Number of Doses of Measles-Mumps-Rubeola Vaccine Applied in Brazil Before and During The COVID-19 Pandemic

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Abstract

Background

Due to the social isolation measures adopted in an attempt to mitigate the risk of transmission of SARS-CoV-2, there has been a reduction in vaccination coverage of children and adolescents in several countries and regions of the world.

Objective

Analyze the number of doses of vaccine against Measles-Mumps-Rubeola (MMR) applied before and after the beginning of mitigation measures due to COVID-19 pandemic in Brazil.

Methods

Ecological study, with data from the National Immunization Program. The Mann-Whitney test evaluated differences between the median number of MMR vaccine doses applied in Brazilian regions, states and municipalities during April/2019 to March/2020 (before the beginning of mitigation measures) and April/2020 to September/2020 (after the start of mitigation measures). Spatial analysis identified clusters with a high percentage of reduction in the median of applied doses, and interpreted according to the Global Moran's Index (I). All analyzes considered the significance level of 5%.

Results

There was a reduction in the median of doses applied in the Regions: North (-33.03%), Northeast (-43.49%) and South (-39.01%). In States: Acre (-48.46%), Amazonas (-28.96%), Roraima (-61.91%), Paraíba (-41.58%), Sergipe (-47.52%), Rio de Janeiro (-59.31%) and Santa Catarina (-49.32) ($p < 0.05$). High-high type spatial clusters (reduction between 34.00 to 90.00%) were formed in the five regions of Brazil (Moran's I = 0.055; p = 0.01).

Conclusion

A reduction in the number of MMR vaccine doses was evidenced as a possible effect by the restrictive actions of COVID-19 in Brazil.

Background

During the Coronavirus Disease Pandemic 2019 (COVID-19), national and international health agencies recommended that immunization services to continue, uninterrupted, their activities, due to the possibility of a return of vaccine-preventable diseases, controlled or eliminated, in response to low vaccination coverage [1]. However, studies have shown that, due to the social isolation measures adopted in an attempt to mitigate the risk of transmission of SARS-CoV-2, the etiological agent of COVID-19 [2, 3], there has been a reduction in vaccination coverage of children and adolescents in several countries and regions of the world [4, 5].

The impact on vaccine coverage was not an exclusive event of the COVID-19 pandemic. Studies conducted after catastrophes and epidemics that occurred in human history also pointed to a decline in vaccination coverage as a response to the reduction in the population's supply and access to health services [6]. After the Ebola outbreak that occurred in Liberia, Sierra Leone and Guinea, in West African countries, starting in 2013 and extending to 2015, there was a 25% decline in measles vaccination coverage, favoring the formation of pockets of susceptible individuals in these countries [6, 7]. In response to low vaccination coverage, since 2017, two years after the end of the Ebola outbreak, these countries are facing rising measles cases and deaths [7]. Recently, Liberia and the Democratic Republic of Congo, located in Central Africa, face the collapse of health services due to the overlapping of cases and deaths from COVID-19, measles and Ebola [6, 8].

Difficult access to immunization services and child malnutrition are factors that act synergistically, placing communities living in a situation of social vulnerability more susceptible to the development of severe forms and death as a result of measles [9]. Even with the widespread diffusion of the Measles-Mumps-Rubella vaccine (MMR vaccine) in 2019, the world's measles rates reached the highest level in the last two decades [9, 10]. It is estimated that in 2018, more than 140,000 people died from measles, with the majority of deaths reported in underdeveloped countries, affecting mainly malnourished children [10]. In this sense, health strategies and policies aimed at improving MMR vaccine coverage indicators are needed, especially in low- and middle-income countries[9].

In Brazil, in 2018, two years after receiving certification for the elimination of measles in the Americas [11], 10,346 cases of the disease were confirmed, resulting in the loss of certification as a “measles virus-free country” [12]. In 2019 and 2020, there were 20,901 and 8,448 measles cases confirmed, respectively and by April 2021, another 318 cases were confirmed [12]. The recently reported cases of measles can be explained by the progressive drop in the coverage of the MMR vaccine in Brazil over the last decade and by the formation of clusters of susceptible individuals in the States of Acre, Amazonas, Pará, Amapá, located in the North region, and in the State of Maranhão, located in the Northeast region of the country [13].

Given the immense size of Brazil and the challenge experienced by the COVID-19 pandemic, this study advances by showing the inequalities in coverage of the MMR vaccine in different locations in the country, pointing to the formation of pockets of individuals susceptible to measles, rubella and mumps. Using the results and lessons learned from this study, it will be possible to improve health strategies and policies thus working at substantially improving the country’s immunization indicators for these areas.

Regional inequalities in vaccine coverage in Brazil [13, 14], can be attributed, in part, to differences in investments in the health sector in the North and Northeast regions when compared to other Brazilian regions, which culminated in the precariousness of the nationally mandated Primary Healthcare Services (*Atenção Primaria* - AB), responsible for offering free immunization through the National Immunization Program (PNI) [15]. Considering that the historical reduction in MMR vaccine coverage rates in Brazil [16, 17], may have been aggravated by the sanitary measures adopted due to the COVID pandemic-19 and that in Brazil the distribution of health services and the allocation of health resources is known to be heterogeneous [18], this study aims to analyze the number of doses of the MMR vaccine applied before and after the beginning of measures of social distancing in response to the pandemic of COVID-19 in the municipalities, states and regions of Brazil. In addition, this study aims to identify, through spatial analysis, clusters formed by municipalities with a high contingent of individuals susceptible to measles.

Methods

Study design

This was an ecological study, with data taken from the Brazilian National Immunization Information Program System (SI-PNI), available at http://sipni.datasus.gov.br/. The SI-PNI provides the number of doses of vaccines applied monthly throughout the country.

Data collection

The data collected refer to the number of doses of the MMR vaccine administered in the period from April 2019 to December 2020. Data extraction was performed by the number of doses applied monthly to the target population over the period: children aged 12 months (first dose) and 9-year-old children (second dose).

Variables

The independent variable was the number of doses applied. The independent variables were geographical, including the five regions of the country (North, Northeast, Central, Southeast and South), the 27 States of the Federation which are comprised of 5,568 Brazilian municipalities.

Statistical analysis

First, the doses of the MMR vaccine applied before (April 2019 to March 2020) and after the beginning of social distancing measures in Brazil (April to September 2020) in the 27 states were added. Next, the differences between the median number of doses applied before and after social distancing measures were evaluated by the Mann-Whitney U test, considering the interquartile range (IQR) and the significance level of 5%. The percentage of variation of the median doses applied was estimated using the equation:

[(median of doses applied by States before social distancing measures-median doses applied by State after social distancing measures) / median of doses applied by States before social distancing measures x 100].

These analyzes were processed using the Statistical Package for Social Sciences software (IBM-SPSS, v.19, IBM, Chicago, IL).

For the general spatial analysis, the percentage variation of the median doses of the MMR vaccine was considered, before and after the beginning of social distancing measures in Brazil in each Brazilian municipality. The percentage variation of the median of applied doses was estimated using the equation previously mentioned.

Techniques for spatial analysis of area data were used considering the digital grids of Brazilian municipalities, using two Geographic Information System (GIS) programs. To examine the existence of a spatial correlation of the median reduction of doses of the MMR-Triple Viral vaccine, the Global Moran's Index (I) was calculated, which ranges from − 1 to + 1, with positive values (between 0 and + 1) indicating direct correlation and negative values, between 0 and − 1 (an inverse correlation). Spatial correlation is interpreted according to the I and can be weak ($I < 0.3$), moderate ($I \geq 0.3$; < 0.7) or strong ($I > 0.7$) [19].

From the cartographic base of the Brazilian municipalities acquired on the IBGE website, cartograms were created for the presentation of clusters with statistical significance ($p < 0.05$). The Moran Eigenvector Maps (MEM) show the high-high spatial clusters (red color) with statistical significance, formed by municipalities with a high percentage reduction in the median of applied doses of the MMR vaccine and surrounded by municipalities with the same trend. Municipalities that did not present significant spatial correlation ($p > 0.05$) or that formed spatial clusters of low-low, low-high or high-low types, were not represented on the map. The regions of the country, namely: North, Northeast, Central, Southeast and South, will be represented in the cartogram with different shades of gray.

In this study, the 95% of Global Moran I level of significance was considered after 999 permutations [19], that is, the areas with statistically significant spatial correlation were those whose p-value was less than or equal to 0.05 after 999 random permutations. For these spatial analyses, the following software was used: Spatial Analysis Laboratory, University of Illinois, Urbana Champaign, United States (GeoDa 0.9.9.10) and TerraView, version 4.1.0.

Ethical aspects

Due to the nature of the study of using freely accessible data, it was not necessary to submit the present study to the Research Ethics Committee, in accordance with Resolution 466/2012 of the National Health Council [20].

Results

From April 2019 to September 2020, 25,717,742 doses of the MMR vaccine were applied throughout Brazil (46.55% after the beginning of the social distancing measures). In the period before measurements, the median number of doses applied was 1,645,527 (IQR = 794,667–2,176,287). During this period of evaluation, the median dropped to 934,991 (IQR: 757,329–1,260,678), equivalent to a reduction of 43.17%.

Of the five regions of the country, the North, Northeast and South showed a statistically significant reduction in the median number of doses applied during the duration of the public health emergency measures. Among the states, seven showed a statistically significant reduction, ranging from 47.52% in Sergipe, to 64.91% in Roraima (Table 1).

Table 1
Median and percentage change in the median number of Triple Viral vaccines (MMR) administered.

States and Regions	**April/19 – March/20** **Median (P25 - P75)**	**April/20 – September/20** **Median (P25 - P75)**	**Variation (%)**	***p****
Brazil	1.645.527 (794.667–2.176.287)	934.991 (757.329–1.260.678)	-43.17	0.180
North	8.249 (5.352–21.528)	5.524 (2.398–13.289)	-33.03	**0.007**
Acre	3.725 (2.313–5.795)	1.920 (1.749–2.283)	-48.46	**0.007**
Amapá	4.210 (1.887–7.736)	1.811 (889–3.698)	-56.97	0.067
Amazonas	24.865 (21.693–29.212)	17.662 (10.487–18.842)	-28.96	**0.002**
Pará	70.60 (26.514–104.196)	47.808 (30.658–93.943)	-32.31	0.682
Rondônia	9.853 (6.993–14.417)	7.309 (6.554–9.199)	-25.81	0.250
Roraima	8.164 (7.188–8.527)	2.864 (2.082–4.460)	-64.91	**0.000**
Tocantins	6.519(5.352–11.474)	5.471(4.786–6.606)	-16.07	0.180
Northeast	31.180 (16.254–49.693)	17.618 (9.827–42.954)	-43.49	**0.009**
Alagoas	24.748 (12.334–38.047)	12.669 (8.606–80.190)	-48.80	0.553
Bahia	72.075 (46.428–170.581)	62.320 (52.049–82.323)	-13.53	0.494
Ceará	49.394 (25.703–74.028)	38.333 (26.499–52.847)	-22.39	0.494
Maranhão	41.476 (25.737–72.172)	25.885 (14.096–37.853)	-37.58	0.063
Paraíba	18.047 (12.741–39.194)	10.543 (8.397–12.917)	-41.58	**0.010**
Pernambuco	45.644 (30.999–100.597)	41.979 (33.530–52.866)	-8.03	0.553
Piauí	22.437 (9.216–37.044)	12.136 (8.894–14.780)	-45.90	0.125
Rio Grande do Norte	14.910 (8.979–31.871)	10.454 (6.909–26.816)	-29.89	0.437
Sergipe	14.318(8.395–21.643)	7.513(7.040–8.925)	-47.52	**0.041**
Central	17.733 (11.175–30.369)	13.181 (11.255–20.263)	-25.66	0.075
Distrito Federal	16.022 (10.382–26.444)	11.968 (10.298–18.516)	-25.29	0.437
Goiás	26.599 (16.504–50.864)	22.884 (19.098–26.081)	-13.96	0.553

Note: P = Percentile; * Mann-Whitney test (difference between medians).
Source: National Immunization Program, Brazil, April 2019 to March 2020 and April 2020 to September 2020.Source: National Immunization Program, Brazil, April 2019 to March 2020 and April 2020 to September 2020.

States and Regions	April/19 – March/20 Median (P25 - P75)	April/20 – September/20 Median (P25 - P75)	Variation (%)	*p**
Mato Grosso	12.770 (9.150–21.261)	12.194 (10.183–15.190)	-25.84	0.180
Mato Grosso do Sul	12.769(9.149–21.260)	12.193(10.182–15.190)	-4.51	0.682
Southeast	106.908 (35.384–220.958)	76.034 (35.558–177.384)	-28.87	0.351
Espírito Santo	21.798 (19.825–32.589)	25.013 (18.680–46.157)	14.74	0.892
Minas Gerais	110.574 (91.922–212.637)	140.480 (95.501–176.163)	27.04	0.750
Rio Janeiro	89.087 (41.172–129.471)	36.248 (34.224–37.285)	-59.31	**0.018**
São Paulo	246.595(209.330-662.975)	226.283(166.472-371.318)	-8.23	0.335
South	54.250 (41.475–93.080)	33.084(27.607–54.533)	-39.01	**0.007**
Paraná	81.645 (44.428–164.329)	57.506 (51.821–66.180)	-29.56	0.750
Santa Catarina	56.141(36.571–93.080)	28.447(26.736–31.991)	-49.32	**0.007**
Rio Grande do Sul	43.931 (26.408–71.409)	30.522 (25.086–34.712)	-30.52	0.151

Note: P = Percentile; * Mann-Whitney test (difference between medians).
Source: National Immunization Program, Brazil, April 2019 to March 2020 and April 2020 to September 2020.Source: National Immunization Program, Brazil, April 2019 to March 2020 and April 2020 to September 2020.

Weak spatial autocorrelation (I = 0.055; p = 0.01) and the presence of High-High spatial clusters were identified, formed by 262 municipalities that presented a reduction in the median of applied doses between 34 and 90%, 88 of which were located in the North Region, 107 in the Northeast region, 41 in the Southeast region and 26 in the South region (Fig. 1).

Discussion

The COVID-19 pandemic resulted in a reduction in the number of applied doses of the MMR vaccine as a possible effect of the restrictive actions of COVID-19. The North, Northeast and South regions and the States of Acre, Amazona, Roraima, Paraiba, Sergipe, Rio de Janeiro and Santa Catarina showed a significant reduction in the median of MMR vaccine doses applied during the period that recommendations for social distancing were put in place in Brazil. High-High spatial clusters were formed by municipalities located mostly in the Northeast and North regions of the country.

National and international studies attributed a reduction of the population's demand for health services, with a consequent drop in vaccination coverage, to the restrictive mitigation measures adopted during the COVID-19 pandemic [1, 5, 21, 22]. However, there has been an observed trend in a decline in vaccine doses applied in Brazil over the last two decades [22], especially those immunobiologicals recommended in early childhood [13, 23]. Contextual and individual factors that have been cited in recent studies [15, 22] have attributed the decline based on vaccination coverage including the lack of planning by the Brazilian National Universal Healthcare System (SUS), social and cultural aspects effecting vaccination acceptance, logistical difficulties cited by the PNI in offering several routine vaccines as part of the national vaccine schedule, anti-vaccination movements, and inconsistencies in the availability of immunobiologicals offered by Primary Healthcare services.

In this study, three of the five Brazilian regions demonstrated a statistically significant reduction in the median of doses of the MMR vaccine applied during the period of social distancing measures. This scenario, added to the drop in vaccination coverage rates in recent years, point to a problem for collective immunity and the risk of outbreaks caused by measles [14, 23]. Furthermore, it is worth noting that the regional inequalities in vaccination coverage in Brazil has favored the formation of pockets of susceptible individuals [13, 23, 24].

Between 2015 and October 2018, Brazil experienced a significant drop in MMR vaccine coverage, from 96.1 to 86.7% and, only after the national vaccination campaign, in September 2018, did it reach the 95.0% target. These low vaccination coverage indicators, added to measles cases imported from Venezuela, triggered an epidemic of the disease that affected several Brazilian states, mainly states in the Northern regions [25].

A study that evaluated the availability of the MMR vaccine in Brazil from 2013 to 2014 indicated that the immunization services located in the North region had a inefficient structure for immunization actions and demonstrated a lower frequency of vaccine availability [15]. The lack of vaccine in the Northern region, even during short period of time, incurs a lost opportunity for vaccination and can compromise the achievement of vaccination coverage goals, increasing the number of susceptible individuals in this region [15].

The lower frequency of availability of the MMR vaccine, on top of the logistical and structural problems of the AB services in the Northern region, may have contributed to the formation of clusters with a higher percentage reduction in the coverage of the MMR vaccine in this region. Furthermore, it is noteworthy that measles is one of the most contagious infectious diseases known [26], making it necessary to adopt emergency strategies for vaccinating communities that formed clusters with a significant reduction in immunization coverage during the COVID-19 pandemic period. This strategy aims to reduce the chances of overlapping cases of measles and COVID-19, which could favor the collapse of healthcare services in these regions.

Furthermore, the collapse of health services in some states in the North and Northeast regions, due to the increasing demand for hospital beds for patients with COVID-19, may have contributed to the reduction in the population's demand for immunization services in these regions [27, 28]. Strategies to contain the pandemic in states and regions of Brazil were also not uniform, which may explain the percentage variations in the median of applied doses of the MMR vaccine, from 47.52% in the State of Sergipe ($p = 0.041$) to 64.91% in the State of Roraima ($p = 0.000$). While in some locations, the response to the epidemic phase of acceleration of the number of cases and deaths from COVID-19 was the mitigation by means of social distancing, other locations resorted to the strategy of total confinement, that is suspending all non-essential activities and limiting the circulation of people [29, 30].

In Brazil, more than a year after the first case of COVID-19, the country continues to lag behind many developing countries in an effort to immunize its population against COVID-19 [31] and many public health officials agree that long-term social isolation strategies will continue for several years to come [32]. Under this scenario, it is necessary to adopt health strategies and policies that ensure the population's universal access to immunization programs. The consequences of a lack of access would means living with the overlapping cases and deaths from COVID-19 with other infectious diseases, such as measles, rubella and mumps.

Limitations and study strengths

One of the weaknesses of the present study was in relation to the intrinsic limitations of studies that use secondary data, in addition to the fact that the available data were not specifically collected to answer the questions proposed in this research. Another point that deserves to be highlighted was the possible influences related to the standardization and quality of filling in the SI-PNI records, which may be subject to information bias. However, in this study, the SI-PNI registered population data was used during the study period, and the generalization of these results is relatively safe for national estimates. Also, to control biases, methodological rigor was taken into account during all of the stages of the study execution.

Conclusions

The COVID-19 pandemic resulted in a reduction in the number of applied doses of the MMR vaccine as a possible effect of the restrictive actions of COVID-19. In Brazil, few studies have evaluated the impact of the COVID-19 pandemic on the vaccination of children and adolescents, and this is the first study in the country to consider the MMR vaccine. The results of this work may support public health policies to guarantee immunization strategies against measles, rubella and mumps in the country, even during the current epidemic phase, which continues to result in increases in the number of COVID-19 cases in Brazil. In this sense, this work may point out priority areas for which public health policies and health strategies should be adopted to improve immunization indicators, in order to prevent the spread of potentially vaccine-preventable infectious diseases.

List Of Abbreviations

Coronavirus Disease Pandemic 2019 - COVID-19

Measles-Mumps-Rubella vaccine - MMR vaccine

Global Moran's Index - I

Moran Eigenvector Maps - MEM

National Immunization Program - PNI

Interquartile range - IQR

Brazilian National Immunization Information Program System - SI-PNI

Declarations

Ethics approval and consent to participate

Due to the nature of the study of using freely accessible data, it was not necessary to submit the present study to the Research Ethics Committee, in accordance with Resolution 466/2012 of the National Health Council.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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None.

Authors' contributions

TMRS: conception, worked on study design, analysis and interpretation of data, co-wrote this manuscript, critical content review and approval of the final version.

ACMGNS: worked on study design, analysis and interpretation of data, co-wrote this manuscript, critical content review and approval of the final version.

EJSP: interpretation of data, co-wrote this manuscript, critical content review and approval of the final version.

EWRV: data interpretation, co-wrote this manuscript, critical content review and approval of the final version.

MAB: data interpretation, co-wrote this manuscript, critical review of content and approval of the final version.

FPM: data interpretation, co-wrote this manuscript, critical review of content and approval of the final version.

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Figures

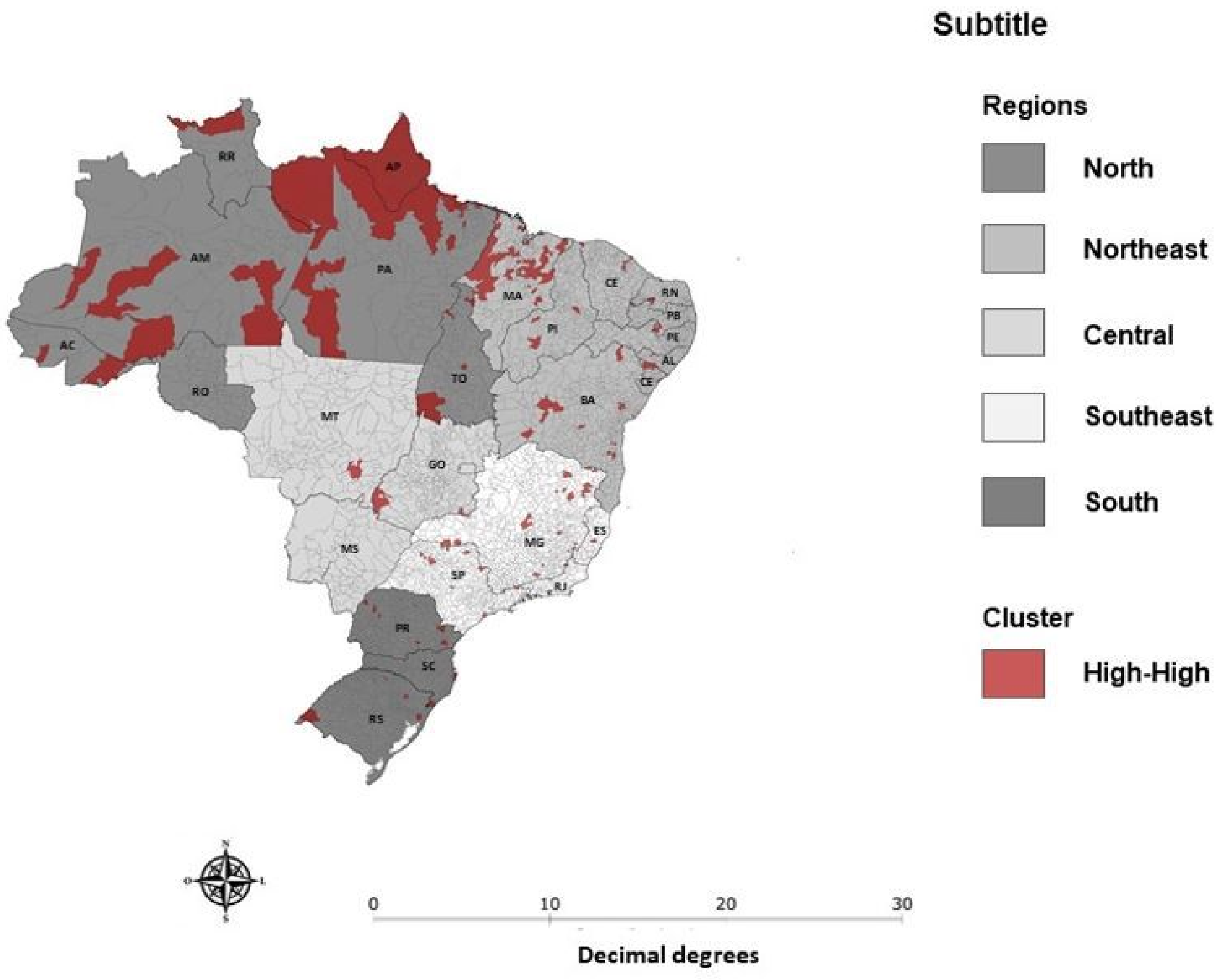

Figure 1

High-high spatial clusters with statistical significance. Source: National Immunization Program, Brazil, April 2019 to March 2020 and April 2020 to September 2020.