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The impact of COVID-19 on routine pediatric vaccination delivery in Brazil



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ABSTRACT

Introduction: Childhood vaccination rates have decreased significantly during the COVID-19 pandemic. The Brazilian immunization program, Programa Nacional de Imunização (PNI), is a model effort, achieving immunization rates comparable to high-income countries. This study aimed to evaluate the impact of the COVID-19 pandemic in pediatric vaccinations administered by the PNI, as a proxy of adherence to vaccinations during 2020.

Methods: Data on the number of vaccines administered to children under 10 years of age nationally and in each of Brazil's five regions were extracted from Brazil's federal health delivery database. Population adjusted monthly vaccination rates from 2015 through 2019 were determined, and autoregressive integrated moving average (ARIMA) models were used to forecast expected vaccinated rates in 2020. We compared the forecasts to reported vaccine administrations to assess adequacy of pediatric vaccine delivery during the COVID-19 pandemic.

Results: From January 2015 to February 2020, the average rate of vaccine administration to children was 53.4 per 100,000. After February 2020, this rate decreased to 50.4, a 9.4% drop compared to 2019 and fell outside of forecasted ranges in December 2020. In Brazil's poorest region, the North, vaccine delivery fell outside of the forecasted ranges earlier in 2020 but subsequently rebounded, meeting expected targets by the end of 2020. However, in Brazil's wealthiest South and Southeast regions, initial vaccine delivery fell and remained well below forecasted rates through the end of 2020.

Conclusion: In Brazil, despite a model national pediatric vaccination program with an over 95% national coverage, vaccination rates decreased during the COVID-19 pandemic. Coordinated governmental efforts have ameliorated some of the decrease, but more efforts are needed to ensure continued protection from preventable communicable diseases for children globally.

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1. Introduction

Nearly 70% of the Brazilian population, approximately 150 million people, depend on Sistema Único de Saúde (SUS), the public health system which oversees the national vaccine program, the Programa Nacional de Imunizações (PNI) [1]. SUS is Brazil's feder-

ally funded healthcare system founded in 1988 under the precepts of universality, integrality, and equity [1]. SUS has already made great strides towards Universal Health Coverage (UHC), and the PNI has been considered a global standard in providing vaccination coverage for the past 30 years [2,3]. It is estimated that 90–95% of all vaccines administered in Brazil are offered by PNI [4,5]. This success has led to the control of a number of communicable diseases across Brazil and serves as a model for the delivery of vaccinations across a large, socially and geographically diverse middle-income country [3].

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In Brazil, when a birth certificate is issued or at a child's first visit to a health clinic, a profile is created in an online medical record system that also records immunization records [6]. The Information System of the National Immunization Program (SIPNI) contains data on vaccine coverage, individual vaccine doses, the incidence of adverse effects, and the number of vaccines in stock [7]. Through the efforts of the PNI in combination with a federally funded system of UHC, Brazil has achieved nearly 100% essential vaccine coverage free of charge to the public [3]. As a result of the COVID-19 pandemic, of which the first recorded case occurred in Brazil in February 2020, a reduction in routine health and preventative care occurred [8]. Despite the pandemic, the World Health Organization (WHO) and the Pan American Health Organization (PAHO) recommend that vaccination programs be maintained as an essential health service [9].

The United Nations International Children's Emergency Fund (UNICEF) estimates that due to the suspension of 93 vaccination campaigns around the world, approximately 80 million children may be at risk for vaccine-preventable illnesses including diphtheria, polio, and measles [10]. Regardless of government efforts to promote immunization, vaccination coverage may be hampered by public concerns about being exposed to SARS-CoV-2 as well as anti-vaccination movements [9]. The aim of this study is to assess the adequacy of vaccination rates among children under 10 during the COVID-19 pandemic in Brazil. This research hopes to encourage Brazilian authorities to create programs and policies aimed at post-pandemic vaccination coverage to address the gap in childhood immunizations.

2. Methods

We performed a retrospective cross-sectional study to assess the impact of the COVID-19 pandemic on childhood vaccination coverage by Brazil's SUS system. The analysis focused on the delivery of immunizations to children under 10 in accordance with the PNI calendar.

2.1. Data sources

Publically available data on vaccine distribution tabulated by state per month from 2015 through 2020 were obtained from Brazil's open access federal health delivery database DataSUS [11]. DataSUS is a publicly accessible database maintained by the Department of Strategic and Participatory Management of the Ministry of Health which publishes monthly reports of disaggregated data at the municipal level for a broad array of diagnoses and procedures [11]. All data available for the years 2015–2020 were retrieved following the regulations of Resolution No. 466/12 on Research Ethics of the National Health Council, Brazil. Annual population estimates were obtained for 2017 through 2020 from the Brazilian Institute of Geography and Statistics [12]. The number of cases of COVID-19 was obtained at a national level from Johns Hopkins COVID-19 Dashboard maintained by the Center for Systems Science and Engineering [13]. Children from birth to age ten, the main age group of the vaccination program in Brazil, were included. Monthly totals for vaccines were based on the vaccine calendar according to PNI and included Hepatitis B, BCG, Pentavalent (Bacterial triple, Hepatitis B, *H. influenzae*), Bacterial triple (Diphtheria, Tetanus, Pertussis), *H. influenzae*, Poliomyelitis (inactivated and oral vaccines), Pneumococcal, Rotavirus, Meningococcal, Yellow Fever, Triple viral (Measles, Mumps, Rubella), Varicella, and Hepatitis A. For the purposes of our study, vaccine coverage refers to the population adjusted rate of individual vaccine doses delivered for vaccines covered under Brazil's standard immunization program, PNI.

2.2. Statistical analysis

Descriptive statistics were performed. The total number of vaccines administered to children age ten and younger was calculated and population standardized vaccine rates were compared among regions. An autoregressive integrated moving average (ARIMA) model was used to forecast vaccination rates for 2020 based on historical monthly vaccine administration rates prior to February 2020; the first documented case of COVID-19. A log transformation was used to induce stationarity. Partial autocorrelation function (PACF) and autocorrelation function (ACF) were used to identify the AR and MA components and the stationarity of the square root transformed series. Model parameters were then estimated based on least squares. The goodness of fit of the models was evaluated based on the lowest normalised Bayesian information criterion (AIC) being considered the optimal model. The partial autocorrelation and autocorrelation of residuals was diagnosed using the Ljung-Box (Q) test to confirm if the series of residuals was white noise. $P < 0.05$ was considered statistically significant. Finally, the optimal model was used to predict the expected number of vaccines administered in Brazil from February 2020 through December 2020. Separate models were constructed for each region based on the number of population-adjusted vaccine administrations. Estimates were then plotted against actual vaccine administration during the COVID-19 pandemic. Statistical analysis was performed in Microsoft Excel and R V3.62 [14].

2.3. Ethics

Ethical approval was not required as the database accessed contains open-access, de-identified, aggregated data.

3. Results

In 2020, Brazil vaccinated 68% of 35.5 million children that should be vaccinated at age under 10. Between January 2015 and February 2020, SUS delivered 331 million first doses of vaccines - of the 14 vaccines recommended by the PNI for children under age ten - with an average monthly rate of 53.4 vaccines delivered per 100,000 population. Between February 2020 and December 2020, 50 million doses were delivered at an average monthly rate of 50.4 per 100 k inhabitants. The largest decrease in dose distributions from 2019 to 2020 were from Hepatitis B (-31.89%), Triple viral (-27.26%), Meningococcal (-25.02%), and BCG (-20.00%). Hepatitis A dropped 15.14%, and Polio (inactivated vaccine) dropped 10%. Influenza, Bacterial Triple, Yellow Fever, and Pentavalent were the only vaccines from pediatric PNI that showed an increase in 2020 vaccination rates, with a rise of 385%, 58.34%, 20%, and 6.20%, respectively, specifically in the month of October. In 2020, overall vaccine coverage was 68% for Brazilian children under age 10 (compared to 77.12% in 2019). Also, 78% of children under ten received the first of two doses for measles "triple viral", and 61% were covered with both doses in 2020 (versus 93% coverage in 2019).

The number of delivered vaccinations in April 2020, after the first wave of COVID-19, was less than 4 million doses. Furthermore, in December 2020, 2.2 million doses were distributed during the second wave of COVID-19. In Brazil, the number of COVID-19 cases reached its height in December. Thus, the number of vaccinations delivered decreased as COVID-19 cases were on the rise (Fig. 1). Comparing a monthly vaccination dose distribution in 2020 to the average monthly rate from years prior (2015–2019), vaccination rates dropped 27% in April 2020, 29% in November 2020, and 25% in December 2020. The vaccine with the largest decrease in distribution during April was *H. influenzae* at 55%, while Hepati-

Number of Vaccinations Delivered to Children Under 10 (2020)

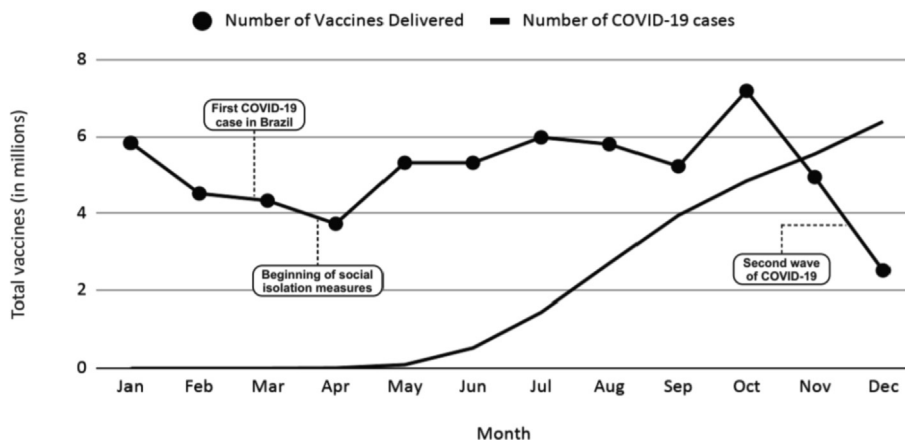


Fig. 1. Trends in vaccination rates (PNI) after COVID-19. Caption Fig. 1: As COVID-19 cases raised, the total number of vaccines delivered by the PNI declined.

tis B showed the largest decrease in November at 43.8%. By region, the South had the most significant vaccination rate drop, with a decrease of 14.12%, followed by Southeast (-12.84%), North (-9.07%), Northeast (-3.87%). The Central-west was the only region that showed an increase (+0.91%).

ARIMA forecast models demonstrated that the total number of vaccinations delivered in December 2020 fell well below the forecasted range and outside of the 95% confidence interval. Regionally, the South and Southeast regions also fell outside the predicted lower 95% confidence interval for the month of December 2020. The North region fell below the expected ranges early in the pandemic in April and May, but rates increased to within expected ranges by mid-August.

4. Discussion

Brazil's national healthcare system has been a model program when it comes to vaccinations with relative success in maintaining high levels of vaccinations despite large geographic variation [15–17]. Our results demonstrate that the number of vaccinations delivered to children under the age of ten in Brazil have not only decreased since the start of the pandemic, but that trends in childhood vaccination rates continue to fall outside of historical norms nearly a year after the start of the pandemic. Furthermore, there has been significant regional variation in vaccine delivery during the pandemic that highlights the need for context specific strategies to remedy reductions in vaccine coverage for children. Our results are consistent with data published in the literature on vaccination trends in Brazil over the last five years [18]. The reductions in administration of childhood vaccines quantified in our study will likely bring with it increases in childhood disease over the next several years and raise significant concern for the health and wellbeing of Brazilian children even after resolution of the COVID-19 pandemic. Thus, the attention of Brazilian authorities should be drawn to the creation of targeted catch-up vaccination campaigns to increase vaccine coverage and to attempt to reduce the transmission of vaccine-preventable diseases.

The first COVID-19 case in Brazil was reported on February 26th, 2020 and social isolation measures started in March, at a point when 6,836 people were already infected [13,19]. The first wave of COVID-19 cases in March likely caused the abrupt decrease in the number of vaccinations administered in April, and similarly, the second wave of COVID-19 cases in October

may be responsible for the drastic decrease in vaccinations seen in November and December [13,19]. Decreases in seasonal vaccination rates are not new to Brazil, and historically, the Brazilian government has hosted an annual vaccination campaign to close the gap in pediatric vaccinations. In 2020, during the pandemic, an October multi-vaccination campaign was created. The target audiences were children and adolescents under age 15, and all vaccines offered by the PNI were distributed [20]. Increased vaccination coverage for Yellow Fever, Influenza, and Bacterial triple could be observed (see Fig. 1). Such increases can be explained by historically low vaccination coverage. For example, yellow fever was added to the PNI vaccine schedule in 2018 due to an outbreak, especially in the Southeast region, and in 2020, the Ministry of Health started to distribute a booster dose for children aged 4 [18]. Historically, the adherence of children to vaccination campaigns against Influenza has always been low [18]. However, since respiratory symptoms from COVID-19 overlap with other viral diseases, such as Influenza, there may have been greater interest from parents in vaccinating their children during the pandemic.

However, due to the unprecedented number of vaccinations missed secondary to lack of routine primary child healthcare during the initial pandemic, the number of doses distributed in 2020 did not adequately close the gap (see Fig. 2). We found that specifically, BCG, Hepatitis B, and Triple Viral (measles, mumps, and rubella) experienced dramatic decreases compared to the other vaccines. The significant decrease in the Triple Viral vaccine may be because parents did not want to take their children into the clinic for vaccines for fear of interacting with other people and becoming infected with COVID-19. BCG and Hepatitis B are vaccines distributed to newborns before leaving the maternity hospital. Some studies referring to the PNI, prior to the pandemic, had already observed a drop over the years, mainly in BCG and Hepatitis B. It is speculated that the explanation for this drop is the increase in popularity of the anti-vaccination movement in Brazil and the fear of parents about possible adverse effects [21].

Brazil's five distinct regions are uniquely diverse, ranging in parallel from low to high-income countries. The regions have broad socio-economic differences represented by dramatic differences in both GDP per capita and Human Development Index (HDI) (see Table 1) [22]. Our results found that the Northern region, an area with the lowest GDP per capita and one of the second lowest HDI, experienced a larger decrease in vaccination doses administered in 2020. Overall, vaccination rates have improved since

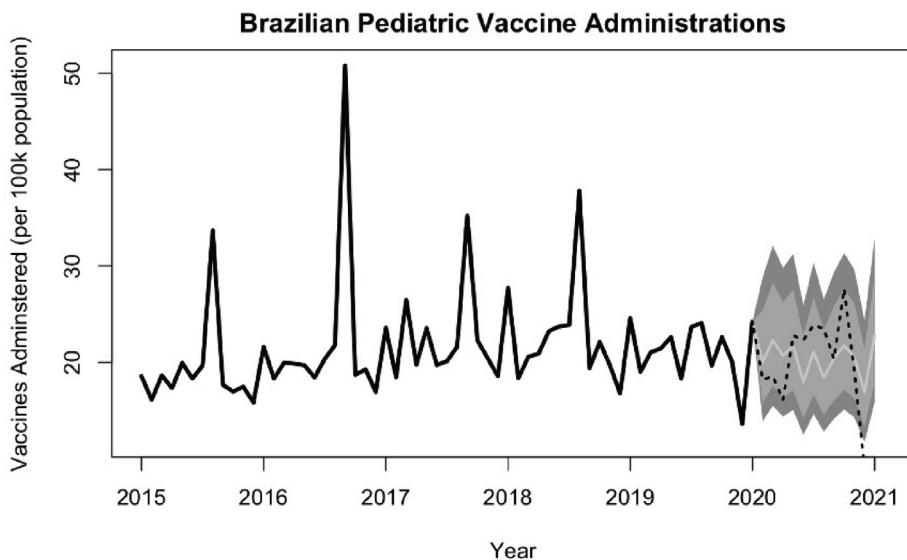


Fig. 2. National vaccine trend. Caption Fig. 2: ARIMA model of monthly vaccine administration for Brazil. Solid black represents historical data, dashed line represents true vaccine administration between February 2020 and December 2020. Light grey (90%), and dark grey (95%) represent confidence intervals for predicted vaccine administrations based on historical trends. All the vaccines delivered by the PNI were included.

April/May, while in the South and Southeast regions with higher HDIs, rates continue to be below expected and are now solidly out-

side of historical norms. Although the poorest areas of Brazil saw initial reductions in vaccine coverage, they have demonstrated

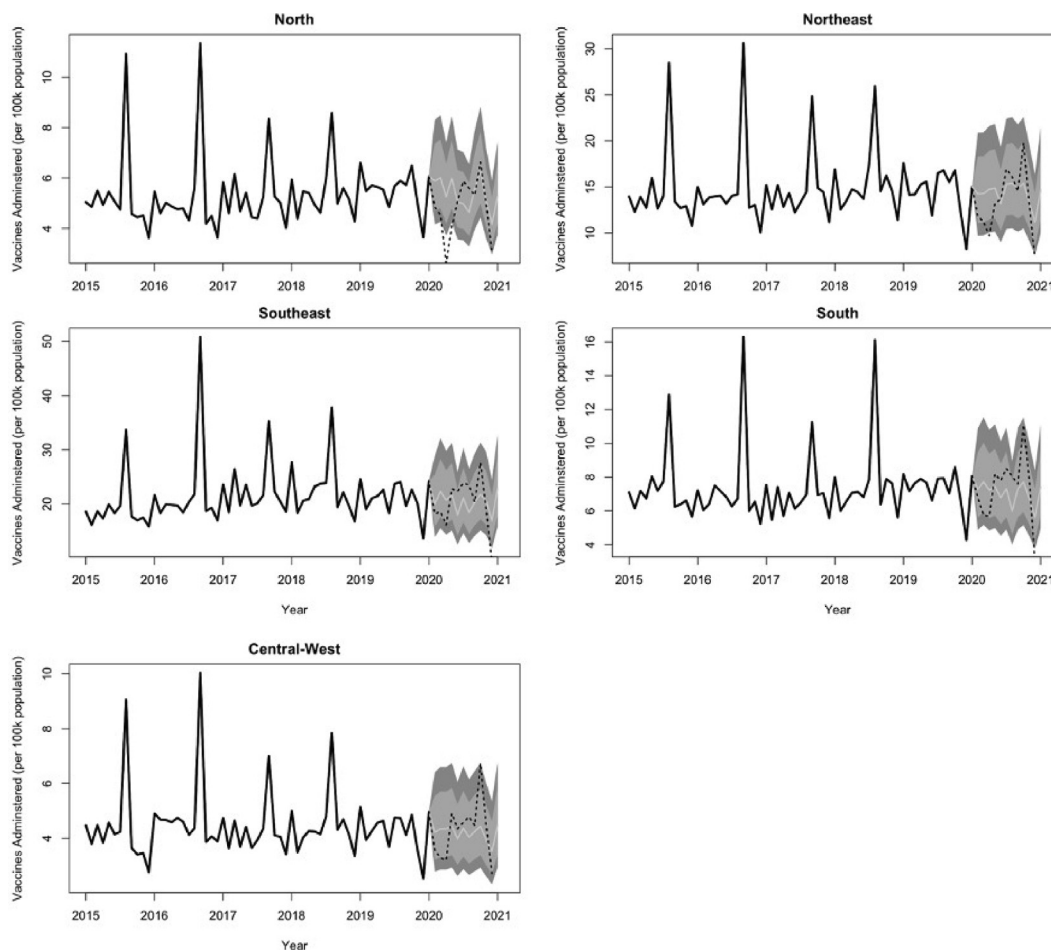


Fig. 3. Trends by region. Caption Fig. 3: Regional ARIMA models of population adjusted vaccine administrations for children under age ten in Brazil. Solid black represents historical data, dashed line represents true vaccine administration between February 2020 and December 2020. Light grey (90%), and dark grey (95%) represent confidence intervals for predicted vaccine administrations based on historical trends. All the vaccines delivered by the PNI were included.

Table 1
Annual vaccination delivery and average population adjusted monthly rate by region.

Table: Annual Vaccinations Delivered to Children Under Ten														
Region	GDP (R\$) per capita [35]	HDI [22]	Total Vaccines Delivered (millions)						Average Population Adjusted Monthly Rate					
			2015	2016	2017	2018	2019	2020	2015	2016	2017	2018	2019	2020
Northeast	9,848.97	0.608	17.4	17.7	17.5	18.6	17.4	16.2	14.4	14.8	14.6	15.4	14.5	13.5
Southeast	27,141.92	0.753	23.0	26.6	26.9	27.4	25	24.5	19.1	22.1	22.4	22.8	20.8	20.4
North	13,041.58	0.683	63.7	63.1	63.4	65.3	66.2	58.8	53.1	52.6	52.8	54.4	55.23	48.9
South	22,647.46	0.831	87.8	88.2	83.5	93	87.5	88.3	73.2	73.5	69.6	77.5	72.9	73.5
Central-west	25,253.47	0.757	51.8	58.5	51.5	54.2	50.7	51.9	43.1	48.7	42.9	45.2	42.2	44.4
Total	20,371.64	0.765	60.7	65.3	64.3	67.2	62.9	60.7	53.1	52.6	52.8	54.4	55.2	48.9

HDI: Human Development Index.
GDP: Gross Domestic Product.

Table 2
Strategies for vaccination in the literature.

Table 2: Strategies Proposed for Improved Childhood Vaccinations	
Strategy	Country/Continent Examples
Continue immunization programs during the COVID-19 pandemic to prevent new outbreaks	Africa (Abbas et al [17]) Pakistan (Chandir et al [26]) Italy (Bechini et al [27])
Implement more stringent sanitary measures such as use of individual protective equipment, physical distancing, and handwashing in all clinic facilities	Africa (Abbas et al [17]) Italy (Bechini et al [27]) USA (Bramer et al [28])
Actively monitor vaccination rates in the country in order to identify children who have missed vaccination	Sierra Leone (Buonsenso et al [15]) Italy ((Bechini et al [27]) USA (Bramer et al [28]) Pakistan (Chandir et al [26]) Japan (Shimizu et al [30])
Create catch-up vaccination campaigns	Indonesia (Suwantika et al [16]) Italy ((Bechini et al [27]) Japan (Shimizu et al [30])
Create specific vaccination rooms so that healthy children can be separated from where sick patients are seen Close down waiting room areas Schedule appointments in advance	Brazil (Sato [31]) USA (Bramer et al [28]) Italy (Bechini et al [27])
Develop alternative vaccination modes, such as vaccination in vehicles or at home to target the most vulnerable population	Brazil (Sato [31]) USA (Bramer et al [28]) Pakistan (Chandir et al [26]) Saudi Arabia (Alsuhaibani et al [32])
Develop revenue-generating plans in order to finance additional vaccination campaigns i.e: funding sources via sectors that the population trusts (for example religious leaders, health professionals) or increasing taxes on alcohol and tobacco	Indonesia (Suwantika et al [16])
Assemble an interdisciplinary team of researchers, policymakers and society members to solve this public health problem	Brazil (Matos et al [29])

recovery. On the other hand, the wealthiest areas of Brazil saw a delayed occurrence of below average vaccination rates, yet these areas are also the ones who have performed the worst in catching up on vaccination coverage. The possible explanation for this discrepancy is the rise of fake news about vaccines and the potential

risks of some of them during the pandemic, especially in the richest regions of the country [23]. However, this difference is not yet fully comprehensive and certainly deserves further research in the future.

This is all to suggest that regional disparities likely play a large role in the ability of health systems to respond to and adapt to the COVID-19 pandemic. Therefore, the country will require a nuanced approach to ensure adequate availability of scheduled vaccines for children.

Concerted efforts are needed to ensure rapid catch-up for children who have missed recommended vaccinations. If this catch-up does not occur quickly, countless outbreaks could erupt, affecting the country’s most vulnerable populations. For example, measles is one of the most contagious viruses with an effective reproductive number (R) of 12–18 [24]. In order to achieve herd immunity for measles in a population, 95% of the population in each age group must be vaccinated [24]. According to DataSUS in 2020, only 50% of Brazilian total population were vaccinated against measles, rubella, mumps, and chickenpox (compared to 70% vaccinated in 2019), far below the target of 95% vaccination coverage, leaving people particularly vulnerable to outbreaks from measles and other viral infections [11]. One model of vaccination coverage in low-and-middle income countries suggests that without vaccination, all-cause under-5 mortality would be approximately 45% higher [25]. These findings, in concert with ours in Brazil suggest that rapid adoption of strategies to improve vaccination coverage are needed.

A number of strategies have been proposed to overcome the decline in pediatric vaccinations seen during the COVID-19 pandemic. Strategic measures include continuing existing immunization programs during the COVID-19 pandemic in order to prevent new outbreaks [26,27], and actively monitoring vaccination rates in order to effectively monitor the situation [15,26,27,30]. Others have suggested targeted catch-up vaccination campaigns [16,27,30], use of mobile units to be dispatched to vaccinate children in vulnerable areas [26,28,29,31,32], and the development of revenue-generating plans in order to finance additional vaccination campaigns [16]. The effectiveness of these strategies has yet to be determined, but our results suggest that even for countries with experience delivering annual vaccination campaigns, there may be significant under delivery of vaccinations for children due to the unprecedented drop in vaccination rates during the pandemic. Countries must be vigilant in monitoring the effectiveness of individual campaigns to ensure that adequate coverage is achieved. Brazil, for example, may need to add an additional campaign for unvaccinated children to make up for the deficit incurred during the COVID-19 pandemic. Additionally, as COVID-19 vaccination programs are expanded and new infrastructure is developed to deliver the vaccine, consideration should be given to harness these systems to deliver other critical vaccines

to overcome the large deficiency in childhood immunizations seen in Brazil and other countries.

Implementing these strategies on a national or global level is no easy task. Success will depend on the cooperation and support of local, regional, and national governments as well as international health organizations. Financing these strategies presents a problem that likely requires a complex solution involving a large group of investors including national governments, international organizations, and private donors. International agencies such as the WHO and the UN have a long history of implementing policies and guidelines for vaccination worldwide. In 2012, WHO developed the Global Vaccine Action Plan 2011–2020 (GVAP), a framework to prevent deaths through more equitable access to vaccines for all [33]. More recently in April 2020, WHO, in collaboration with other organizations, developed COVAX, an initiative aimed at providing equitable access to COVID-19 diagnostics, treatments, and vaccines [34]. Childhood mortality is a key Sustainable Development Goal and as such, the UN and WHO must prioritize childhood vaccines in the wake of COVID-19 in order to ensure that the gains made globally in reducing childhood disease and death are sustained.

Our study is not without limitations. Vaccination rates in Brazil are reported on an aggregated level, so it is not possible to determine the number of patients who have met the full schedule of vaccination. Our ARIMA models are based on historical rates which fluctuate annually based on different national strategies and vaccine campaigns. We attempted to make our data as stationary as possible and account for seasonal variation in our ARIMA forecast models, but due to changing policies and the aggregated nature of the data, it is difficult to capture the effect of future vaccine related policy within forecast policies.

5. Conclusions

Despite a model national vaccination program that provides free vaccines with historical coverage of nearly 100%, delivery of vaccines for children under 10 has fallen in Brazil during the COVID-19 pandemic with significant regional disparities in the response. Despite a national campaign in October to catch up on missed vaccinations, the number of vaccines delivered monthly remains lower than expected and well below historical norms. Additional efforts aimed at reversing these deficits are needed not only in Brazil, but globally, to ensure continued protection for children from preventable communicable diseases.

6. Summary box key questions:

What is already known?

- The COVID-19 pandemics have affected daily routine with isolation measures and lockdown.
- People stayed at home more often during 2020, and this may be reflected in vaccination distribution rates.
- Brazil's standard immunization program, PNI, is a public system of vaccination that covers 95% of the Brazilian population.

What are the new findings?

- Total number of delivered vaccines have fallen in 2020, with April, November, and December showing the biggest decreases.
- Hepatitis B, Measles, Mumps, Rubella, and Meningococcal had an approximately 30% drop.
- Poor regions suffered disproportionately with the reduction in the number of vaccines in Brazil.

What do the new findings imply?

- Data suggests the atypical year of 2020 has impacted vaccination delivery in Brazil.
- The pandemic was probably responsible for social behaviors that led to fewer distributions of vaccines by PNI.
- New outbreaks of severe diseases may occur if this trend continues, and new vaccination campaigns and strategies must be carried out so that preventable diseases do not become new outbreaks.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2022.02.076>.

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