

Analysis of vaccination coverage in children under one year and its implications in the state of Maranhão, Brazil

Título Resumido: Infant Vaccination Coverage and Its Impacts in Maranhão

Análise da cobertura vacinária em menores de um ano e suas implicações no estado do Maranhão, nordeste do Brasil

Título Resumido: Cobertura vacinal infantil e seus impactos no Maranhão

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ABSTRACT

Active immunization through vaccination is the most effective method to reduce the spread of infectious diseases. Therefore, this study analyzed vaccination rates in the state of Maranhão in the periods of 2013-2022, in order to understand the implications of the reduction in this

coverage for the re-emergence of previously eradicated diseases and the main outcomes. This is an ecological type of time series and spatial correlation research carried out in the state of Maranhão. In this study, the vaccination coverage of immunobiologicals recommended for children under 1 year of age was analyzed, namely: vaccine against Bacillus of Calmette and Guérin (BCG), human rotavirus vaccine, pneumococcal 10 vaccine, pentavalent vaccine, meningococcus C vaccine, polio vaccine and yellow fever (YF) vaccine. Of the seven immunobiologicals studied, the only ones to reach the recommended target for vaccination coverage were BCG and polio, during the period of data analysis. Regarding the trend, none showed an increasing pattern during the analyzed period and the formation of clusters indicating risk areas. Undoubtedly, vaccines are indispensable tools for preventing and combating diseases, in addition to being excellent cost-effectiveness. Given the results, it can be said that the population is certainly the main protagonist in this scenario, since the success or failure of immunization actions are closely associated with society's adherence. Therefore, supporting and encouraging actions that contribute to community awareness and access to vaccines are essential in this context.

Keywords: Vaccine, Immunization, Primary prevention, Primary attention.

RESUMO

A imunização ativa através da vacinação é o método mais eficaz para reduzir a propagação de doenças infecciosas. Portanto, este estudo analisou as taxas de vacinação no estado do Maranhão de 2013 a 2022. Trata-se de uma pesquisa do tipo ecológico de séries temporais e de correlação espacial realizada no estado do Maranhão. Neste estudo foi analisada a cobertura vacinal dos imunobiológicos recomendados para menores de 1 ano, a saber: vacina contra Bacillus Calmette Guérin (BCG), vacina contra rotavírus humano, vacina pneumocócica 10, vacina pentavalente, vacina contra meningococo C, vacina contra a poliomielite e a vacina contra a febre amarela (FA). Dos sete imunobiológicos estudados, os únicos que atingiram a meta de cobertura vacinal recomendada foram BCG e poliomielite, no período de análise dos dados. Quanto à tendência, nenhuma apresentou padrão crescente no período analisado e formação de clusters indicando áreas de risco. As vacinas são ferramentas essenciais para prevenção e combate a doenças, além de apresentarem excelente custo-benefício. Concluiu-se que os estados apresentaram tendência decrescente nos indicadores de vacinação em menos de um ano no período analisado. Tais indicadores podem sobrecarregar os serviços de média e alta complexidade do SUS, além de aumentar as já elevadas taxas de mortalidade infantil no estado.

Palavras-Chave: Vacina, Imunização, Prevenção primária, Análise espacial, Atenção primária.

INTRODUCTION

Active immunization through vaccination is established as the most effective method to reduce the spread of infectious diseases, thus serving as a major predictor of the reduction in morbidity and mortality of preventable diseases¹. In this context, Brazil's National Immunization Program (NIP), formulated in 1973, coordinates and oversees vaccination activities in the country, currently providing over 15 immunogens free of charge to the entire Brazilian population^{2,3}. This provision is offered according to various vaccination schedules that cover specific calendars for infancy, adolescence, adults, pregnant women, and also the elderly.

All of this program's strategy was consolidated over time, following the organizational principles of the Brazil's Unified Health System (*Sistema Único de Saúde [SUS]*), established in 1990, thus allowing the gradual decentralization of the National Immunization Program (PNI). Consequently, more than 5,000 municipalities in Brazil gained access to vaccination schedules, including even the most remote ones^{3,4}. On the other hand, despite the numerous achievements over the years, the PNI has faced current challenges related to declining vaccination rates⁴.

The source of this problem is multifaceted, involving issues such as underfunding of the Brazil's Unified Health System, ineffective dissemination, and inequality in the availability of immunogens between private and public networks⁵. Nevertheless, this latter disparity is exemplified in the influenza vaccine, which has a coverage rate of around 32.4 years of age when obtained in the private sector, a proportion that is not observed to the same extent in the PNI⁵.

The deviation of vaccination coverage rates is not limited to Brazil and is also observed in developed countries like the United States, where the term 'non-medical exemptions (NMEs)' based on philosophical beliefs has gained prominence⁶. Furthermore, the downward trend in vaccination coverage in Brazil since 2013 is strongly linked to unsubstantiated and misleading information consistently spread on social media⁷.

Finally, starting in 2020, the COVID-19 pandemic also contributed to the decline in vaccination coverage in children due to the suspension of vaccination campaigns for a few days and parents' concerns about their children contracting Sars-CoV-2 at vaccination centers⁸. In Maranhão, the lower coverage was associated, according to some studies, with socioeconomic differences, being more pronounced in children in situations of social vulnerability².

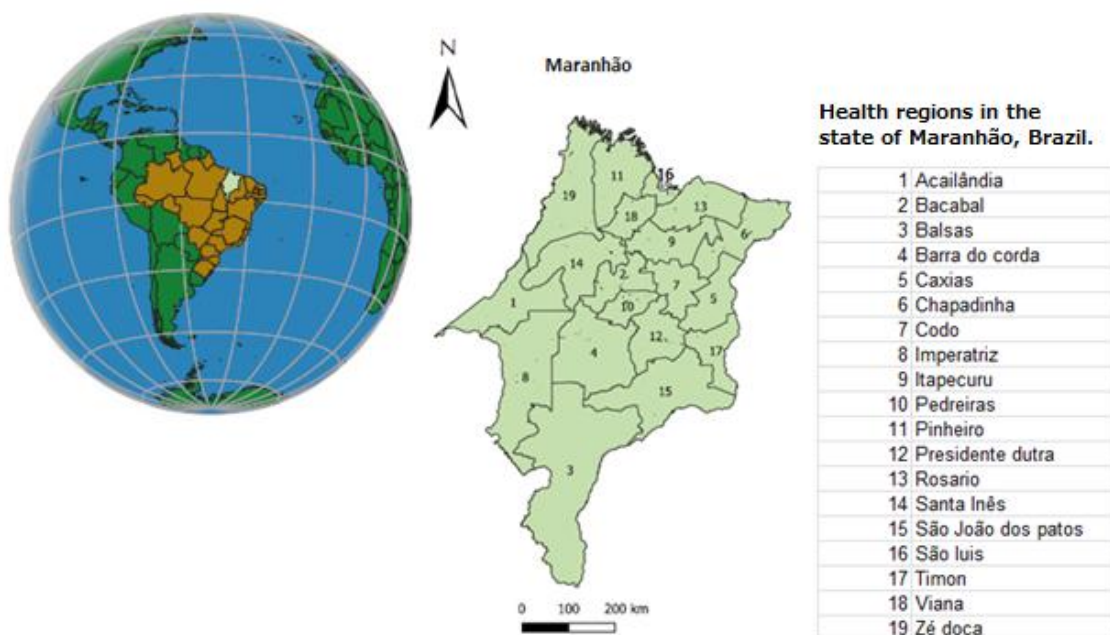
In this context, the influence of the challenging social conditions in Maranhão on the proper adherence to vaccination schedules, particularly in children under one year of age, is undeniable. This situation justifies the rise in reported cases of diseases such as measles, pertussis, hepatitis B, and tuberculosis in the state⁹. Therefore, it is crucial to understand the vaccination coverage conditions in the state of Maranhão to consolidate the impact of low vaccination adherence on the resurgence of vaccine-preventable diseases, pinpoint regions experiencing significant declines, and ultimately develop systematic approaches to counteract this deviation.

Hence, it is necessary to analyze vaccination rates in children under one year residing in the state of Maranhão during the periods 2013-2022, in order to comprehend the implications of the reduction in this coverage for the resurgence of diseases that were previously eradicated and the main outcomes.

METHODOLOGY

This is an ecological time series study conducted in the state of Maranhão. The state cover an approximate area of 329,651,496 km², with an estimated population of 7,153,262 people. Concerning population density, according to the last census in 2010, Maranhão had 19.81 inhabitants/km² ¹⁰.

Fig 1. State of Maranhão and Health Districts.



The state is characterized by a large number of municipalities in conditions of high social vulnerability, low per capita GDP, families in extreme poverty, illiteracy, and high infant mortality rates. It is the 17th most robust economy in Brazil, standing out for its main economic activities, such as industry (involving the transformation of aluminum and alumina, cellulose production, food and timber sectors), services, plant extraction (especially babaçu), agriculture (cultivation of soy, cassava, rice, and corn), and livestock. However, among the federal units, it has the lowest Human Development Index (HDI) in Brazil, with 0.676 points.

As such, it is imperative to analyze vaccination rates in children under one year residing in the state of Maranhão for the periods 2013-2022. This analysis aims to comprehend the implications of the reduction in this coverage for the resurgence of diseases that were previously eradicated and to identify the primary outcomes.

The state comprises 217 municipalities distributed among the 19 regional health units (RHUs), which, in turn, aim to integrate the organization, planning, and execution of health actions and services¹¹. The data under study were extracted from the National Immunization Program Information System (SI-PNI) regarding vaccination coverage in the state of Maranhão from 2013 to 2022. Descriptive analysis of this data was conducted through tables, as well as choropleth maps (figure 01).

This study analyzed vaccination coverage for immunobiologicals recommended for children

under 1 year, including the Bacillus Calmette-Guérin (BCG) vaccine, human rotavirus vaccine (human Rotavirus G1P1), 10-valent pneumococcal vaccine (Pneumococcal 10-valent), pentavalent vaccine (DTP+Hib+HB), meningococcal C vaccine (conjugated Meningococcal C), inactivated poliovirus vaccine (VIP), and yellow fever vaccine.

Vaccination coverage estimates in children under 1 year were considered based on achieving the target coverage set for each immunobiological annually and by RHU¹². The coverage calculation formula considered the number of administered doses of the specified dose (1st, 2nd, 3rd dose, or single dose, depending on the vaccine) divided by the target population (children under one year), multiplied by 100¹³. For the hepatitis B immunobiological, a complete vaccination schedule was considered when all 3 doses of the pentavalent vaccine were administered.

For the trend analysis, Prais-Winsten autoregressive models were employed, with vaccination coverage levels per regional health unit (RHU) as dependent variables and study years (2013 to 2022) as independent variables. The Prais-Winsten regression model was adopted to correct the serial autocorrelation in time series.

To perform the Prais-Winsten regression, vaccination coverage for each immunobiological was transformed both annually and by RHU to the logarithmic scale. This process was carried out to reduce the variance heterogeneity of residuals resulting from time series regression analysis.

The calculation of the annual percent change (APC) was also conducted for each analyzed dependent variable, using the formula: $APC = (-1 + 10[b1]*100\%)$, where b1 refers to the angular coefficient (beta) of the Prais-Winsten regression¹⁴.

Furthermore, 95% confidence intervals (CI95%) of APC measures were calculated using the following formula: *CI95% minimum* $(-1 + 10 [b1 - t*e]100\%)$ and *CI95% maximum* $(-1 + 10 [b1 + t*e]100\%)$. The values of the angular coefficients (b1) from the Prais-Winsten regression and standard errors were generated by the statistical analysis program. The 't' in the formula corresponds to the Student's t-test, which equaled 9 degrees of freedom (t=2.262 for the ten-year period) and 10 degrees of freedom for other proportions of gestational and congenital syphilis (t=2.228 for the eleven-year period), both with a 95% confidence level.

The regression results were interpreted as follows: increasing trend when the p-value was less than 0.05 and the regression coefficient was positive; decreasing trend when the p-value was less than 0.05 and the regression coefficient was negative; or stationary trend when the p-value was greater than 0.05. The statistical package used for data analysis was the Statistical Software for Professional (Stata), version 16.0.

For the statistical analysis of spatial dependence, the Moran's Spatial Autocorrelation Coefficient was employed, which is subdivided into Global Moran's Index and Local Moran's Index. The variables analyzed were vaccination indicators, with the geographic unit of analysis being the municipalities of the state of Maranhão.

The Local Moran's Index was used to identify clusters of areas with similar risks for the occurrence of the outcome of interest, in case a significant spatial autocorrelation was identified by the Global Moran's Index. This index allows analyzing the extent to which the value of a variable for a specific area is similar or different from its neighboring areas¹⁵.

Clusters formed from the analysis of the Local Moran's Index can be divided into four parameters: high-high, representing municipalities with high rates and neighbors with high rates; low-low, representing municipalities with low rates and neighbors with equally low rates; low-high, representing cities with low rates and neighbors with high rates; and high-low, identifying cities with high rates and neighbors with low rates. The presentation of these data used the LISA (Local Indices of Spatial Association) Map, which allows expressing spatial dependence patterns locally through choropleth maps¹⁶.

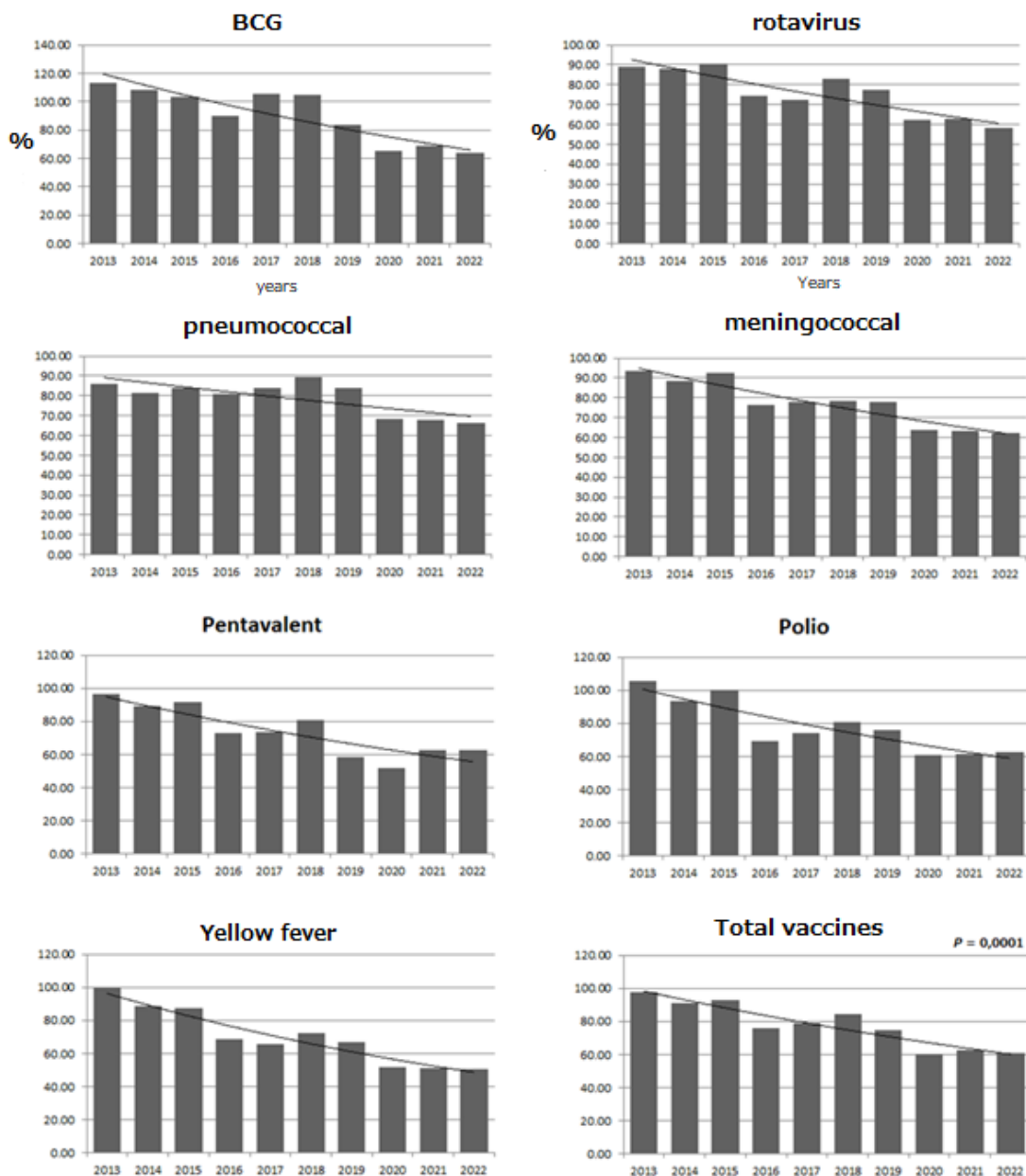
A significance level of 5% was considered. The statistical analyses were conducted using GeoDa software version 1.18, and the maps were created using QGIS software version 3.10.

As these are non-nominal public data available from the Datasus public database, the study was not submitted for review by an Ethics Research Committee.

RESULTS

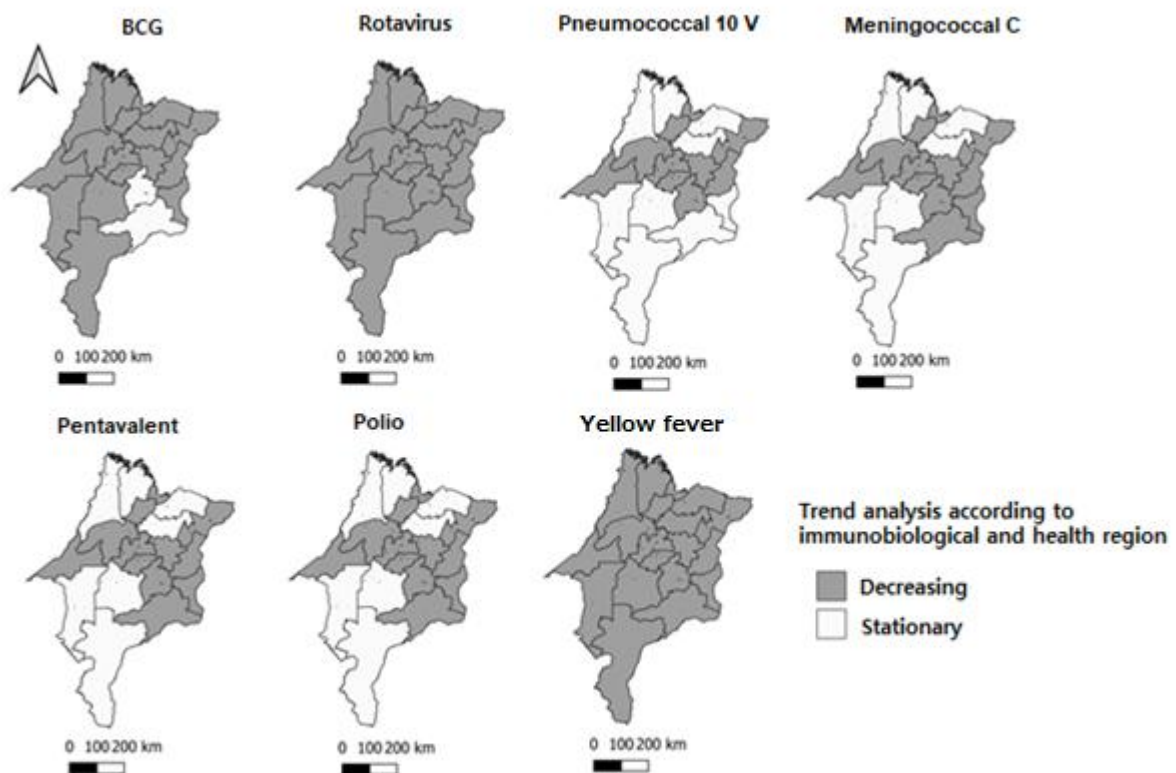
Seven immunobiologicals were analyzed, corresponding to the infant vaccination schedule for children under 1 year of age. Of these, only the BCG and polio vaccines achieved the recommended target for vaccination coverage during the data analysis period (2013-2022). Thus, within this timeframe, the BCG vaccine achieved the target most frequently, between the years 2013-2015, 2017, and 2018. However, from then on, the coverage for this vaccine experienced a decline, reaching levels below 70% in the year 2022. Although the polio vaccine achieved the coverage target, it did so only once, specifically in the year 2013 (Figure 2).

Fig 2. Time trend of vaccination coverage levels in children under one year of age in the state of Maranhão, according to immunobiological and year, from 2013 to 2022.



As for the trend in coverage, at least ten out of the 19 Regional Health Units (RHUs) showed a declining trend for six out of the seven immunogens investigated in this study (Fig 3). The RHUs in question are Açailândia, Bacabal, Caxias, Chapadinha, Codó, Pedreiras, Presidente Dutra, Santa Inês, São Luís, and Viana. Of these, only Presidente Dutra did not exhibit a decreasing trend for the coverage of all the immunogens analyzed in this study.

Fig 3. Trend analysis by vaccine in children under one year old by Health Districts (RS) in the State of Maranhão from 2013 to 2022.



With regard to the investigated immunobiologicals, none showed an increasing trend during the analyzed period. There is a notable decrease in the Yellow Fever vaccine and the Rotavirus vaccine, both exhibiting a declining trend in 100% of the Regional Health Units (RHUs). Following them, the BCG vaccine showed an 89.5% decline, while the Pentavalent, Polio, and Meningococcal vaccines all had a 63.2% declining trend. Lastly, the Pneumococcal-10 immunogen showed the smallest decrease at 52.7% (Table 1).

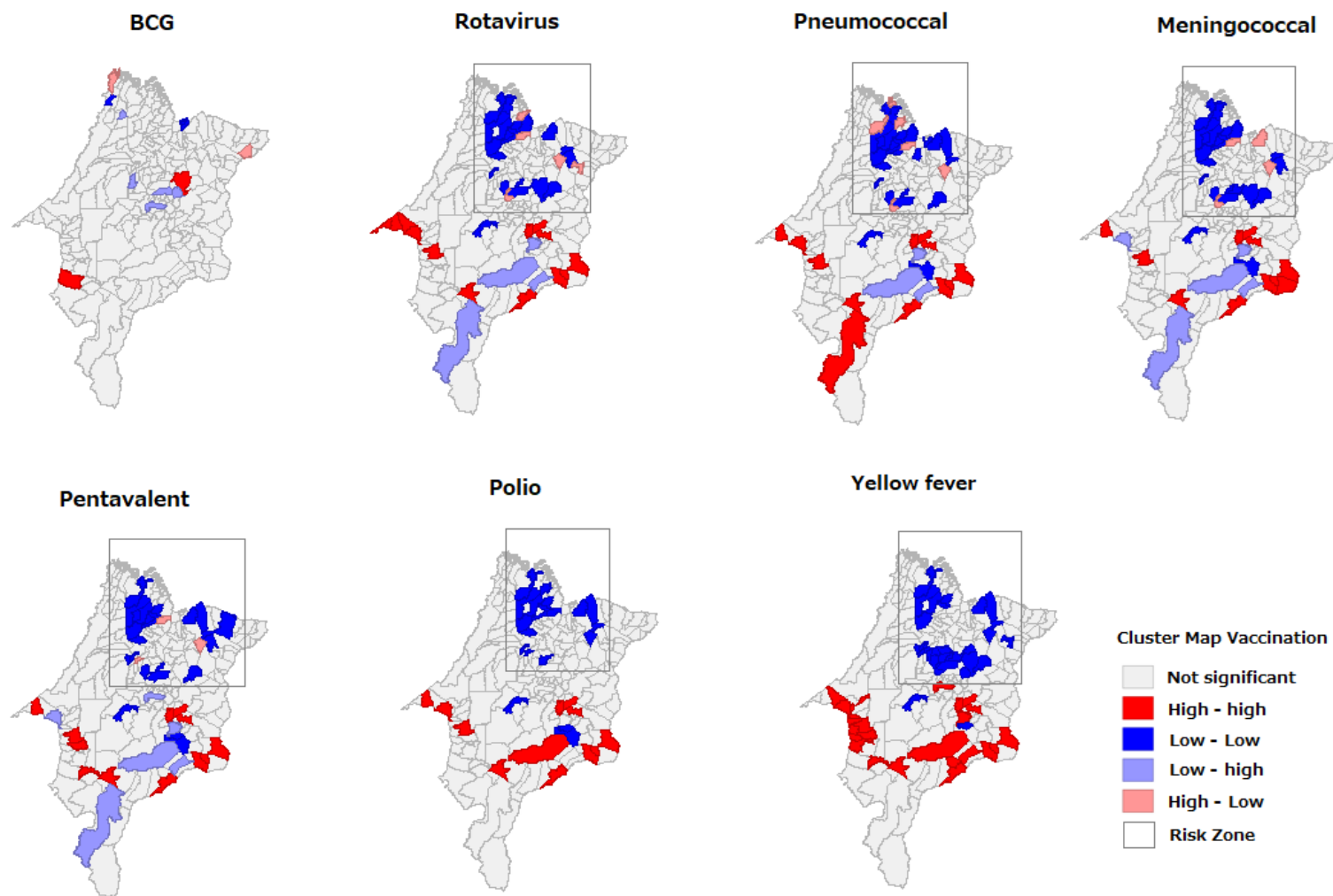
Based on the analyzed data, a decreasing trend in vaccination coverage was observed for all immunogens in at least ten out of the nineteen health regions in the state of Maranhão between the years 2012-2023. There is a specific emphasis on two immunogens, Rotavirus and Yellow Fever, which showed a decreasing trend in all health regions during the analyzed period. Thus, this declining trend in Maranhão is similar to the national scenario, where inadequate coverage has been observed since 2016 (less than 95% for most immunogens, except for Rotavirus and BCG vaccines, with a target of 90%). However, compared to other states in the federation, Maranhão exhibits higher rates of vaccination incompleteness¹⁷.

Taking a closer look at the RHUs, it is evident that none of them exhibited an increasing trend for the seven immunogens investigated in the study at hand. Nevertheless, 10 out of the 19 RHUs in the state showed a declining trend for all vaccines examined in this study, namely: São Luís, Santa Inês, Viana, Bacabal, Açailândia, Pedreiras, Presidente Dutra, Codó, Chapadinha, and Caxias. Thus, given the geographic proximity of these RHUs, they present as an area with a higher risk factor for the transmission of vaccine-preventable diseases in Maranhão. This finding raises questions about the effectiveness of vaccination campaigns promoted in the state of Maranhão, particularly in the northern region of the state.

Table 1. Number of Regional Health Units (URS) according to trend analysis by immunobiological in children under one year old in the State of Maranhão in the period from 2013 to 2022.

Immunobiological	Decreasing		Stationary		Growing	
	n	%	n	%	n	%
BCG	17	89.5	2	10.5	0	0
Rotavirus	19	100	0	0	0	0
Pneumococcal 10	10	52.7	9	47.3	0	0
Meningococcal C	12	63.2	7	36.8	0	0
Pentavalent	12	63.2	7	36.8	0	0
Polio	12	63.2	7	36.8	0	0
Yellow Fever (YF)	19	100	0	0	0	0

Another point to be highlighted is the formation of risk areas for the emergence of new outbreaks, as the clustering with neighboring areas exhibiting low vaccination rates was systematically prevalent in the municipalities located in the health regions of Pinheiro, Viana, Itapecuru, Bacabal, and Rosário for the majority of the analyzed immunobiologicals (Fig 04).

Fig 4. Identification maps for areas forming clusters of municipalities with high and low vaccination levels.

DISCUSSION

Active immunization through vaccination is recognized as the most effective method for preventing, reducing, and controlling many infectious diseases. In addition to protecting the individual who receives it, vaccines prevent the spread of the disease to others, known as herd immunity¹⁸. Therefore, it is crucial that children receive immunization with vaccines specified by the childhood immunization schedule from birth, especially since they have an immature immune system. In this regard, Brazil stands out for the availability of immunobiologicals since the creation of the National Immunization Program (PNI) in 1973².

In light of this scenario, it is worth noting that the data found in the study, particularly regarding the immunogen against yellow fever, point to an imminent outbreak of the disease in the state. Considering that Maranhão comprises an enzootic area of yellow fever in Brazil, meaning regions where the disease is naturally maintained in a constant cycle of transmission due to the presence of primary hosts associated with the characteristics of the Amazon biome¹⁹. Thus, in accordance with the Brazilian childhood vaccination schedule, it is necessary for children to be vaccinated at 9 months old, especially those residing in endemic regions of the disease. This emphasizes the need for measures to be taken to reverse the decline in yellow fever vaccination coverage in Maranhão.

Furthermore, the effort to combat infectious diseases led to the elimination of polio in 1989, as well as a reduction in cases of pertussis and diphtheria²⁰. This progress also resulted in the title of measles eradication in 2016 given by the World Health Organization (WHO), considering the notification of the last autochthonous case of the disease that year²¹. However, despite the previously achieved success, the decline in vaccination rates in Brazil has led to the resurgence of these once-eradicated diseases, with Brazil recording around 1,100 cases of measles in 2017²².

On the other hand, there has been a decline in vaccine coverage for immunogens such as BCG and polio, with this decrease occurring at the national level, establishing a reduction of 0.9% per year for BCG and 1.3% for polio². Among the key players in this reduction in childhood vaccination coverage is the phenomenon of vaccine hesitancy, which refers to a delay or refusal of vaccination by parents²³. This encompasses aspects such as a lack of confidence in the effectiveness of immunogens, fear of adverse reactions, and even sociocultural and religious factors¹.

It is also noteworthy that the dissemination of fake news on social media contributes to the discourse of vaccine hesitancy. This includes spreading news that questions the efficacy of vaccines, pointing to DNA damage, teratogenicity, and the development of neuropsychomotor developmental disorders in children, such as autism²⁴. The appropriation of such unfounded information does not assist, only contributes to the decline

in childhood vaccination coverage and the potential scenario of reemergence of vaccine-preventable diseases.

Souto and Kabad (2020)²⁵ identified three variables that contribute to the phenomenon of vaccine hesitancy: trust, complacency, and convenience. Trust relates to questioning the efficacy and safety of immunobiologicals, as well as suspicion of the healthcare system, legislators, healthcare professionals, among others. Complacency in this context is understood when the risks of vaccine-preventable diseases for a particular immunobiological are low, making vaccination seem less relevant. Convenience involves logistical and everyday issues in healthcare practices, especially regarding the practicality and ease of obtaining the vaccine by the population. Problems such as vaccination center operating hours, availability of immunobiologicals, human resources, among others, can be determining factors.

Furthermore, it is known that the incompleteness of the vaccination schedule is multifactorial. It is also influenced by other factors such as socioeconomic factors, among which parity, the number of prenatal visits, and low socioeconomic levels stand out²⁶. It is understood that with a higher number of children, there is a certain difficulty in individual care, thus reducing the time to seek a healthcare facility on the appropriate date for the application of each immunogen²⁶. Nevertheless, the low number of prenatal visits reflects the lack of instructions about the importance of vaccination and the completeness of the vaccination schedule, contributing to the deviation in vaccination rates.

It is worth noting that the main and most concerning consequence of the reduction in vaccination coverage is the reemergence of previously eradicated vaccine-preventable diseases²⁷. As an example, the yellow fever epidemic that occurred in Brazil between 2016 and 2019, with a record of more than 2,200 cases of infected individuals and a total of more than 750 deaths between December 2016 and June 2019²⁸.

The presence of areas with clusters of low vaccination coverage (low-low) may pose a higher risk of outbreaks, making them priority areas for the development of actions that engage the population along with healthcare services to reverse this scenario^{19, 27}.

Moreover, the downward trend of 63.2% in the Pentavalent vaccine (DTP+Hib+HB) can contribute to strengthening the high rate of hospital admissions related to vaccine-preventable diseases in Maranhão. Thus, the scenario envisioned in 2019, where the state reached 7.8% of these admissions due to pertussis, could persist²⁹. This should concern the health authorities of the state, especially as it represents a problem that could be preventable with the application of the aforementioned immunogen.

Therefore, the study indicated that the decrease in vaccine coverage can lead to serious consequences for the state, especially in the northern region of this federal unit, where 10 URS showed a declining trend for all immunogens. As Maranhão faces serious

issues regarding social inequalities, reflecting in deficient quality of life and health compared to other federal units in Brazil³⁰.

Despite the concerning vaccine coverage rates, the Brazil's Unified Health System is one of the largest, most complex, and comprehensive public health systems in the world^{3,24}. In this sense, the state of Maranhão, like other federal units already equipped with this healthcare system, has the full capacity to reverse this disturbing scenario. Supported by recommendations from national and international organizations, aiming to improve vaccination rates.

CONCLUSION

Such indicators related to low immunization rates can place an additional burden on SUS's medium and high complexity services, in addition to increasing the already high rates of infant mortality in the state, which, in turn, has one of the most concerning rates in Brazil. Therefore, considering means to combat the deviation of vaccination rates is essential to reduce the vulnerability of the population in this state.

Given the identified indicators in this study, it is suggested, primarily, to intensify and maintain immunization efforts. Nevertheless, it is recommended to keep vaccine centers open during the entire operating hours of healthcare units and vaccination points with flexible schedules, eliminate access barriers, combat fake news, actively search for those missing vaccinations, train healthcare professionals, promote collective health education actions for public awareness, among others.

Undoubtedly, vaccines are indispensable tools in the prevention and control of infectious diseases, and they also exhibit excellent cost-effectiveness. In light of the results, it can be affirmed that the population is certainly the key player in this scenario since the success or failure of immunization actions is closely associated with society's adherence. Therefore, supporting and encouraging actions that contribute to community awareness and access to vaccines are fundamental in this context.

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Carvalho BCM.; De Jesus AG.; Gomes H. contributed to the conception and design of the study, data collection, image processing, analysis and interpretation of results, writing and critical review of the manuscript's content. All authors have approved the final version of the manuscript and are responsible for all aspects of it, including ensuring its accuracy and integrity.