








Spatial analysis of pentavalent immunobiological vaccine coverage in children under one year of age

Análise espacial da cobertura vacinal do imunobiológico pentavalente em crianças menores de um ano

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ABSTRACT

Objective: to analyze the spatial distribution of pentavalent immunobiological vaccine coverage in children under one year of age. **Methods:** this is an ecological time series study which used data from the National Immunization Program Information System on the pentavalent vaccine coverage rate in a southern Brazilian state, between 2013 and 2022. Vaccination coverage was expressed in percentages, by year, health region and immunobiological type. In addition, distribution and spatial autocorrelation analyses of municipal rates were used. **Results:** the average pentavalent vaccination coverage in the state was 90.94%, with the highest rate in 2013 (101.94%) and the lowest in 2019 (79.03%). The Western macroregion had the highest average coverage, while the Northern macroregion had the lowest. Low coverage clusters were evident in the Eastern region. **Conclusion:** vaccination coverage in Paraná has been decreasing over the years, possibly due to the rise of anti-vaccine movements and the impact of the pandemic in the last three years. **Contributions to practice:** the results highlight the need for awareness campaigns and targeted actions for regions with low vaccination coverage. Health professionals, especially nurses, can use these data for interventions which promote greater vaccination adherence.

Descriptors: Spatial Analysis; Vaccination; Child Health; Vaccination Coverage.

RESUMO

Objetivo: analisar a distribuição espacial da cobertura vacinal do imunobiológico pentavalente em crianças menores de um ano. **Métodos:** estudo ecológico do tipo séries temporais que utilizou dados do Sistema de Informação do Programa Nacional de Imunização sobre a taxa de cobertura vacinal da pentavalente em um estado sul-brasileiro, entre 2013 e 2022. As coberturas vacinais foram expressas em porcentagens, por ano, regional de saúde e tipo de imunobiológico; e empregadas análises de distribuição e autocorrelação espacial das taxas municipais. **Resultados:** a cobertura vacinal média da pentavalente no estado foi de 90,94%, com o maior índice em 2013 (101,94%) e o menor em 2019 (79,03%). A macrorregião Oeste teve a maior média de cobertura, enquanto a macrorregião Norte teve a menor. Agrupamentos de baixa cobertura foram evidenciados na região Leste. **Conclusão:** a cobertura vacinal no Paraná tem diminuído ao longo dos anos, possivelmente devido à ascensão de movimentos antivacinas e ao impacto da pandemia nos últimos três anos. **Contribuições para a prática:** os resultados destacam a necessidade de campanhas de conscientização e ações direcionadas para regiões com baixa cobertura vacinal. Profissionais de saúde, especialmente enfermeiros, podem utilizar esses dados para intervenções que promovam uma maior adesão à vacinação.

Descritores: Análise Espacial; Vacinação; Saúde da Criança; Cobertura Vacinal.

Introduction

Immunization of children in Brazil, especially in the first year of life, continues to be an important strategy for promoting health and preventing infant mortality. It is a safe, effective and advantageous method, both from an economic and social point of view, compared to treating the diseases that vaccines help prevent. Data from the World Health Organization (WHO) reinforce the importance of vaccination in reducing infant mortality and preventing outbreaks of vaccine-preventable diseases⁽¹⁾.

Brazil's National Immunization Program (*Programa Nacional de Imunizações - PNI*) was created in 1973, initially providing five vaccines free of charge: against tuberculosis (BCG), against diphtheria, tetanus and pertussis (DTP), and against measles, polio and smallpox. New immunobiological vaccines were incorporated over time, and the age range covered by the vaccines was expanded. The pentavalent conjugate vaccine, which protects against diphtheria, tetanus, whooping cough, hepatitis B and Haemophilus influenzae type b (Hib), was incorporated into the national calendar in 2012⁽²⁾.

The PNI currently provides more than 20 vaccines free of charge, and is recognized as one of the largest vaccination programs in the world, especially due to the success of the smallpox eradication campaigns⁽²⁾. The eradication and/or control of some infectious diseases depends on the immunogenic power of the vaccine in question, but also on its coverage rate, which is determined based on information about the number of doses of a given vaccine administered and the number of children who should have received it⁽³⁾.

The PNI aims to vaccinate all children under one year of age, but national data indicate a reduction in vaccination coverage in all regions of Brazil⁽⁴⁻⁵⁾. This decline has caused the resurgence of vaccine-preventable diseases, such as whooping cough, despite lower incidences than in the pre-vaccination era. Among the factors which interfere with vaccination rates, misinformation about the effectiveness of immunobiologi-

cal vaccines, cultural beliefs and the dissemination of fake news⁽⁶⁻⁷⁾ stand out.

Vaccine hesitancy – characterized by refusal or delay in vaccination – is one of the greatest threats to global health⁽⁸⁾. Fear of adverse events, lack of adequate information and vaccine shortages contribute to this phenomenon, aggravated by fake news and denialist actions which undermine the population's trust in vaccines and professionals⁽⁹⁻¹⁰⁾. This decline challenges the achievement of the Sustainable Development Goals (SDG) target of eradicating preventable diseases by 2030⁽¹¹⁾.

Despite the benefits being widely recognized, studies point to a worrying decline in pentavalent vaccination coverage. National data suggest inequalities in coverage distribution between regions and municipalities, influenced by socioeconomic and structural factors of the Unified Health System (*Sistema Único de Saúde - SUS*)⁽⁴⁻⁵⁾. However, studies that explore spatial and contextual patterns of this coverage are still scarce, limiting understanding of the local dynamics which compromise achievement of the PNI goals.

This gap highlights the need for ecological analyses which enable identifying critical areas of low adherence to vaccination campaigns⁽⁷⁻⁸⁾. Investigating these contexts can guide more effective and equitable interventions, optimizing vaccination efforts in vulnerable populations, such as children. Therefore, understanding these scenarios is essential for planning strategies that reinforce the control of vaccine-preventable diseases and contribute to achieving the SDGs⁽¹¹⁻¹²⁾.

Given the importance of assessing and monitoring vaccination coverage, especially for controlling vaccine-preventable diseases and defining targeted strategies, detailed analyses of the spatial distribution of such coverage are necessary for health surveillance and care, creating possibilities for more effective local interventions. In view of the above, the objective of this study was defined as: to analyze the spatial distribution of pentavalent immunobiological vaccine coverage in children under one year of age.

Methods

This is an ecological time series study with its analysis units being the health regions and municipalities of the state of Paraná. Data on vaccination coverage referring to the period from 2013 to 2022 were obtained from the National Immunization Program Information System (*Sistema de Informação do Programa Nacional de Imunização - SI-PNI*), accessed by the Department of Information Technology of the Unified Health System (*Departamento de Informática do Sistema Único de Saúde - Datasus*) on August 2, 2023. This system was implemented in 2010 and enables monitoring vaccination indicators, including an assessment of the impact of vaccination strategies on the Brazilian population⁽¹³⁾.

The study setting was the state of Paraná, located in the southern region of Brazil, which had a population of 11,443,208 people in 2022, the largest for the southern region of Brazil, and a human development index (HDI) of 0.769⁽¹⁴⁾. The state has 399 municipalities, which are grouped into four macro-regions (North, Northwest, West and East) and 22 micro-regions (or health regions) within the scope of the health system aiming at decentralization and capillarity of actions and services.

The variable under analysis consisted of pentavalent vaccine application records to children under one year of age, from January 1, 2013 to December 31, 2022, with this being the last year with data available at the time of this study. The basic regimen of this immunobiological vaccine (which protects against diphtheria, tetanus, whooping cough, hepatitis B and *Haemophilus influenzae* type B) is considered complete with three doses, administered at two, four and six months of age.

The vaccination coverage rate is automatically calculated by the SI-PNI according to the formula standardized by the Ministry of Health: number of doses administered in a given year (3rd dose of the vaccine administered to children under one year of age), divided by the target population residing in the

same place and period, and the result was multiplied by 100. The variables related to the application year were considered according to the health regions and municipalities of the state of Paraná to describe the vaccination coverage rates.

The annual vaccination coverage rates were presented according to macro and micro health regions. Then, the rates were presented by municipality considering the following time periods: 2013; 2014-2016; 2017-2019; 2020-2021; and 2022. The vaccination coverage data for the three- and two-year periods were grouped by arithmetic mean. These periods were defined taking into account that the rates could fluctuate and be affected in relation to the other years of the historical series evaluated, as demonstrated by studies in the area.

A target of 95% was considered to assess the pentavalent vaccination coverage rates by municipality in the state of Paraná, as recommended by the Brazilian Ministry of Health, and these were classified as: inadequate (<95%); adequate ($\geq 95\%$) and overestimated ($> 120\%$)⁽¹⁵⁾. The spatial distribution map was constructed from the shape file of the state's municipal grid obtained from the Brazilian Institute of Geography and Statistics website with the support of the QGIS® version 3.26.3 software.

After distribution of the rates, a spatial dependence analysis was performed using the Moran index, seeking to verify whether the data from each municipality had a correlation with the rates of neighboring municipalities defined by the first-order queen criterion. The global Moran index (I) was initially performed, which varied from 0.00 to 1.00: the closer to 1.00, the greater the correlation, whether direct (+) or inverse (-)⁽¹⁶⁾. The pseudosignificance test for the I was applied with 999 permutations ($p \leq 0.05$).

When significant, the local Moran index (Ii) was applied to verify which areas presented autocorrelation. The municipalities were described in clusters considering the vaccination coverage rate, namely: high-high, municipalities and neighbors with high rates; low-low, municipalities and neighbors with low rates;

high-low, municipalities with high rates and neighbors with low rates; low-high, municipalities with low rates and neighbors with high rates; and non-significant, with no evident spatial association⁽¹⁶⁾. The analysis was performed in GeoDa[®] version 1.20.

The study followed the ethical precepts set forth in Resolution No. 466/2012 of the National Health Council, and was approved by the Research Ethics Committee of the State University of Maringá (Certificate of Presentation of Ethical Appreciation No. 57753722.7.0000.010), under opinion No. 5,385,657/2022. The use of an informed consent form was waived as it deals with secondary and non-nominal data originating from the *SI-PNI*, which is publicly accessible on the Datasus website.

Results

A total of 4,225,176 doses of the pentavalent immunobiological vaccine were administered to chil-

dren under one year of age in the period from 2013 to 2022 in the state of Paraná. Of these, 1,446,680 were registered as the 1st dose; 1,410,868 as the 2nd dose and 1,366,420 as the 3rd dose, therefore corresponding to the total number of children who completed the vaccination schedule. The arithmetic mean of the pentavalent vaccination coverage between 2013 and 2022 was 90.94%, with 2013 being the year with the highest rate (101.9%), and 2019 the year with the lowest rate (79.0%).

The West stood out with the highest average vaccination coverage value for the series analyzed (97.0%) among the state’s health macroregions, while the North had the lowest average value for the period (90.5%). The regions which registered the highest coverage rates in the analysis by health regions were: Toledo (102.9%), Francisco Beltrão (99.2%), Cianorte (98.5%) and Irati (98.4%); on the other hand, the lowest rates were seen in the Paranaguá (77.5%) and Londrina (85.6%) regions (Table 1).

Table 1 – Pentavalent vaccine coverage rates according to macro and micro health regions of Paraná, 2013 to 2022 (n=1,366,420). Maringá, PR, Brazil, 2023

Macro and microregions	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
East	104.3	104.0	100.4	90.4	91.2	90.8	77.1	88.3	81.4	80.6
1st Paranaguá	100.6	99.7	74.0	78.8	72.3	82.5	64.2	70.8	72.4	59.5
2nd Metropolitana	97.0	94.8	99.5	86.6	87.2	89.2	71.6	86.2	79.7	82.8
3rd Ponta Grossa	93.0	98.9	108.4	86.3	86.2	91.2	91.3	91.4	86.3	80.0
4th Irati	100.5	111.6	113.6	101.2	105.7	99.6	70.0	94.2	91.2	96.9
5th Guarapuava	99.58	107.7	109.0	93.3	90.7	89.8	70.2	99.0	82.1	81.8
6th União da Vitória	112.4	126.0	97.6	87.3	92.6	95.2	89.8	89.7	88.3	85.9
21st Telêmaco Borba	127.1	90.0	100.6	99.3	103.8	88.4	82.5	86.6	69.5	77.2
West	107.1	102.0	108.9	96.6	93.0	99.9	92.8	91.7	85.6	92.3
7th Pato Branco	100.0	102.3	106.9	92.6	91.0	89.0	97.4	98.6	89.1	94.4
8th Francisco Beltrão	111.9	105.2	107.1	102.3	99.6	99.5	83.9	94.9	89.3	98.4
9th Foz do Iguaçu	114.5	103.3	120.5	83.7	82.3	89.2	89.6	68.8	72.7	80.3
10th Cascavel	109.6	99.4	102.0	102.0	84.6	96.4	85.2	97.4	89.6	95.7
20th Toledo	99.6	100.2	107.7	102.3	107.5	125.6	107.8	99.0	87.3	92.6
Northeast	109.0	100.1	97.8	97.3	94.8	95.7	81.6	93.2	83.2	89.5
11st Campo Mourão	124.4	114.4	92.0	97.9	96.1	97.3	67.9	78.8	90.4	85.8
12nd Umuarama	94.0	76.4	100.0	92.0	89.7	94.9	86.4	92.8	85.7	92.4
13rd Cianorte	111.0	103.0	101.0	102.20	98.9	100.0	88.7	99.4	86.4	94.1
14th Paranavai	111.3	103.2	98.5	97.4	89.1	94.0	80.6	90.1	71.8	89.2
15th Maringá	104.6	103.4	97.2	96.9	100.0	92.2	84.4	104.7	81.6	86.2
North	98.5	100.6	101.0	92.9	93.5	89.3	76.5	85.5	80.8	86.6
16th Apucarana	105.8	101.5	113.6	88.6	90.3	90.8	73.7	68.2	80.7	78.7
17th Londrina	100.8	93.0	94.5	95.5	94.4	66.9	76.5	76.6	77.8	79.8
18th Cornélio Procopio	94.0	99.8	100.4	91.3	90.5	92.4	63.7	85.5	75.1	88.4
19th Jacarezinho	99.1	103.8	96.5	93.2	95.1	97.8	73.7	98.4	87.9	91.3
22nd Ivaiporã	92.9	104.9	100.2	96.0	97.2	98.5	94.7	98.9	82.6	94.8
Paraná	101.9	99.0	101.3	91.6	90.7	90.9	79.0	88.4	81.7	84.8

When analyzing the vaccination coverage rates by municipality in Paraná, it was noted that adequate rates were predominant in 2013 and in the 2014-2016 triennium (Figures 1A and 1B). These periods presented a greater number of municipalities with

records of adequate coverage distributed homogeneously among the macro-regions (Figure 1B). The presence of spatial autocorrelation was observed for all analyzed periods when applying the global Moran index (Table 2), and so the local index was applied.

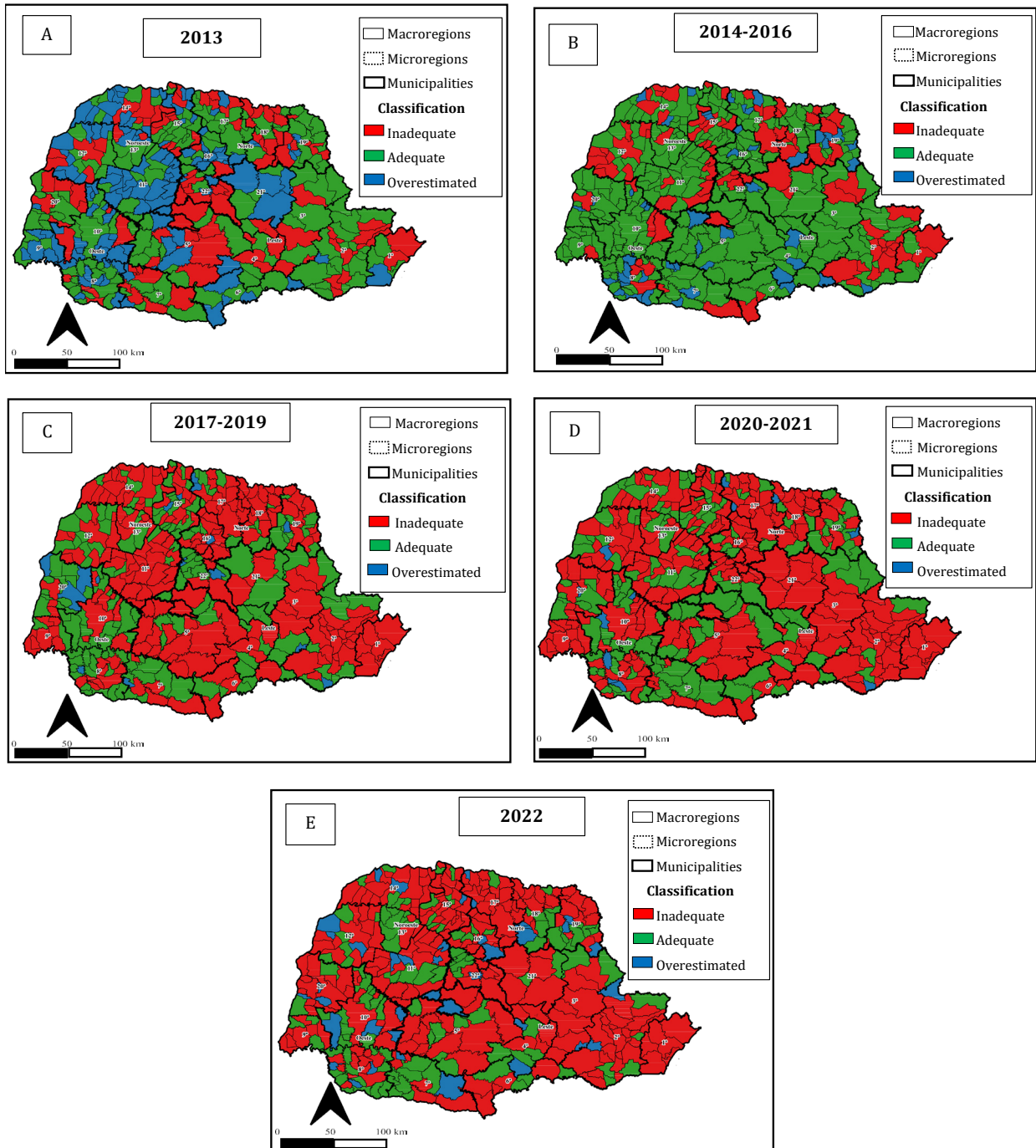


Figure 1 – Spatial distribution of pentavalent vaccine coverage rates according to municipalities in Paraná, 2013 to 2022. Maringá, PR, Brazil, 2023

Table 2 – Global and local Moran index of pentavalent vaccine coverage rates according to municipalities in Paraná, 2013 to 2022. Maringá, PR, Brazil, 2023

Period	I*	p-value [†]	Municipalities by clusters				
			High-high	Low-low	Low-high	High-low	Non-significant
2013	0.12	<0.010	14	26	16	7	336
2014-2016	0.09	<0.010	9	30	13	15	332
2017-2019	0.16	<0.010	17	36	10	10	326
2020-2021	0.05	0.030	9	20	7	12	351
2022	0.04	0.050	7	25	13	10	344

*Global Moran index; [†]pseudosignificance test with 999 permutations

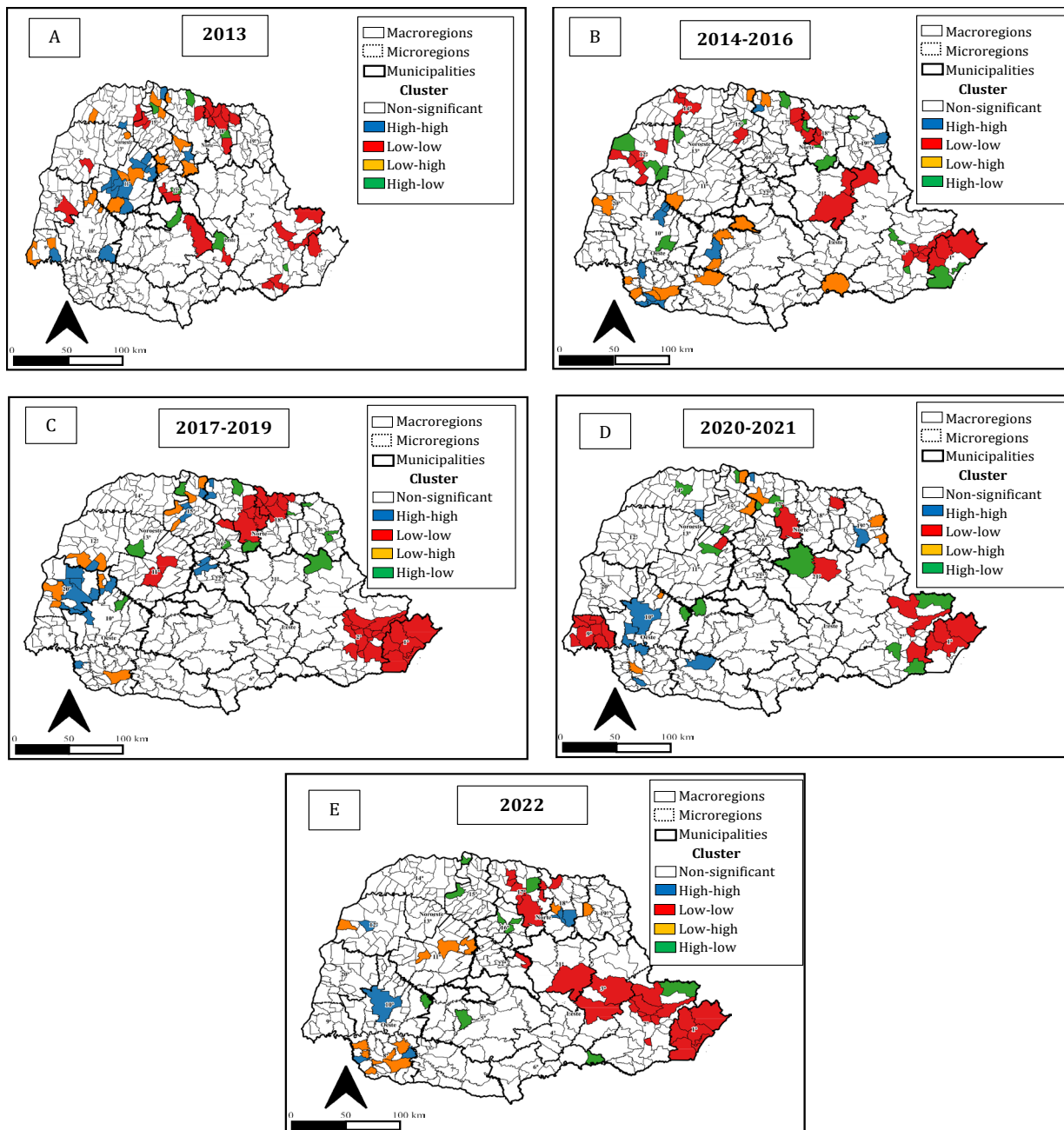


Figure 2 – Spatial dependence of pentavalent vaccine coverage rates according to municipalities of Paraná, 2013 to 2022. Maringá, PR, Brazil, 2023

The largest number of significant clusters was observed in the 2017-2019 triennium, in which 36 clusters of low vaccination coverage rates were observed, especially in the Metropolitan region and in the Paranaguá region (Figure 2C). These clusters were observed in the other periods with the inclusion of other municipalities in the macro East in 2022 (Figure 2E). Few municipalities which had high vaccination coverage rates were observed throughout the period, with the largest number of clusters observed in the 2017-2019 triennium (Figure 2C).

Discussion

Vaccines are among the greatest achievements in public health due to their great potential to prevent some communicable diseases. This is particularly important for more vulnerable populations, such as children, especially those under one year of age. However, it is necessary to achieve the goals related to vaccination coverage rates in order to reduce the incidence and prevalence of diseases preventable by immunization and consequently the number of deaths caused by them⁽¹⁷⁾.

The results revealed marked differences in vaccination coverage between the macro-regions of Paraná. The Western macro-region had the highest average value, while the Northern macro-region had the lowest average. Furthermore, Toledo stood out regionally with the highest coverage rate, in contrast to Paranaguá, which had the lowest rate. These disparities highlight the importance of regionalized strategies to strengthen achievement of vaccination goals and reduce coverage inequalities⁽⁵⁾.

The pentavalent vaccine was included in the National Vaccination Calendar in 2012, bringing benefits to health services and the population. In the context of health services, it reduces costs and improves operational logistics; for the population, it reduces the number of visits to health services and provides greater comfort for children who do not need to receive several immunobiological vaccines in isolation. The

combination of these factors contributes to increased vaccination coverage and prevention of preventable infectious diseases⁽¹⁸⁾.

Municipal analyses in this study indicated groups with low vaccination coverage concentrated in specific regions, such as Metropolitana and Paranaguá, especially in the 2017-2019 triennium. On the other hand, clusters with high coverage were less frequent. Brazil achieved the goals established for all immunobiological vaccines for children under one year of age for a long time; however, this scenario gradually began to change, as pentavalent coverage in the country fell significantly between 2015 and 2019⁽¹⁸⁾.

The Southeast region of the state showed a drop in pentavalent coverage between 2015 and 2020; this result was contributed to by: socioeconomic inequalities, lack of access to information and difficulties in accessing services⁽¹⁹⁾. In this reasoning, it is understood that municipalities in Paraná with lower socioeconomic indicators may face challenges in transportation, communication and infrastructure of health units, making vaccination difficult; as a consequence, they have lower vaccination coverage rates.

Pentavalent vaccination coverage was also lower in Brazilian state capital cities than recommended by the Ministry of Health from 2018 to 2022, with sharper declines from 2019 onwards, especially in the cities of Rio de Janeiro, Florianópolis and Porto Alegre⁽²⁰⁾. Data from this study show that Paraná also did not reach the target established by the Ministry of Health in the same period. However, the average pentavalent vaccination coverage in the state was higher than the national average, ranging from 79% to 90%.

The data from this study showed that 2013 was a standout year, with 101.94% average coverage in the state, in addition to predominantly adequate rates in the 2014-2016 triennium. The homogeneous distribution of coverage among municipalities during these periods suggests a more efficient system and less influence from external factors, such as the low expression of the anti-vaccine movement at the time. The literature also highlights that maintained high vacci-

nation coverage rates was due to a collective effort by the SUS and the population's great trust in the health system⁽²¹⁾.

However, an increase in disparities was observed from 2017 onwards, possibly associated with the deterioration of public policies and growing vaccine hesitancy. One of the contributing factors to the low pentavalent vaccination coverage in the country in 2019 was the failure of batches in the quality test by the National Institute for Quality Control in Health and in the analysis by the National Health Surveillance, which resulted in unavailability or insufficiency in the country⁽¹²⁾.

The low vaccination coverage rates in 2020 were due to the COVID-19 pandemic, since social distancing and isolation measures made access to health services difficult. This was confirmed in a study that analyzed data from *SI-PNI* and found a 20% reduction in the number of vaccine doses administered to young children in the months of March and April compared to January and February 2020⁽²²⁾.

A study investigating knowledge and practices regarding vaccination conducted between November 2019 and March 2020 with 150 adults living in the city of São Paulo found that 15.3% did not consider vaccines to be completely safe, 16% were afraid of being vaccinated, and 16% did not agree with mandatory vaccinations. This suggested that the drop in vaccination coverage may be related to lack of trust in vaccines, fear of adverse events, and the spread of fake news on digital media⁽²³⁾.

This scenario culminated in actions of low confidence in vaccination and uncertainty regarding its real effects on the population. This fact was more prominently evidenced after the emergence of COVID-19 and vaccines to combat it, which generated a large volume of fake news circulating on social media. This highlights a warning for health surveillance issues, since many people began to join the anti-vaccine movement, resulting in an alarming drop in vaccination rates⁽²⁴⁾.

Another important factor in reducing vaccination coverage is not vaccinating at the appropriate

age, since there is a limit to the age at which the vaccine can be administered. For example, according to the vaccination schedule proposed by the National Immunization Program, the pentavalent vaccine can only be administered up to 6 years, 11 months and 29 days of age. When the established deadlines are not respected, vaccination rates are affected. Therefore, it is essential to respect the ideal age and the recommended intervals between doses⁽¹²⁾.

This study also highlighted the evolution of spatial dependence, revealing significant low coverage clusters, especially in the eastern region. The coastal region of the state may concentrate areas which are difficult to access, which may in turn complicate vaccine distribution and the population's movement to health services. It is worth noting that spatial patterns not only reflect socioeconomic factors, but also local administrative capacity and the availability of focused educational campaigns⁽²⁵⁻²⁶⁾.

A comparative study between municipalities in different regions of Brazil found that those which achieved the recommended vaccination coverage had higher proportions of the population covered by primary care and a greater number of community health workers per thousand inhabitants⁽²⁷⁾. This relationship reinforces the importance of primary care in ensuring high vaccination coverage, especially in vulnerable regions, such as the coast of Paraná. The presence of community health workers can facilitate an active search for unvaccinated children and education to families about the importance of vaccines. Furthermore, well-structured and accessible health units, combined with strategies such as local campaigns, are essential to overcome logistical and cultural barriers that compromise adherence to vaccination campaigns.

Reflecting on pentavalent vaccination in the context of Brazilian public health leads to prioritizing planning actions to be developed within the PNI and in health teams, thereby allowing strategies to be implemented which ensure achieving established goals⁽²⁰⁾. This is crucial for states and municipalities to recognize the weaknesses in their health systems and seek to

implement more proactive and effective strategies to achieve better vaccination coverage rates, especially in the first year of life.

According to the Project to Regain High Vaccination Coverage proposed by Fiocruz, it is possible to reverse the current condition marked by low vaccination coverage through articulation of structural and interinstitutional actions, accompanied by valuing and strengthening public policies and implementing measures whose results can be observed in the short, medium and long-term⁽²⁶⁾.

Actions such as actively seeking out children who are behind on their vaccinations and campaigns to raise awareness and educate the population about the importance of vaccines in different settings such as schools, social media and companies, as well as facilitating access to immunization by extending the opening hours of vaccination rooms are strategies to increase vaccination coverage rates. These initiatives not only promote individual protection, but also strengthen collective immunity, contributing to prevent outbreaks and eradicate diseases.

Therefore, all of these actions require effective work with health professionals, especially those who work at the frontline of the system, in order to raise awareness about the importance of their role in direct contact with the population. Furthermore, these professionals also need to be willing to make changes related to restructuring services.

Study limitations

The main limitations of this study are related to the ecological method, which does not capture individual variations that affect vaccination coverage. The data representativeness may also be a limitation, since secondary data from the *SI-PNI* were used, which may result in inconsistencies in recording or underreporting. A lack of information on the specific reasons for vaccine hesitancy and local barriers are also relevant limitations which may affect the accuracy of the results.

Contributions to practice

The results of this study have important implications for practice in the public health and nursing areas. Identifying macroregions, microregions, and municipalities with low vaccination coverage rates allows health managers and professionals to more efficiently direct efforts to areas with greater deficiencies. Awareness campaigns can be intensified in these regions, focusing on educating the population about the importance of vaccination, especially among the target audience.

For nursing, the results highlight the importance of initiatives such as actively seeking out unvaccinated children and health education, promoting greater adherence to immunization campaigns. In addition, the study provides a basis for planning strategies which seek to reverse the decline in vaccination coverage, especially considering the impact of the COVID-19 pandemic. These findings can contribute to formulating public policies that promote more equitable and comprehensive vaccination.

Conclusion

The pentavalent vaccine coverage in the state of Paraná has declined over the years. This decline is worrying, as it puts the state at risk of outbreaks of preventable diseases. Therefore, considering that vaccines are essential for preventing vaccine-preventable diseases, especially in children under one year of age, developing actions to increase coverage is necessary, such as awareness campaigns, improvements in access to vaccination, combating misinformation and fake news, as well as investments in the health network.

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Authors' contributions

Conception and design or data analysis and interpretation; writing the manuscript or critical review relevant to intellectual content; final approval of the version to be published; and responsibility for all aspects of the text in ensuring the accuracy and integrity of any part of the manuscript: Carvalho JMG, Lima LV, Nardi EFR, Barreto MS, Marcon SS. Writing the manuscript or critical review relevant to intellectual content; final approval of the version to be published; and responsibility for all aspects of the text in ensuring the accuracy and integrity of any part of the manuscript: Gomes BJO, Garcia GMC.

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