to rent, real estate prices, and taxes. Additional information collected during the interview included status as internally displaced by the armed conflict (yes vs. no), time residing in the municipality, maximum education level attained by the informant (complete high-school or above vs. less than high-school), employment status of the mother (paid employment vs. unpaid/unemployed), and self-identification as belonging to a racial/ethnic minority (yes vs. no). Finally, the child's gender, birth date, birth order, number of siblings, and affiliation to the health system (insured in the regular contributive regime, in any of the special regimes, in the subsidized regime, or not insured) were collected

2.5. Statistical analyses

We estimated ratios of vaccinated and timely vaccinated children to the total number of children with an immunization record card, at the municipality level and for the 80 municipalities combined. We estimated totals for the numerator and the denominator of each ratio using expansion factors inverse to the inclusion probabilities of the sampled units. Then, we calculated the ratios along with their bounded 95% confidence intervals (CIs). The standard errors used in the CIs calculation took into account the intraclass correlation coefficients and sampling weights to adjust for the complex design effect of the survey.

Finally, we calculated odds ratios (ORs) to estimate the association of sociodemographic factors with absolute immunization coverage and timeliness of vaccine administration. We used generalized linear latent and mixed models to simultaneously adjust for the correlation induced by the sampling scheme, to evaluate between-municipalities differences in vaccination coverage, and to allow for random intercepts accounting for betweencluster differences in the baseline odds of immunization that remained unexplained by the variables in the models at the municipality, census block group, and block levels.

All the analytical procedures were conducted using Stata Statistical Software release 12.1 [15], along with the Stata program gllamm, documented by Rabe-Hesketh and Skrondal [16], for the generalized linear latent and mixed models. All procedures used a statistical significance level α = 0.05.

3. Results

In total, we identified 18,232 children living in 12,846 households across 80 municipalities (successful contact rate at the household level = 81%). Demographic data were obtained for 17,860 children whose parents agreed to participate in the survey (participation rate among successfully contacted = 98%). Of them, 14,805 (82.9%) had an immunization card available at the time of the interview. Table 1 provides a summary description of the 14,805 children with an immunization card. Among the 3055 without an immunization card, only 0.72% reported not having it due to not being vaccinated. According to the informants, other reasons for not having the immunization record card were that it was kept in a relative's house (45%), it was lost (16%), or it was archived in a daycare facility (16%).

The overall estimated averages for absolute and timely immunization coverage with different vaccines in the 80 municipalities are shown in Tables 2 and 3, respectively. The above defined indicator subset of vaccines had an overall absolute coverage of 78.1% (95% CI: 76.6–79.5), whereas timely coverage for this subset was 32.7% (95% CI: 31.0–34.4). Only 13 of the 80 evaluated municipalities had an absolute immunization coverage above the 90% goal, while 21 had an absolute coverage below 70%. Regarding timely coverage, no single municipality achieved the proposed goal of 90% for the same indicator subset of vaccines, with point estimates ranging from 8% to 52%. Mean delays in immunization with the different vaccines are presented in Table 4, along with the acceptable immunization timeframe according to the guidelines of the CMH.

Multivariable analyses using generalized linear latent and mixed models showed that child's age, number of siblings, belonging to the lowest SEP category, identifying as racial/ethnic minority, and lack of health insurance, were all inversely and significantly associated with immunization status in terms of absolute coverage (Table 5); by contrast, a mother completing high

Table 1

Sociodemographic characteristics of study participants in a survey of immunization coverage with an indicator vaccine schedule (BCG, pentavalent, MMR, DTP) among children less than 6 years of age living in 80 municipalities of Colombia in 2012.

variables ^a	Total n = 14,805	Incompletely immunized n = 3513	Immunized n = 11,292	Timely immunized n = 4416
Male gender: n (%)	7624 (52.0)	1787 (51.5)	5837 (52.1)	2273 (51.8)
Age in years: mean (sd)	2.9 (1.7)	3.6 (1.7)	2.6 (1.6)	1.8 (1.6)
Belonging to the lowest SEP category: n (%)	8635 (59.7)	2261 (66.3)	6374 (57.7)	2325 (53.5)
Mother completed high school: n (%)	7424 (50.8)	1558 (45.1)	5866 (52.5)	2545 (58.0)
Mother is a paid worker: n (%)	4689 (32.1)	1070 (31.0)	3619 (32.5)	1362 (31.3)
Self-identification as belonging to an ethnic minority: n (%)	7200 (50.0)	1817 (53.7)	5383 (48.9)	2115 (49.0)
Health insurance: n (%)				
Not insured	1201 (8.28)	365 (10.7)	836 (7.5)	348 (8.0)
Subsidized health insurance	8917 (61.5)	2140 (62.6)	6777 (61.2)	2400 (55.4)
Contributive health insurance	3821 (26.4)	772 (22.6)	3049 (27.5)	1394 (32.2)
Special regimes	561 (3.9)	140 (4.1)	421 (3.8)	190 (4.4)
Number of siblings: mean (sd)	1.3 (1.4)	1.6 (1.6)	1.2 (1.4)	1.0 (1.2)
Time living in municipality > 1 year: n (%)	13,464 (94.4)	3141 (93.9)	10,323 (94.5)	4054 (94.5)
Internally displaced by the armed conflict: n (%)	2491 (17.0)	709 (20.4)	1782 (15.9)	638 (14.6)

^a Percentages shown here may differ slightly from those calculated directly from column totals due to missing data. No single variable had more than 3.6% missing values.

Table 2

Average immunization coverage for different vaccines in Colombia in 2012, estimated from a survey of children less than 6 years of age living in 80 municipalities

Type of vaccine	Average coverage estimate	95% CI for the average	Range of coverage across municipalities
BCG at birth	95.7%	95.1-96.4	77.2–100
Hepatitis B at birth	91.9%	91-92.8	64.6-100
Pentavalent, 3 doses	93.3%	92.4-94.3	72.8-100
DPT, 1st booster dose	87.9%	86.4-89.4	59.5-100
DPT, 2nd booster dose	66.4%	62.6-70.1	7.0–100
Yellow fever, single dose	91.6%	90.2-93.1	67.6-100
MMR, initial dose	94.5%	93.5–95.6	62.5-100
MMR, booster dose	57.1%	52.7-61.5	8.0-98.9
Oral polio, three initial doses	93.8%	92.8-94.8	31.1-100
Oral polio, first booster dose	89.8%	88.7–91	60.0-100
Oral polio, second booster dose	69.8%	65.9-73.6	7.0–100
Influenza, two doses	48.4%	45.9-50.8	13.5-86.4
Rotavirus, two doses	80.0%	77.8-82.1	41.8-100
Pneumococcal conjugate, two initial doses	77.9%	75.5-80.3	37.0-100
Pneumococcal conjugate, booster dose	14.6%	13.1-16.1	1.4–32.1
Indicator subset (BCG, pentavalent, MMR, DTP)	78.1%	76.6–79.5	46.3-96.8

Table 3

Average timely immunization coverage for different vaccines in Colombia in 2012, estimated from a survey of children less than 6 years of age living in 80 municipalities.

Type of vaccine	Average timely coverage estimate	95% CI for the average	Range of coverage across municipalities
BCG at birth	87.7%	86.6-88.8	63.5-98.2
Hepatitis B at birth	86.9%	85.8-88	55.1-97.4
Pentavalent, 3 doses	48.9%	47.1-50.7	19.0-68.8
DPT, 1st booster dose	44.4%	42.1-46.7	9.7-69.0
DPT, 2nd booster dose	61.8%	58.1-65.4	7.0-93.9
Yellow fever, single dose	71.7%	69.6-73.7	40.4-90.1
MMR, initial dose	75.0%	73.1–77	38.2-90.8
MMR, booster dose	48.3%	43.5-53.2	8.0-93.4
Oral polio, three initial doses	49.6%	47.9-51.3	17.2–71.4
Oral polio, first booster dose	45.9%	43.6-48.2	17.6–70.8
Oral polio, second booster dose	66.1%	62.3-69.8	7.0-100
Influenza, two doses	7.4%	6.6-8.1	1.0-18.3
Rotavirus, two doses	66.2%	64.2-68.3	32.0-88.9
Pneumococcal conjugate, two initial doses	47.3%	44.8-49.8	11.8–95.1
Pneumococcal conjugate, booster dose	11.2%	10-12.4	0.9-31.0
Indicator subset (BCG, pentavalent, MMR, DTP)	32.7%	31-34.4	7.9–51.7

school or above was associated with a 16% higher odds of being immunized.

Regarding timely vaccination coverage, we also found that child's age, number of siblings, belonging to the lowest SEP category, lack of health insurance, and having subsidized health insurance, were inversely associated with timely immunization status. On the other hand, children whose mother completed high school, children with older siblings, and those whose families were living in the town for more than one year had higher odds of timely immunization. In contrast to what was observed for absolute coverage, identifying as a racial/ethnic minority was not associated with timely immunization (Table 5). A graphical summary of the main findings described above is presented in Fig. 1.

In the absolute coverage analysis, we found statistically significant and sizable heterogeneities in the baseline odds of immunization at the municipality level, the census block group level, and the block level (p-values < 0.0001 from likelihood ratio tests for the contribution of random intercepts). Random effects for heterogeneity in the baseline odds of timely immunization were also significant at the municipality and census block group levels, but not at the block level.

4. Discussion

This survey evaluated the differences between absolute and timely immunization rates among children less than 6 years in Colombia in 2012. While absolute immunization coverage is routinely estimated by countries and reported by the WHO and UNI-CEF as part of the surveillance of immunization programs, thus allowing comparisons between countries and along time [3], it may be insufficient to describe some of the more recent challenges experienced by immunization programs, such as the persistence of low coverage pockets, and the missed opportunities for vaccination resulting in untimely immunization [4]. In this study, the observed gap between absolute and timely coverage was as large as 40 percent points for pentavalent (three doses) and oral polio (three initial doses) vaccines, suggesting that absolute immunization coverage may importantly overestimate the success of the CEPI, and that indicators of timeliness of immunization, in addition to indicators of absolute coverage, may help to depict a more comprehensive evaluation of the performance of immunization programs.

The observed discrepancies are consistent with studies in other countries [17–20] that have raised questions about the utility of absolute coverage as an indicator of success of the immunization programs. Since absolute coverage does not necessarily reflect timely administration of vaccines, it may be a biased estimator of the fraction of the population truly protected [19], and relying exclusively on it may place the population at risk of outbreaks [20]. On the other hand, routine estimation of indicators of timeliness of immunization may suffer from challenges related to data quality and availability. In that regard, the relative advantages and disadvantages of different data sources for the estimation of absolute coverage have been previously described [21,22], and the same strengths and limitations apply to estimators of timely

Table 4

Ranges of age for timely immunization as defined in the Colombian Expanded Program of Immunization, and mean delay in immunization (days) among children less than 6 years of age living in 80 municipalities of Colombia in 2012.

Type of vaccine	Range of timely administration as defined in the Colombian Expanded Program of Immunization	Mean (SD) delay in days counted from last possible day of timely administration	n delayed
BCG at birth	From 0 to 28 days of life	128 (244)	1369
Hepatitis B at birth	From 0 to 28 days of life	135 (271)	876
Pentavalent, 3 doses	At 2, 4 and 6 months; each dose with a 1 month leeway	117 (191)	4547
DPT, 1st booster dose	Between 15 and 18 months	233 (264)	1903
Yellow fever, single dose	Between 12 and 15 months	211 (265)	1614
MMR, initial dose	Between 12 and 15 months	232 (289)	1461
Oral polio, three initial doses	At 2, 4 and 6 months; each dose with a 1 month leeway	112 (185)	4524
Oral polio, first booster dose	Between 15 and 18 months	222 (244)	1934
Influenza, two doses	Initial dose at 6 months, second at 7 months; each dose with a 1 month leeway	275 (287)	5335
Rotavirus, two doses	First dose between weeks 8 and 15; second dose between 4 and 7 months	130 (153)	241
Pneumococcal conjugate, two initial doses	At 2 and 4 months; each dose with a 1 month leeway	87 (108)	1567
Pneumococcal conjugate, booster dose	Between 12 and 15 months	130 (112)	225

Table 5

Factors associated with absolute immunization and timely immunization among children less than 6 years of age living in 80 municipalities of Colombia in 2012, using an indicator subset of vaccines as a proxy for total coverage

Risk factors ^a	Absolute coverage		Timely coverage	
	OR	95% Conf. interval	OR	95% Conf. interval
Male sex	1.07	0.98-1.17	1.01	0.93-1.09
Continuous age in months (centered at 36)	0.69	0.67-0.71	0.55	0.53-0.57
Lowest SEP category vs. all other categories	0.79	0.69-0.90	0.77	0.69-0.86
Mother completed high school vs. less than high school	1.16	1.03-1.29	1.23	1.12-1.36
Mother is a paid worker vs. not paid or unemployed	1.00	0.90-1.11	0.99	0.90-1.09
Self-identified as belonging to race/ethnic minority	0.85	0.75-0.97	0.97	0.88-1.07
Health insurance (compared to contributive regime):				
Subsidized health insurance	1.04	0.91-1.18	0.85	0.76-0.95
Not insured	0.64	0.52-0.79	0.66	0.56-0.79
Special regimes of health insurance	0.77	0.59-1.00	0.91	0.73-1.15
Number of siblings (as continuous variable)	0.87	0.80-0.95	0.78	0.70-0.86
Birth order (1st born as reference vs. not 1st born)	1.08	0.99-1.18	1.13	1.01-1.26
More than one year living in the municipality	1.20	0.96-1.50	1.32	1.11-1.58
Internally displaced family	0.96	0.83-1.10	0.94	0.82-1.09

^a Bold font indicates a statistically significant association at α = 0.05.

coverage; however, there may be additional difficulties related to the lack of standardization of the definitions of timely immunization. For instance, the definitions used along this paper and detailed in Table 4 are not identical to those described in prior studies of missing opportunities for vaccination and timeliness of immunization [4]. The large difference between absolute and timely coverage observed in our study is not unprecedented: in Uganda in 2008, this difference was reported to be as large as 75% vs. 18% [18].

This survey also demonstrated important disparities between municipalities: the absolute coverage for the indicator subset of vaccines varied between 46% and 97%, while for timely coverage the range was from 8% to 52%. This shows immunization coverage in Colombia is far from homogeneous, and a summary measure like the mean coverage across the entire study population may be insufficient to capture and describe within-country disparities. This is in agreement with a 2005 study in Papua New Guinea, where sub-national areas had much lower immunization rates than the national average [23]. Although the present analysis was not specifically aimed to contrast the coverage between rural and urban areas, a secondary analysis of our data showed that absolute coverage and timely coverage were not different comparing 21 municipalities with more than 50% rural population vs. the other 59 (77% vs. 78% for absolute coverage, and 30 vs. 34% for timely coverage). However, in 4 municipalities were the sample

was predominantly taken from rural settings, we identified a significantly lower timely coverage in the rural area (32% vs 16%, p = 0.001), although this was not the case for absolute coverage (77% vs. 86%, p = 0.14). This suggests that urbanicity may be another factor driving within-country heterogeneity, insufficiently explored in the present survey, but worth to examine in future studies.

Heterogeneities in vaccine access have been linked to material deprivation/wealth [24–26], lack of health insurance [27], lack of education [22,24,25], distance to health centers [25], and racial/ ethnic inequities [28]. In the present study too, sociodemographic inequalities contributed to explain immunization coverage. Mother's education at the high school level or beyond was associated with higher odds of absolute and timely immunization. In comparison, older age, a greater number of siblings, low SEP, and lack of health insurance contributed to lower absolute and timely immunization. Analogous findings have been observed in the United States, where racial/ethnic minorities and groups served by public vaccination providers remain persistently under-reached by immunization programs [29]. However, as opposed to previous reports [27], internal displacement was not linked to lower immunization coverage in this analysis. We hypothesize this may be a result of the efforts of governmental and non-governmental agencies to provide internally displaced families with basic health and social assistance.



Fig. 1. Immunization coverage, timely immunization, variation with age, and coverage of new or underutilized vaccines in Colombia, 2012. The vertical bars represent 95% confidence intervals for immunization coverage and the central marks are the point estimates. (a) The red arrow illustrates the gap between national absolute immunization coverage and timely coverage. (b) The red arrow illustrates the difference in mean absolute coverage between the top half and bottom half of the studied municipalities, classified according to coverage levels. (c) The red line illustrates the stated goal for national immunization coverage. (d) The red line illustrates the decay in immunization coverage through age. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Most factors associated with immunization coverage and timely coverage in our models are to some degree inherent to the studied individuals (e.g. age, race, birth order), their families (e.g. mother's education, number of siblings), or are structurally related to the organization of the society they live in (e.g. types of health insurance, low SEP). These constitute barriers for immunization that can and should be addressed by public health systems. In order to do so, associations of these factors with immunization coverage must be translated into interventions on modifiable events that contribute to explain such associations [30]. For instance, identifying as a racial minority is not in itself modifiable, but racial disparities in immunization can be interpreted as the result of a complex set of social disadvantages experienced by persons who belong to a racial minority, and policies can be put into effect to ameliorate these disadvantages. For instance, incentives to households and health care workers have been suggested by the WHO as strategies to reach underserved populations, as long as the autonomy of the beneficiaries is respected [2].

Another relevant finding concerns the differences between recently introduced vaccines and traditional ones. Absolute coverage for rotavirus and pneumococcal vaccines was only 80%, and for seasonal influenza vaccine was less than 50%, while traditional vaccines targeted towards children of the same age range reported absolute coverage greater than 90%. These low coverage levels may leave room for outbreaks among the unprotected population. Specific reasons for the low uptake of vaccines were not ascertained in this study, but other studies suggest this may be due to socio-economic and geographic barriers [25], barriers related to the organization of the immunization program [31], patterns of utilization of health care services [32], and beliefs and attitudes from parents and guardians [33].

One important limitation of this study is related to the use of immunization record cards as the primary source of information. It has been shown in countries with robust health information systems that methods based on record cards tend to underestimate immunization rates when compared to health care provider sources, because a substantial proportion of children lacking immunizations on the card may actually be vaccinated [34]. However, the limitations of health information systems in Colombia [35] do not allow to use that approach. A nominal electronic EPI registry is currently under implementation and may serve to this purpose in the future. Additionally, the absolute coverage indicator for many of the individual vaccines in this study was above 90%, leaving little room for a substantial underestimation.

Although this study was initially conceived as a national survey, generalizability of the results to specific municipalities not included in the sample may be limited by the profound heterogeneity revealed by this study, and the non-probabilistic nature of the initial selection of the municipalities provided by the Colombian Ministry of Health. Thus, the conclusions of this study apply to the 80 municipalities included in the survey, and possibly to others within a similar spectrum of geographic, cultural, and demographic characteristics, but the results should not be regarded as a quantitative summary of the national immunization coverage. Additionally, direct comparison of these results to the routine surveillance of the CEPI may be limited by the methodological differences between these two assessment approaches. Routine surveillance is based on administrative coverage and rapid monitoring surveys, but these methodologies may be affected by inaccuracies in the administrative population denominators and disparities in immunization practices between and within municipalities [21].

4.1. Conclusions

Immunization of children with the basic schedule of traditional vaccines included in the CEPI in Colombia in 2012 met the proposed WHO goal of 90% coverage, although coverage of booster doses in older children fell far below that goal. In addition, coverage for the more recently introduced vaccines was low. Delayed immunization is a common problem in Colombia, which may result in reduced levels of individual protection and create a pool of susceptible individuals who can spread infection throughout the population. This study showed that socioeconomic inequities are important determinants of immunization coverage and delayed immunization in Colombia. The identification of vulnerable sub-populations may help to focus interventions aimed at creating incentives and addressing barriers for immunization, as well as to improve the efficacy and reaching capacity of immunization programs until a more comprehensive social response is put in effect in order to tackle health inequities.

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6. Conflicts of interest

None.

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References

- WHO, UNICEF, World Bank. State of the world's vaccines and immunization. 3rd ed. Geneva: World Health Organization; 2009.
- [2] WHO. Global vaccine action plan 2011-2020. World Health Organization; 2013.
- [3] Burton A, Monasch R, Lautenbach B, Gacic-dobo M, Neill M, Karimov R. WHO and UNICEF estimates of national infant immunization coverage: methods and processes 2009:535–41. <u>http://dx.doi.org/10.2471/BLT.08.053819</u>.
- [4] Pan American Health Organization. Methodology for the evaluation of missed opportunities for vaccination. Washington DC: PAHO; 2013.
- [5] Pan American Health Organization. Coverage in the Americas by Country 2016 <<u>http://ais.paho.org/phip/viz/im_coveragebycountry.asp></u> [accessed September 27, 2016].

- [6] Ministerio de Salud y Protección Social República de Colombia. [Vaccination: Achievements of the Government] [Spanish]. 2012 <https://www. minsalud.gov.co/DocumentosyPublicaciones/Logros+del+Gobierno+en +vacunacion.pdf> [accessed September 27, 2016].
- [7] de La Hoz F, Perez L, de Neira M, Hall AJ. Eight years of hepatitis B vaccination in Colombia with a recombinant vaccine: factors influencing hepatitis B virus infection and effectiveness. Int J Infect Dis 2008;12:183–9. <u>http://dx.doi.org/ 10.1016/j.ijid.2007.06.010</u>.
- [8] Morón L, Espitia M. A Rapid Evaluation of Vaccination Coverage in Bogotá, 2006. Rev Salud Pública 2009;11:237–46. <u>http://dx.doi.org/10.1590/S0124-00642009000200008</u> (Spanish).
- [9] National Administrative Department of Statistics DANE (Colombia). Estimates and projections of the total national, departmental and municipal population by area, 1985-2020; 2009 https://www.dane.gov.co/files/ investigaciones/poblacion/proyepobla06_20/Municipal_area_1985-2020.xls [accessed September 27, 2016].
- [10] Särndal E, Swensson B, Wretman J. Chapter 3.6. Probability proportional-tosize sampling. Model Assist. Surv. Sampl.. New York: Springer-Verlag; 1992. p. 87–99.
- [11] National Administrative Department of Statistics DANE (Colombia). [Methodological Summary Sheet of the General Census, 2005][Spanish]; 2006 http://www.dane.gov.co/files/censo2005/ficha_metodologica.pdf [accessed September 27, 2016].
- [12] WMA General Assembly. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects (as amended by the 59th WMA General Assembly, Seoul, October 2008). World Med Assoc 2008.
- [13] Ministerio de Salud y Protección Social República de Colombia. [Vaccination Week in the Americas 2012: a framework document][Spanish]; 2012:28–30 https://www.minsalud.gov.co/Lineamientos/Documento_Marco_Jornada_ de_Vacunacion_de_las_Américas_abril2012.pdf> [accessed September 27, 2016].
- [14] Congreso de la República de Colombia. Ley 142 de 1994. The Congress of the Republic of Colombia; 1994.
- [15] StataCorp LP. Stata Data Analysis and Statistical Software: release 12.1; 2014.
 [16] Rabe-Hesketh S, Skrondal A. Multilevel and Longitudinal Model Using Stata. 2nd ed. College Station, TX: Stata Press; 2008.
- [17] O'Grady K-A, Krause V, Andrews R. Immunisation coverage in Australian Indigenous children: Time to move the goal posts. Vaccine 2009;27:307–12. http://dx.doi.org/10.1016/i.vaccine.2008.09.096.
- [18] Fadnes LT, Nankabirwa V, Sommerfelt H, Tylleskär T, Tumwine JK, Engebretsen IMS, et al. Is vaccination coverage a good indicator of age-appropriate vaccination? A prospective study from Uganda. Vaccine 2011;29:3564–70. http://dx.doi.org/10.1016/i.vaccine.2011.02.093.
- [19] Akmatov MK, Kretzschmar M, Krämer A, Mikolajczyk RT. Timeliness of vaccination and its effects on fraction of vaccinated population. Vaccine 2008;26:3805–11. <u>http://dx.doi.org/10.1016/j.vaccine.2008.05.031</u>.
- [20] Dannetun E, Tegnell A, Hermansson G, Törner A, Giesecke J. Timeliness of MMR vaccination-influence on vaccination coverage. Vaccine 2004;22:4228–32. <u>http://dx.doi.org/10.1016/i.vaccine.2004.04.018</u>.
- [21] Dietz V, Venczel L, Izurieta H, Stroh G, Zell ER, Monterroso E, et al. Assessing and monitoring vaccination coverage levels: lessons from the Americas. Rev Panam Salud Pública = Pan Am J Public Heal 2004;16:432–42. <u>http://dx.doi.org/10.1590/S1020-49892004001200013</u>.
- [22] Casey RM, Dumolard L, Danovaro-Holliday MC, Gacic-Dobo M, Diallo MS, Hampton LM, et al. Global Routine Vaccination Coverage, 2015. MMWR Morb Mortal Wkly Rep 2016;65:1270–3. <u>http://dx.doi.org/10.15585/mmwr.mm6545a5</u>.
- [23] Toikilik S, Tuges G, Lagani J, Wafiware E, Posanai E, Coghlan B, et al. Are hardto-reach populations being reached with immunization services? Findings from the 2005 Papua New Guinea national immunization coverage survey. Vaccine 2010;28:4673–9. <u>http://dx.doi.org/10.1016/j.vaccine.2010.04.063</u>.
- [24] Kawakatsu Y, Honda S. Individual-, family- and community-level determinants of full vaccination coverage among children aged 12–23 months in western Kenya, Vaccine 2012;30:7588–93. <u>http://dx.doi.org/</u> 10.1016/i.vaccine.2012.10.037.
- [25] Rahman M, Obaida-Nasrin S. Factors affecting acceptance of complete immunization coverage of children under five years in rural Bangladesh. Salud Pública de México 2010;52:134–40. <u>http://dx.doi.org/10.1590/S0036-36342010000200005</u>.
- [26] Konstantyner T, Taddei JA de AC, Rodrigues LC. Risk factors for incomplete vaccination in children less than 18 months of age attending the nurseries of day-care centres in Sao Paulo, Brazil. Vaccine 2011;29:9298–302. <u>http://dx. doi.org/10.1016/i.vaccine.2011.10.02</u>.
- [27] Ruiz-Rodríguez M, Vera-Cala LM, López-Barbosa N. [Health insurance for infants and infant vaccination related to forced-displacement in Colombia]. Rev Salud Pública 2008;10:49–61. <u>http://dx.doi.org/10.1590/S0124-00642008000100005</u> (Spanish).
- [28] Bárcenas-López RM, Curiel-Reyes R, Caballero-Hoyos R, Villaseñor Sierra A. Low vaccine coverage in indigenous migrant boys and girls. Salud Pública de México 2012;54:361–2. <u>http://dx.doi.org/10.1590/S0036-36342012000400001.</u>
- [29] Zhao Z, Smith PJ. Trends in vaccination coverage disparities among children, United States, 2001–2010. Vaccine 2013;31:2324–7. <u>http://dx.doi.org/10.1016/j.vaccine.2013.03.018</u>.

- [30] Greenland S. Epidemiologic measures and policy formulation: lessons from potential outcomes. Emerg Themes Epidemiol 2005;2:5. <u>http://dx.doi.org/</u> 10.1186/1742-7622-2-5.
- [31] Ransom J, Schaff K, Kan L. Is there an association between local health department organizational and administrative factors and childhood immunization coverage rates? J Health Hum Serv Adm 2012;34:418–55.
 [32] Glanz JM, Newcomer SR, Narwaney KJ, Hambidge SJ, Daley MF, Wagner NM,
- [32] Glanz JM, Newcomer SR, Narwaney KJ, Hambidge SJ, Daley MF, Wagner NM, et al. A population-based cohort study of undervaccination in 8 managed care organizations across the United States. JAMA Pediatr 2013;167:274–81. <u>http:// dx.doi.org/10.1001/jamapediatrics.2013.502</u>.
- [33] Favin M, Steinglass R, Fields R, Banerjee K, Sawhney M. Why children are not vaccinated: a review of the grey literature. Int Health 2012;4:229–38. <u>http:// dx.doi.org/10.1016/j.inhe.2012.07.004</u>.
- [34] Miles M, Ryman TK, Dietz V, Zell E, Luman ET. Validity of vaccination cards and parental recall to estimate vaccination coverage: a systematic review of the literature. Vaccine 2013;31:1560–8. <u>http://dx.doi.org/10.1016/ i.vaccine.2012.10.089</u>.
- [35] Pan American Health Organization. Health in the Americas: 2012 Edition. Regional outlook and country profiles. 2012 ed. Washington DC: PAHO; 2012.