

# Vaccination coverage according to doses received and timely administered based on an electronic immunization registry, Araraquara-SP, Brazil, 2012-2014\*

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## Abstract

**Objective:** to describe vaccine coverage by type of vaccine at 12 and 24 months of age. **Methods:** descriptive cohort study with children born in 2012, living in Araraquara-SP, Brazil, recorded in the Information System on Live Births (Sinasc); a manual linkage of Sinasc data with an electronic immunization registry (EIR) was performed; the assessment was based on vaccination status according to São Paulo State recommendations, and on doses received and timely administered. **Results:** 2,740 children were registered on Sinasc and 99.6% of them were included into EIR; among the 2,612 (95.3%) children studied, the triple viral vaccine (measles, mumps and rubella) had the lowest coverage at 12 months for received dose (74.8%) and at 24 months for timely vaccination (53.5%) and received doses (88.0%). **Conclusion:** coverage was higher than 90% for most vaccines; however, delayed vaccination was observed, which indicates the need to intensify actions aimed at timely vaccination.

**Keywords:** Child; Immunization Coverage; Electronic Health Record; Epidemiology, Descriptive; Cohort Studies.

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## Introduction

Brazil has a routine immunization schedule, of universal and free access. Besides the vaccination routine in health services, the National Immunization Program (NIP) uses the strategy of national vaccination days in order to increase vaccination coverage.<sup>1</sup> The coverage achieved by NIP vaccines is usually high,<sup>2</sup> although it is not always homogeneous among different social groups and different vaccines.<sup>3,4</sup>

The estimates of vaccination coverage in Brazil are obtained through administrative method, where the numerator is defined by the number of vaccine doses administered that are registered in the health units, and the denominator is defined by the population estimates.<sup>5</sup> This method supports the planning of NIP actions, but it is inaccurate, because it does not allow the identification of micro areas of low coverage; therefore, it is necessary to carry out periodic vaccination coverage surveys.<sup>6</sup>

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An electronic and nominal registration system of vaccination is especially important when it comes to understanding the vaccination coverage, particularly in a scenario where there is periodic incorporation of new vaccines.<sup>5</sup> Electronic immunization registry (EIR) assist in the scheduling of vaccines and identification of absent patients. They are useful instruments for achieving and maintaining high vaccination coverage, which helps preventing the reoccurrence of diseases that are already under control. The EIR also allow an analysis of vaccination opportunity, that is, vaccination at the recommended age with proper intervals between doses, once they provide individual data, with date and batch of each dose received.<sup>7</sup>

Studies based on electronic vaccination systems in Brazil are scarce.<sup>5</sup> This fact enables researches that use these systems as data sources, especially in the current process of implementation of NIP Information System (IS-NIP), which has national coverage.<sup>5</sup> In Latin America, only a few studies have assessed vaccination opportunity regarding the schedule compliance over time.<sup>8,9</sup> For the immunization programs,

monitoring the immunization status at the appropriate age is essential to identify missed immunization opportunities, and to define the disease risk in the population, especially those diseases in which age is a risk factor related to severity or higher occurrence of complications<sup>8,10</sup> – for instance, the vaccine against tuberculosis (Calmette-Guérin bacillus [BCG]), administered at birth, preventing tuberculous meningitis in the first year of life.

Regarding the assumptions presented, this study aimed to describe the vaccine coverage according to vaccine type at 12 and 24 months of age, in the municipality of Araraquara, São Paulo State, Brazil.

## Methods

This is a descriptive cohort study, carried out in Araraquara-SP, from 2012 to 2014.

In 2011, Araraquara had an estimated population of 210,673 inhabitants;<sup>11</sup> 2,569 were recorded as live births in that year.<sup>2</sup> In 2010, the local Human Development Index (HDI) was 0.815, ranking 14<sup>th</sup> in the national HDI classification by municipality.<sup>12</sup> In that same year, the proportion of resident population with monthly per capita household income of up to half a minimum wage was 12.6%; and the proportion of illiterates aged 15 or more, 3.3%.<sup>2</sup>

Since 1987, the Special Health Service of Araraquara (SHSA), a school health unit of the School of Public Health of the University of São Paulo (USP), assisted by São Carlos IT Center also from USP, has been managing the first EIR implemented in the country. In 2011, this registry was reformulated and became part of the online information and management system in Public Health, named 'Juarez' in honor of Professor Edmundo Juarez, of the School of Public Health/USP, who directed SHSA for many years and founded EIR. This system has four components: (i) outpatient registration and control; (ii) health program and epidemiological surveillance; (iii) laboratory control; and (iv) vaccination control. In the 'vaccination control' component, it is possible to obtain detailed vaccination data from children born and/or residents in the municipality.<sup>15</sup>

As it is a consolidated program, Araraquara EIR allows detailed analyses of the vaccination coverage in this medium-sized municipality. The individuals' immunization schedules are filed in it, in order to reduce the possibility of information loss, as well as to allow access to this information from any primary health care unit of the municipality.

In Araraquara, at the time of the study, there were 28 primary health care units that performed vaccination activities, and the health professionals of each unit had access to EIR data in real time, including vaccination data into the system daily. In turn, the five private services from the municipality sent periodically nominal information, regarding vaccination activities, to SHSA, so that it could be included into Juarez System (information collected by the SHSA team).

The study population was composed by the cohort of live births of mothers resident in Araraquara, registered at the Information System on Live Births (Sinasc) from January 1<sup>st</sup> to December 31<sup>st</sup>, 2012. Children who moved from the municipality were excluded, as well as those who died before 13 months of age, whose death was recorded at the Mortality Information System (SIM). The identification of the children who moved from the municipality was based on EIR data, and it was not possible to obtain the moving date. Sinasc is filled in with the Declaration of Live Birth (DLB), an official standardized document that is mandatory throughout the country and required in order to register the child at the civil registry office.<sup>14, 15</sup>

The study variables were those related to the immunization status, that is, date of birth and age at the time of vaccination, vaccines received according to the recommendations of São Paulo State Health Department in 2012 and 2013, date of vaccine administration, doses received and dose intervals.

The sources of data used were Sinasc and SIM, databases provided by the Municipal Health Department; and Juarez System EIR, database provided by SHSA.

In order to verify if all live births in 2012 of mothers resident in Araraquara-SP and registered at Sinasc (2,740 records) had also been included into EIR (3,194 records), these databases were manually linked. Previously, the consistency of the data was verified: for example, the dates of vaccines that were not registered in ascending order, along with the doses administered, were reorganized. We also verified the existence of duplications in both databases. After organizing the mothers' names alphabetically in both databases, the variables 'child's birth date', 'child's sex', 'residence address' and 'gestation type' were used to verify possible duplicities, one by one.

Afterwards, deaths were excluded according to SIM data from 2012 to 2014 (30 records), through manual search, by checking the pairs according to mother's

name, child's date of birth, child's sex, birth weight and DLB number. Therefore, the final database used in the analysis was constituted.

The EIR analysis was based on two indicators: coverage and duplication of records. Coverage was calculated in percentage; the number of children registered at EIR was the numerator, and the denominator was the total number of children born to women living in the municipality of Araraquara, registered at Sinasc. A study published in 2008, when the databases of the civil registry and Sinasc were linked, showed that there was a difference of less than 1% between these two bases, which is why, in this study, Sinasc was considered gold standard.<sup>16</sup> Duplicity was calculated considering the number of children duplicated at EIR as the numerator and the total number of children registered at EIR as the denominator.

The immunization status was assessed based on recommendations of São Paulo State Health Department, published in 2012 and 2013.<sup>17</sup> Figure 1 presents a table adapted from the recommendations of the Brazilian National Immunization Program<sup>18</sup> and the Centers for Disease Control and Prevention of the United States (CDC/US).<sup>19</sup> The delay was defined by a vaccine received a month after the age recommended by the immunization routine. The vaccination coverage was analyzed according to the doses received – doses recommended according to the vaccination schedule up to the maximum ages of 12 months (394 days) and 24 months (730 days) –; and timely doses – recommended doses according to the vaccination schedule, taking into account the minimum and maximum age when each vaccine was administered, and the appropriate intervals between doses.<sup>17</sup>

Vaccination coverage was calculated by considering the children recorded at EIR who received all doses of each vaccine as the numerator and, as the denominator, the total number of children recorded at Sinasc and EIR (after excluding deaths and those who had moved from Araraquara).

Vaccine coverage, according to vaccine type, was estimated in accordance with the respective 95% confidence intervals (95% CI), at 12 and 24 months of age, according to doses received and timely administered doses.

The vaccination opportunity was verified by the analysis of time spent until the event, and presented in proportion. From 2002, this type of analysis has also been applied to characterize vaccination over time.<sup>20</sup>

| Vaccine Dose   | Age Recommended | Minimum age to the dose | Minimum interval recommended to the next dose | Age to consider as a delay | Minimum and maximum ages (in days) |
|--|-----------------|-------------------------|---|----------------------------|------------------------------------|
| BCG <sup>a</sup>   | At birth        | At birth                | –   | 1 month                    | 0-30                               |
| HB <sup>b</sup> – 1 <sup>st</sup> dose                     | At birth        | At birth                | 4 weeks                                       | 1 month                    | 0-30                               |
| HB <sup>b</sup> – 2 <sup>nd</sup> dose                     | 2 months        | 4 weeks                 | 8 weeks                                       | 3 months                   | 28-89                              |
| HB <sup>b</sup> – 3 <sup>rd</sup> dose                     | 6 months        | 6 months                | –   | 7 months                   | 182-212                            |
| RV <sup>c</sup> – 1 <sup>st</sup> dose                     | 2 months        | 1 month and 15 days     | 4 weeks                                       | 3 months                   | 45-89                              |
| RV <sup>c</sup> – 2 <sup>nd</sup> dose                     | 4 months        | 3 months and 15 days    | –   | 5 months                   | 105-151                            |
| Hib <sup>d</sup> – 1 <sup>st</sup> dose                    | 2 months        | 6 weeks                 | 4 weeks                                       | 3 months                   | 42-89                              |
| Hib <sup>d</sup> – 2 <sup>nd</sup> dose                    | 4 months        | 10 weeks                | 4 weeks                                       | 5 months                   | 70-151                             |
| Hib <sup>d</sup> – 3 <sup>rd</sup> dose                    | 6 months        | 14 weeks                | –   | 7 months                   | 98-212                             |
| DPT <sup>e</sup> – 1 <sup>st</sup> dose                    | 2 months        | 6 weeks                 | 4 weeks                                       | 3 months                   | 42-89                              |
| DPT <sup>e</sup> – 2 <sup>nd</sup> dose                    | 4 months        | 10 weeks                | 4 weeks                                       | 5 months                   | 70-151                             |
| DPT <sup>e</sup> – 3 <sup>rd</sup> dose                    | 6 months        | 14 weeks                | 6 months                                      | 7 months                   | 98-212                             |
| DPT <sup>e</sup> – booster                                 | 15 months       | 12 months               | –   | 16 months                  | 365-486                            |
| Polio <sup>f</sup> – 1 <sup>st</sup> dose                  | 2 months        | 6 weeks                 | 4 weeks                                       | 3 months                   | 42-89                              |
| Polio <sup>f</sup> – 2 <sup>nd</sup> dose                  | 4 months        | 10 weeks                | 4 weeks                                       | 5 months                   | 70-151                             |
| Polio <sup>f</sup> – 3 <sup>rd</sup> dose                  | 6 months        | 14 weeks                | 6 months                                      | 7 months                   | 98-212                             |
| Polio <sup>f</sup> – booster                               | 15 months       | 12 months               | –   | 16 months                  | 365-486                            |
| MenC <sup>g</sup> – 1 <sup>st</sup> dose                   | 3 months        | 6 weeks                 | 4 weeks                                       | 4 months                   | 42-120                             |
| MenC <sup>g</sup> – 2 <sup>nd</sup> dose                   | 5 months        | 10 weeks                | 8 weeks                                       | 6 months                   | 70-181                             |
| MenC <sup>g</sup> – booster                                | 12 months       | 12 months               | –   | 13 months                  | 365-394                            |
| P10 <sup>h</sup> – 1 <sup>st</sup> dose                    | 3 months        | 6 weeks                 | 4 weeks                                       | 4 months                   | 42-120                             |
| P10 <sup>h</sup> – 2 <sup>nd</sup> dose                    | 5 months        | 10 weeks                | 4 weeks                                       | 6 months                   | 70-181                             |
| P10 <sup>h</sup> – 3 <sup>rd</sup> dose                    | 7 months        | 14 weeks                | 8 weeks                                       | 8 months                   | 98-242                             |
| P10 <sup>h</sup> – booster                                 | 15 months       | 12 months               | –   | 16 months                  | 365-484                            |
| YF <sup>i</sup>  | 9 months        | 9 months                | –   | 10 months                  | 273-303                            |
| MMR <sup>j</sup> – 1 <sup>st</sup> dose                    | 12 months       | 12 months               | 4 weeks                                       | 13 months                  | 365-394                            |
| MMR <sup>j</sup> /MMRV <sup>k</sup> – 2 <sup>nd</sup> dose | 15 months       | 15 months               | –   | 16 months                  | 452-486                            |

a) BCG: Bacillus Calmette-Guérin vaccine.

b) HB: hepatitis B vaccine.

c) RV: rotavirus oral vaccine.

d) Hib: *Haemophilus influenzae* type b vaccine.

e) DPT: triple bacterial vaccine (combined vaccine against diphtheria, tetanus and whole-cell pertussis, includes the acellular bacterial vaccine [DPaT]).

f) Polio: includes the attenuated poliomyelitis 3-valent oral vaccine (VOP) and the inactivated poliomyelitis 3-valent injectable vaccine (VIP).

g) MenC: meningococcal C conjugate vaccine.

h) P10: pneumococcal 10-valent conjugate vaccine.

i) YF: yellow fever vaccine.

j) MMR: measles, mumps and rubella vaccine.

k) MMRV: measles, mumps, rubella and varicella vaccine.

Note: The table was adapted from the recommendations of the Brazilian National Immunization Program<sup>18</sup> and the Centers for Disease Control and Prevention/EUA.<sup>19</sup>

Figure 1 – Age recommended per vaccine dose and interval between doses

The modified Kaplan-Meier curve<sup>21</sup> was used in order to visualize the proportion of children timely vaccinated, in agreement with the vaccine schedule up to 24 months of age. Time zero indicates the birth of the children and, for the analysis of time spent until the event, we considered as event not receiving the vaccine doses recommended in the indicated time interval (Figure 1), that is:

- a) event 1 (BCG; hepatitis B vaccine [HB 1]);
- b) event 2 (combined vaccine against diphtheria, tetanus and pertussis [DTP 1], polio vaccine [Polio 1], *Haemophilus influenzae* type b vaccine [Hib 1], rotavirus oral vaccine [RV], HB 2);
- c) event 3 (10-valent pneumococcal conjugate vaccine/13-valent conjugated pneumococcal vaccine [PCV 1]; meningococcal C conjugate vaccine [MenC 1]);
- d) event 4 (DTP 2, Polio 2, Hib 2, RV 2);
- e) event 5 (PCV 2; MenC 2);
- f) event 6 (DTP 3, Polio 3, Hib 3, HB 3);
- g) event 7 (PCV 3);
- h) event 8 (yellow fever vaccine [YF]);
- i) event 9 (measles, mumps and rubella vaccine [MMR 1], MenC 3); and
- j) event 10 (DTP 4, Polio 4, PCV 4, MMR 2)

Children who did not receive the vaccine(s) timely were no longer eligible to be followed up and, therefore, were excluded from the analysis (of the proportion numerator). The child was censored when all the recommended doses of vaccine up to 24 months old had been timely administered.

The modified Kaplan-Meier curve  $[1-s(t)]^{20}$  was used to describe the time spent until each dose of DTP (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> or 4<sup>th</sup> dose) and to estimate vaccine coverage in different moments. The observation period of each child started at birth (time zero) and continued until the date when the last child in the cohort received a certain dose of DTP vaccine. The total period of observation was divided into short time intervals, limited by the date when each child received a dose of DTP. The DTP vaccine was chosen for this analysis because it is (i) one of the vaccines recommended by the World Health Organization,<sup>22</sup> it is (ii) injectable and multi-dose (three doses and a booster) and because of (iii) the long period since it has been included into the vaccination schedule.<sup>23</sup> The softwares used in the analyses were SPSS Statistics version 21 and Microsoft Office Excel for Mac® 2011.

The research project was approved by the Research Ethics Committee of the School of Public Health, University

of São Paulo, on July 3<sup>rd</sup>, 2014: Protocol No. 707,588 and Certificate of Presentation for Ethical Appreciation (CAEE) No. 30987314.0.0000.5421.

## Results

In 2012, 2,740 children born to mothers resident in Araraquara were registered at Sinasc, and no duplicity was found. Out of this total, 2,731 (99.7%) were at Juarez System EIR and 3 (0.1%) were duplicated in this system (n=2,728). EIR coverage was estimated at 99.6% (2,728/2,740). Out of the total number of children identified on Sinasc, 98 (3.6%) were excluded because they had moved from the municipality and 30 (1.1%) were excluded because they had died; all of them were less than 13 months old. Thus, 2,612 children (95.3%) were included in the study.

The number of vaccine schedules identified and included in the study for Polio, DTP, HB, PCV, MMR and Hib vaccines is presented on Table 1. Some explanations for the different vaccine schedules are related to:

- a) vaccines' availability at the time of vaccination;
- b) change of schedules in the period – for example, the inclusion of the 5-valent vaccine (DTP/Hib/HB) in the second half of 2012 and the MMRV vaccine in 2013 –;
- c) recommendation for the child to receive combined vaccine against diphtheria, tetanus and acellular pertussis (DTaP) because of the high risk of post-vaccination adverse event; and
- d) the vaccines offered by the private service are not the same as those offered by the public service – for example, 13-valent pneumococcal conjugate vaccine (P13) instead of 10-valent pneumococcal conjugate vaccine (P10).

The vaccination coverage at 12 months old for doses received ranged from 74.8% (95%CI 73.2; 76.5) regarding MMR to 99.9% (95%CI 99.9; 100.0) regarding BCG; and, at 24 months old, it ranged from 88.0% (95%CI 86.7;89.2) regarding MMR/MMRV to 99.9% (95%CI 99.9;100.0) regarding BCG (Table 2). With regard to doses timely administered, they ranged from 68.7% (95%CI 66.9;70.5) for MenC to 98.5% (95%CI 98.0;99.0) for BCG at 12 months old; and at 24 months, from 53.5% (95%CI 51.6;55.4) regarding MMR/MMRV to 98.5 regarding BCG (Table 2). Among the doses of vaccines to be administered after 12 months old (DTP, Polio, PCV and MMR/MMRV), Polio and DTP

**Table 1 – Number of vaccine schedules included into the study in Araraquara, São Paulo, 2012-2013**

| Vaccines                            | Number of Vaccine Schedules |
|-------------------------------------|-----------------------------|
| HB <sup>a</sup>                     | 3                           |
| Hib <sup>b</sup>                    | 10                          |
| DPT <sup>c</sup>                    | 24                          |
| Polio <sup>d</sup>                  | 7                           |
| PCV <sup>e</sup>                    | 3                           |
| MMR <sup>f</sup> /MMRV <sup>g</sup> | 2                           |

a) HB: hepatitis B vaccine.

b) Hib: *Haemophilus influenzae* type b vaccine.

c) DPT: triple bacterial vaccine (combined vaccine against diphtheria, tetanus and whole-cell pertussis, includes the acellular bacterial vaccine [DPaT]).

d) Polio: includes the attenuated poliomyelitis 3-valent oral vaccine (VOP) and the inactivated poliomyelitis 3-valent injectable vaccine (VIP).

e) PCV: pneumococcal conjugate vaccine; includes pneumococcal 10-valent conjugate vaccine (P10) and pneumococcal 13-valent conjugate vaccine (P13).

f) MMR: measles, mumps and rubella vaccine.

g) MMRV: measles, mumps, rubella and varicella vaccine.

**Table 2 – Vaccine coverage at 12 and 24 months of age according to doses received and timely administered among the live births (N=2,612), Araraquara, São Paulo, 2012**

| Vaccine               | 12 months                   |                    |                                  |                    | 24 months                   |                    |                                  |                    |
|-----------------------|-----------------------------|--------------------|----------------------------------|--------------------|-----------------------------|--------------------|----------------------------------|--------------------|
|                       | Received doses <sup>a</sup> |                    | Timely administered <sup>b</sup> |                    | Received doses <sup>a</sup> |                    | Timely administered <sup>b</sup> |                    |
|                       | %                           | 95%CI <sup>c</sup> | %                                | 95%CI <sup>c</sup> | %                           | 95%CI <sup>c</sup> | %                                | 95%CI <sup>c</sup> |
| BCG <sup>d</sup>      | 99.9                        | 99.9;100.0         | 98.5                             | 98.0;99.0          | 99.9                        | 99.9;100.0         | 98.5                             | 98.0;99.0          |
| HB <sup>e</sup>       | 98.0                        | 97.4;98.5          | 78.9                             | 77.3;80.4          | 98.4                        | 97.9;98.9          | 78.9                             | 77.3;80.4          |
| RV <sup>f</sup>       | 95.0                        | 94.2;95.8          | 90.0                             | 88.8;91.1          | 95.0                        | 94.2;95.9          | 90.0                             | 88.8;91.1          |
| Hib <sup>g</sup>      | 96.6                        | 95.9;97.3          | 77.5                             | 75.9;79.1          | 97.7                        | 97.1;98.3          | 77.5                             | 75.9;79.1          |
| DTP <sup>h</sup>      | 97.4                        | 96.8;98.0          | 78.0                             | 76.4;79.6          | 93.4                        | 92.5;94.4          | 63.0                             | 61.2;64.9          |
| Polio <sup>i</sup>    | 97.5                        | 96.9;98.1          | 78.1                             | 76.6;79.7          | 93.4                        | 92.5;94.4          | 63.1                             | 61.3;65.0          |
| MenC <sup>j</sup>     | 75.6                        | 73.9;77.2          | 68.7                             | 66.9;70.5          | 95.1                        | 94.2;95.9          | 68.7                             | 66.9;70.5          |
| PCV <sup>k</sup>      | 95.5                        | 94.7;96.3          | 71.8                             | 70.1;73.5          | 89.3                        | 88.1;90.5          | 55.4                             | 53.5;57.3          |
| YF <sup>l</sup>       | 93.0                        | 92.0;94.0          | 80.5                             | 79.0;82.0          | 95.6                        | 94.8;96.4          | 80.5                             | 79.0;82.0          |
| MMR/MMRV <sup>m</sup> | 74.8                        | 73.2;76.5          | 74.6                             | 73.0;76.3          | 88.0                        | 86.7;89.2          | 53.5                             | 51.6;55.4          |

a) Received doses: doses recommended according to the vaccine schedule up to the maximum age of 12 months (394 days) and 24 months (730 days).

b) Timely administered: doses recommended according to the vaccine schedule, considering the minimum and maximum age for each vaccine and the appropriate intervals between doses.

c) 95%CI: confidence interval of 95%.

d) BCG: Calmette-Guérin bacillus vaccine – at birth.

e) HB: hepatitis B vaccine – at birth, at 2 and at 6 months old.

f) RV: rotavirus oral vaccine – at 2 and 4 months old.

g) Hib: *Haemophilus influenzae* type b vaccine – at 2, 4 and 6 months.

h) DTP: triple bacterial vaccine (combination vaccine against diphtheria, tetanus and whole-cell pertussis, includes the acellular bacterial vaccine [DTaP]) – at 2, 4, 6 and 15 months old.

i) Polio: includes the attenuated poliomyelitis 3-valent oral vaccine (VOP) and the inactivated poliomyelitis 3-valent injectable vaccine (VIP) – at 2, 4, 6 and 15 months –; 23 (0.9%) children received at least one dose of 6-valent (DTaP/Hib/Polio) or inactivated 5-valent (DTaP/VIP/Hib).

j) MenC: meningococcal C conjugate vaccine – at 3, 5 and 12 months –; the booster dose was changed in 2013, from 15 to 12 months; the vaccine coverage of the two doses and the booster up to 15 months old is 91.7% (2,395/2,612) – 95%CI 90.6;92.8.

k) PCV: pneumococcal conjugate vaccine; includes pneumococcal 10-valent conjugate vaccine (P10) and pneumococcal 13-valent conjugate vaccine (P13); 20 (0.8%) children received at least one P13 doses – indicated at 3, 5, 7 and 15 months old.

l) YF: yellow fever vaccine – at 9 months old.

m) MMR/MMRV: measles, mumps and rubella vaccine, or triple viral vaccine (MMR)/ measles, mumps, rubella and varicella vaccine, or 4-valent viral (MMRV) – indicated at 12 and 15 months old; in 2012, one dose of triple viral vaccine was recommended at 12 months old and another at the age of 4 years old; in 2013, the recommendation changed to 1 dose at 12 months old and one 4-valent viral vaccine dose at 15 months old.

had the highest coverage for doses received (93%) and timely administered (63%).

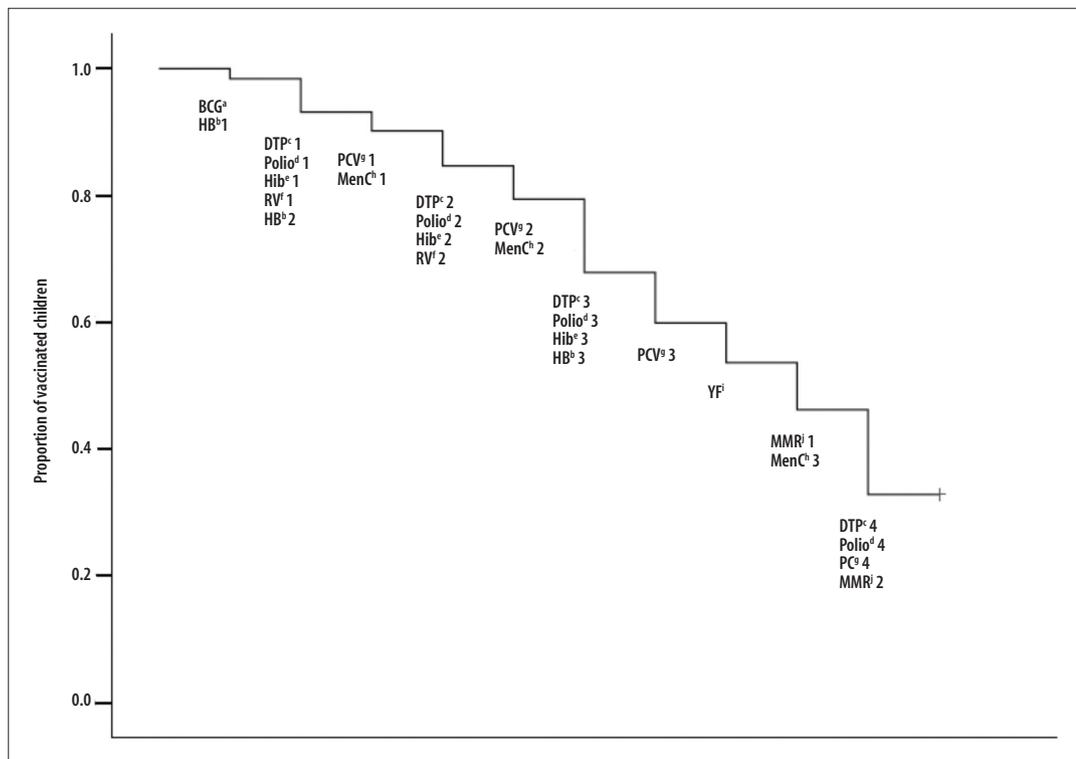
The proportion of children timely vaccinated, in agreement with the recommended doses up to 24 months old, is presented in Figure 2. Among the children followed up, 32.8% timely received all the vaccines. The deepest reduction in the proportion of children timely vaccinated (28.9%) occurred when the vaccines DTP 4, Polio 4, PCV 4 and MMR 2 should have been administered.

The proportion of children vaccinated with each dose of DTP over time can be seen in the four curves of Figure 3. Vaccine coverage for 1st, 2nd, 3rd, and 4th doses were 99.2%, 98.9%, 98, 3% and 94.4%, respectively. Among the children who took the DTP vaccine, there was timely

vaccination for the 1st dose, in 96.6% (2,504/2,592) of the cases, for the 2nd dose, in 91.8% (2,371/2,582), for the 3rd dose in 80.0% (2,054/2,568) and for the 4th dose in 78.6% (1,941/2,468); 50% of the children took the 1st, 2nd, 3rd and 4th doses of DTP at approximately 64, 128, 194 and 464 days, respectively. Vaccine coverage of 1st, 2nd, 3rd and 4th doses of DTP reached approximately 90% at 75, 150, 233 and 528 days, in that order.

## Discussion

Vaccination coverage was above 90% for most of the vaccines analyzed. However, lower percentages were observed concerning the doses timely administered. Analyses over time revealed vaccination delay.

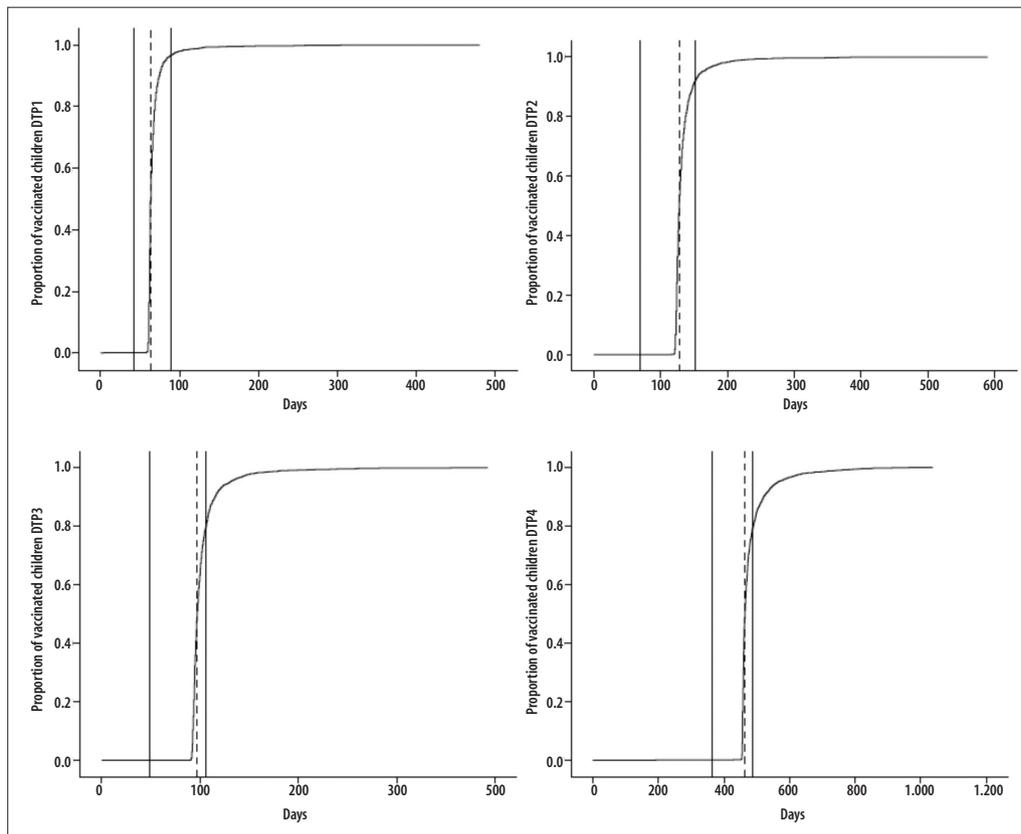


Subtitle:

- a) BCG: Calmette-Guérin bacillus vaccine.
- b) HB: hepatitis B vaccine.
- c) DTP: triple bacterial vaccine (combined vaccine against diphtheria, tetanus and whole-cell pertussis, includes the acellular bacterial vaccine [DTaP]).
- d) Polio: includes the attenuated poliomyelitis 3-valent oral vaccine (VOP) and the inactivated poliomyelitis 3-valent injectable vaccine (VIP).
- e) Hib: *Haemophilus influenzae* type b vaccine.
- f) RV: rotavirus oral vaccine.
- g) PCV: pneumococcal conjugate vaccine; includes pneumococcal 10-valent conjugate vaccine (P10) and pneumococcal 13-valent conjugate vaccine (P13).
- h) MenC: meningococcal C conjugate vaccine.
- i) YF: yellow fever vaccine.
- j) MMR: measles, mumps and rubella vaccine, (includes measles, mumps, rubella and varicella vaccine [MMRV]).

Note: The lines are decreasing due to the occurrence of events (not receiving the recommended vaccine doses according to the time interval indicated).

**Figure 2 – Proportion of children timely vaccinated, according to the recommended doses over time, among live births (N=2,612), Araraquara, São Paulo, 2012**



Note:  
Kaplan-Meier inverse curves [1-s(t)].  
The areas among the continuous vertical lines indicate the recommended period to vaccination.  
The dashed lines mark the medians of the vaccination days of the studied children.

**Figure 3 – Proportion of children who received the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and the 4<sup>th</sup> doses of DTP over time, among live births (N=2,612), Araraquara, São Paulo, 2012**

The limitations of this study are related to the use of secondary data. The exclusion of children who moved from the municipality may have overestimated or underestimated the results; however, as this percentage was small, it is possible that it has not affected – at least significantly – the results. The fact that not all vaccine doses were filled into EIR may have led to an underestimate of vaccine coverage. However, the fact that we considered different vaccine schedules for calculating the vaccination coverage and vaccination opportunities regarding Polio, DTP, HB, PCV, MMR/MMRV and Hib collaborated to improve data quality. It is important to highlight that in Araraquara, there is a routine of search for children in the civil registry and SIM in order to verify if they are registered at Juarez System.

The high coverage of children registered at EIR and the low duplication of records reinforce their

usefulness regarding monitoring and control of the vaccines administered. Moreover, EIR proved to be very useful for research, allowing a good use of information recorded in it.

In the study period, BCG, RV, PCV, Polio, HB, Hib and DTP vaccines administered at the age of 12 months old presented vaccine coverage for doses received over 95%. Nevertheless, we should highlight the importance of opportunity for the recommended vaccines, which was lower than 90% for most of them. It is also important to remember that the MMR/MMRV and MenC vaccines changed in the vaccination schedule of 2013, a measure that may have influenced the vaccination schedule. Another vaccine that deserves attention is PCV: the booster dose, which should be administered at the age of 15 months old, caused a decrease in its coverage at 24 months old. The variety

of vaccine schedules found for Polio, DTP, HB, PCV, MMR/MMRV and Hib vaccines shows the complexity of analyzing coverage data in face of these differences, especially concerning public and private vaccination networks. Moreover, over the years, the vaccination schedule became increasingly complex after vaccines such as PCV, MenC and RV were included.

Similarly to Araraquara, a vaccination coverage research, regarding the age of 18 months old, took place in 2007-2008 in Salvador, capital of Bahia State,<sup>24</sup> and identified greater coverage of BCG, DTP and Polio; and lower MMR coverage. In other capitals of the Brazilian Northeast region, concerning the same period of 2007-2008,<sup>25</sup> lower vaccination coverage was found at the age of 12 months for BCG, DTP, Hib, HB and Polio, and higher coverage for MMR, when compared to Araraquara.

A study carried out in 2004, also based on EIR from Curitiba, capital of Paraná State,<sup>3</sup> on vaccine coverage per doses received at 12 and 24 months old presented similarities to what was found in Araraquara; the exception was the MMR vaccine, which presented lower coverage in Araraquara. The authors suggest that the link to health services was an important factor for these results. As in the present study, the proportion of children registered at the EIR of Curitiba was quite high; however, the percentage of duplicate cases was higher than what was found in Araraquara.

Vaccine coverage according to doses received and doses timely administered are different ways of assessing vaccination schedule; the latter allows visualizing a decrease or increase in vaccination over time. Kaplan-Meier curve proved to be very useful for monitoring the vaccine schedule in its different stages, that is, for every dose(s) included. The graphic presentation provides quick and comprehensive overview of the complex issue of vaccination in a population over time. Estimating the proportion of children vaccinated at any time – and vice versa – enables two measures: (i) the investigation of age when the goal of vaccine coverage for a given disease is achieved in a population; and (ii) checking whether the recommended vaccination schedule is being well implemented, by observing the median of vaccination age of the population.<sup>20</sup>

Except for the BCG and RV, vaccine coverage by timely administered doses was below 90% for the vaccines analyzed. In São Luís, capital of Maranhão State,<sup>26</sup> a household survey conducted in 2006 involving 427 children identified fewer vaccine opportunities at 12 months old for BCG, HB, DTP, and Polio, compared to

the results of Araraquara. In El Salvador,<sup>9</sup> a household survey carried out in 2011, involving 2,550 children, revealed percentages of vaccination opportunity similar to those found in Araraquara, except for BCG and RV, which were better in Araraquara. In Buenos Aires, Argentina,<sup>8</sup> a 2002 population-based survey regarding 1,391 children showed lower percentages of DTP, HB, and MMR vaccines. In the USA,<sup>27</sup> a sample of 11,710 children of the 2012 national survey revealed greater opportunity for MMR vaccine than in Araraquara, but all the other vaccines presented lower percentages.

A study conducted in three municipalities of South Africa,<sup>28</sup> from 2006 to 2008, involving 1,137 children from zero to 24 months old, identified lower percentages of timely vaccine coverage for the 1<sup>st</sup> and 2<sup>nd</sup> doses of DTP, and higher percentage for the 3<sup>rd</sup> dose of this vaccine. In El Salvador,<sup>9</sup> the vaccination opportunities of the three doses of DTP and its booster were lower than in Araraquara.

Still regarding opportunity, in this study, DTP vaccination coverage in the first two doses reached 90% within the recommended period, different from Germany, according to a national survey involving 782 children in the year 1999.<sup>20</sup> There is evidence in the literature that delayed vaccination is clinically important because the child may be exposed to complications from these diseases.<sup>29</sup>

In conclusion, vaccine coverage in the municipality of Araraquara is heterogeneous and experiences delays. Thus, it is relevant to intensify actions aimed at timely vaccination, especially MMRV and PCV (booster). The results of this study may have implications for vaccination programs in Brazilian municipalities with similar characteristics to those of Araraquara, who have implemented – or are implementing – the electronic immunization registry – EIR.

## Authors' Contributions

Tauil MC, Sato APS and Waldman EA contributed to the conception and design of the study, data analysis and interpretation, drafting and critical review of the manuscript's intellectual content. Costa AA, Inenami M and Ferreira VLR contributed to the analysis and interpretation of the results, drafting and critical review of the manuscript's intellectual content. All the authors approved the final version of this article and declared to be responsible for all aspects of the study, ensuring its accuracy and integrity.

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