

## ANALYSIS OF VACCINATION AGAINST HPV IN A CAPITAL IN NORTHEAST BRAZIL

### ANÁLISE DA VACINAÇÃO CONTRA O HPV EM UMA CAPITAL DO NORDESTE DO BRASIL

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#### ABSTRACT

This article aims to analyze vaccination coverage in a capital city in Northeast Brazil. Epidemiological study, with data obtained from the Information System of the National Immunization Program and DATASUS. In Teresina, during the period of 2018, 17,938 doses of the quadrivalent vaccine against Human Papillomavirus were applied, with 9,371 doses applied to boys and 8,567 doses applied to girls. Total vaccination coverage in males corresponds to 11.67 for the first dose and 8.17 for the second dose. In females, the total vaccine coverage for the first dose reaches 7.27 and 10.64 for the second dose. The HPV vaccine is safe and can reduce the number of cervical cancer related to human papillomavirus infection. The low vaccination coverage in Teresina, as well as in Piauí and Brazil, can be multifactorial, such as the population's lack of knowledge about the effectiveness and safety of the vaccine, becoming evident that the other doses are neglected after the first dose.

**Keywords:** HPV. Immunization. Vaccination coverage.

#### RESUMO

O presente artigo tem como objetivo analisar a cobertura vacinal contra o Papilomavírus Humano (HPV) em Teresina, capital do Estado do Piauí, Nordeste do Brasil. Estudo epidemiológico, com dados obtidos no Sistema de Informação do Programa Nacional de Imunizações e no DATASUS. Em Teresina, durante o período de 2018, foram aplicadas 17.938 doses da vacina quadrivalente contra o HPV, sendo 9.371 doses aplicadas em meninos e 8.567 doses aplicadas em meninas. A cobertura vacinal total no sexo masculino corresponde a 11,67% à primeira dose e 8,17% à segunda dose. No sexo feminino, a cobertura vacinal total da primeira dose chega a 7,27% e 10,64% à segunda dose. A vacina contra o HPV é segura e pode reduzir os números de câncer de colo do útero relacionado à infecção pelo papilomavírus humano. A baixa cobertura vacinal de Teresina, assim como do Piauí e do Brasil, pode ser multifatorial, como a falta de conhecimento da população acerca da efetividade e segurança da vacina, ficando evidente que as demais doses são negligenciadas após a primeira dose.

**Palavras-chave:** Cobertura vacinal. HPV. Imunização.

## INTRODUCTION

HPV (Human Papillomavirus) is a virus that infects the skin or mucous membranes, including the oral, genital and anal regions, causing genital warts and cancer, depending on the type of virus, both in men and women. HPV infection is the most common sexually transmitted infection (STI) around the world. Papillomavirus has more than 150 different genotypes, 12 of which are considered to be of high oncogenic risk by the International Agency for Research on Cancer (IARC). Among the types of cancer that HPV can cause, one can include cancer of the cervix, vulva, penis and anus, in addition to oropharyngeal cancer (BRASIL, 2018; SERRANO *et al.*, 2018).

Globally, about 290 million women have HPV (INCA, 2019). According to the National Cancer Institute – INCA (as per its Portuguese acronym), 16,370 new cases of cervical cancer were estimated for each year of the 2018-2019 biennium in Brazil, with an estimated risk of 15.43 cases per 100,000 women, constituting the third most common type of cancer among Brazilian women. Without considering non-melanoma skin cancer, cervical cancer had a lower incidence only than breast and colon and rectal cancers. In the North, cervical cancer was the first most incident (25.62/100 thousand). The Northeast region occupied the second position (20.47/100 thousand). In Piauí, the estimate was 430 new cases of cervical cancer; and, in the capital Teresina alone, the estimate was 140 new cases (INCA, 2017).

Primary prevention of cervical cancer is related to decreasing the risk of contagion by HPV. Due to the consequences of HPV infection and its worldwide prevalence, the development of a vaccine was an immediate necessity, being the most effective measure for the prevention of this infection (ALMEIDA *et al.*, 2020).

Because of the high morbidity and mortality due to cervical cancer in the country, the Brazilian Ministry of Health obtained a favorable result for the incorporation of the HPV vaccine in the Unified Health System (SUS, as per its Portuguese acronym) after conducting studies taking into account the cost-effectiveness, besides the positive manifestation of the Technical Advisory Committee on Immunizations (CTAI, as per its Portuguese acronym) recommending the vaccine. The quadrivalent vaccine was approved in 2006 by the Food and Drug Administration (FDA) as an immunizing agent against HPV; and, in that same year, the National Health Surveillance Agency (ANVISA, as per its Portuguese acronym) regulated marketing in Brazil. Subsequently, the bivalent vaccine from the GlaxoSmithKline laboratory and the quadrivalent vaccine from Merck Sharp and Dohme were approved. These vaccines stimulate the humoral response based on contact with virus-like particles (VLP). In 2014, the Brazilian Ministry of Health, through the National Immunization Program, introduced the quadrivalent HPV vaccine (vq-HPV) in the National Vaccination Calendar. The quadrivalent vaccine is able to provide immunity against viral types 6 and 11 (responsible for 90% of genital warts) and 16 and 18 (responsible for 70% of cases of cervical cancer), while the bivalent vaccine prevents only against types 16 and 18 (BRASIL, 2014; ZARDO *et al.*, 2014).

In Brazil, the implantation of the HPV vaccine was gradual, offered in the routine vaccination of SUS health units and schools in a 3-dose schedule (0, 6 and 60 months). In 2014, the target population was girls aged from 11 to 13 years old; in 2018, the vaccine was available in a 2-dose schedule, with an interval of 6 months, for girls aged from 9 to 14 years old, as well as for the male population from 11 to 14 years old. It was also available for people living with HIV, transplant recipients and cancer patients undergoing chemotherapy and radiotherapy, aged between 9 and 26 years, in three doses (BRASIL, 2018).

An unprecedented study conducted by the Moinhos de Vento Hospital, through the Institutional Development Support Program of SUS (PROADI-SUS, as per its Portuguese acronym), pointed out the national prevalence of HPV infection, which was 53.6% in a total of 6,388 valid samples of uterine cervix, penis and scrotum (5,268 samples from women and 1,120 from men), collected between 2016 and 2017 in individuals aged from 16 to 25 years, with high oncogenic risk HPV being present in 35.2% of participants. The prevalence of HPV in Teresina was 57.2%, of which 31.2% had high-risk HPV (AHMV, 2020).

One of the great challenges for public health is to inform the population about HPV and to develop accurate forms of communication through the media, churches, schools and non-governmental organizations (MONTEIRO *et al.*, 2018). When considering the prevalence of HPV and its close relationship to cervical cancer and low vaccination coverage, this study is of great public relevance, since establishing strategies requires a detailed analysis of vaccination coverage. Accordingly, this study is intended to analyze the vaccination coverage against HPV in Teresina, capital of the State of Piauí, Brazilian Northeast.

## MATERIAL AND METHODS

Quantitative, epidemiological, descriptive and population-based study. The data were obtained from the Information System of the National Immunization Program (SI-PNI, as per its Portuguese acronym) and from DATASUS, SUS Informatics Department, both publicly accessible. The data refer to the applied doses of vq-HPV and vaccination coverage in men and women, in 2018, in Teresina. The first dose (D1) and the second dose (D2), total and by age groups (from 9 to 14 years old), as well as the data from the third dose (D3), were included only for people with HIV (Human Immunodeficiency Virus) and immunosuppressed people, regardless of age group.

The Information System of the National Immunization Program registers the immunobiological agents applied and the population quantity vaccinated, aggregated by age group, time period and geographical area of each health establishment (vaccine rooms) linked to the Brazilian Ministry of Health, with registration in the Immunization Program Evaluation System (API, as per its Portuguese acronym). DATASUS is an organ of the Secretariat for Strategic and Participative Management of the Ministry of Health that provides information that can serve to support objective analyzes of the health situation. It contains vital information (mortality and live births), epidemiological and morbidity, as well as demographic and socioeconomic, information from the health care network.

The data were made available in DATASUS and organized in spreadsheets for further evaluation. Vaccination Coverage (VC) is measured as the percentage of vaccinees in the target population for each vaccine and is the concrete data provided by SI-PNI and DATASUS to demonstrate the effectiveness and efficiency PNI. The obtainment of vaccination coverage is based on population data from the Brazilian Institute of Geography and Statistics (IBGE, as per its Portuguese acronym) and data on applied doses from SI-PNI. This study does not require submission to the Ethics Committee because it involves only publicly accessible data in which participants are not identified, according to CNS Resolution 510/2016.

## RESULTS AND DISCUSSION

In Teresina, during 2018, 17,938 vq-HPV doses were applied, with 9,371 doses applied to boys and 8,567 doses applied to girls. The boys were included in the vaccination routine during 2017; and, in 2018, the number of vaccinated people was already higher in this population. According to Brasil (2018), the vaccination strategy for boys also contributes to reducing the transmission of the virus to women and, thus, reducing the incidence of HPV-related diseases in the female population.

In 2018, Piauí had 69,758 applied vq-HPV doses; and Teresina, which had 104 vaccine rooms and because it contains the largest population in the state, contributes 25.7% of this total. According to Table 1, 9,678 people took the first dose (D1) and 7,999 took the second dose (D2), representing a decrease of approximately 17%. People with HIV and immunosuppressed people are entitled to take a third dose (D3), where 261 doses applied to this public were counted by DATASUS.

**Table 1** - Number of vq-HPV doses applied to both genders and regardless of age, in Teresina, Piauí, Brazil (2018)

	D1	D2	D3	D1+D2+D3
Men	5,097	4,208	66	9,371
Women	4,581	3,791	195	8,567
Total	9,678	7,999	261	17,938

Source: DATASUS (2018).

In 2018, the total vaccination coverage for men corresponded to 11.67% for the first dose and 8.17% for the second dose. In women, the total vaccination coverage for the first dose reached 7.27%, while it was 10.64% for the second dose (Table 2). In both genders, vaccination coverage was well below the target stipulated by the Brazilian Ministry of Health for this respective year, which would be 80% of the vaccinated target population. The data regarding vaccination coverage for the third dose (D3) was not made available by the Information System of the National Immunization Program.

One of the families' concerns about vaccinating female children and adolescents would be a possible change in the sexual behavior of these young women who, influenced by the vaccine, could feel encouraged to start their sex life earlier. In adolescence, physical and emotional changes take place, being the period when human sexuality awakens; but, when this exercise of sexuality happens early and inconsequentially, it can lead to consequences such as unwanted pregnancy, school dropout and sexually transmitted infections (STI) (CALCAVECCHIA, 2018).

**Table 2** - Total HPV vaccination coverage by gender and regardless of age, in Teresina, Piauí, Brazil (2018)

	D1 total (%)	D2 total (%)
Men	11.67	8.17
Women	7.27	10.64

Source: DATASUS (2018).

Regarding the number of doses applied and vaccination coverage for each year of the age group recommended by PNI to receive the vq-HPV vaccine, the data for D1 and D2 are presented in Tables 3 and 4, respectively for women and men. The data referring to the age group of 14 years, in both genders, were not available in SI-PNI. In women, the age group that obtained the greatest coverage was 9 years old (Table 3), obtaining 44.07%; and in men, the greatest coverage was obtained at 11 years of age (Table 4), with 33.11%. These highest coverage levels were found in the early ages of HPV vaccination according to gender. As age progressed, the amount of doses applied decreased significantly. This behavior is noted both in girls (Table 3) and in boys (Table 4).

Analyzing the difference in doses applied between D1 and D2, it is found that, in its entirety, the amount of D2 is less than D1, in both genders. This behavior is also seen in other regions of the Brazilian Northeast. Da Silva and Oliveira (2018), when analyzing the coverage of the HPV vaccine in the town of Cascavel, in the state of Ceará, between the years 2014 and 2017, identified a constancy of low vaccination coverage of D2, being insufficient to ensure the completeness of the scheme for effective prevention against HPV.

Many countries have already seen a significant reduction in HPV after joining vaccination in young people, such as in Australia, Europe, North America and New Zealand, which reduced the number of HPV infections by approximately 90%. In the United States and Australia, the reduction has been proved in less than 4 years (COELHO *et al.*, 2015).

**Table 3** - Doses applied and coverage of the vq-HPV vaccine in women, by age, in Teresina, Piauí, Brazil

Age	Doses applied D1	Coverage D1 (%)	Doses applied D2	Coverage D2 (%)
9 Years	2,878	44.07	1,083	16.58
10 Years	876	12.94	1,232	18.20
11 Years	394	5.58	592	8.39
12 Years	180	2.48	288	3.96
13 Years	102	1.38	220	2.99

Source: DATASUS (2018).

In Piauí, since the incorporation of vq-HPV in the National Calendar until March 2018, the cumulative coverage with the two doses is 42.2% for girls aged from 9 to 14 years and 39% for boys aged from 12 and 13 years, with the first dose. According to Brazil (2018), the age group from 9 to 14 years seems to be the best occasion for vaccination against HPV, because, at this age, parents still maintain the habit of taking their children to take other vaccines, usually precedes the beginning of sexual activity and it is at this time of life that vaccination provides higher levels of antibodies, in amounts from 10 to 100 times greater than in a naturally acquired infection.

**Table 4** - Doses applied and coverage of the vq-HPV vaccine in men, by age, in Teresina, Piauí, Brazil

Age	Doses applied D1	Coverage D1	Doses applied D2	Coverage D2
11 Years	2,409	33.11	671	9.22
12 Years	1,299	17.42	1,311	17.58
13 Years	719	9.64	950	12.74

Source: DATASUS (2018).

Knowledge has a lot of influence on the attitude towards the HPV vaccine. The literature has highlighted some problems in patients' adherence to the vaccine, such as cultural barriers in relation to sexually transmitted infections, coverage of the health network and the knowledge about the clinical implications of chronic HPV infection (PEREIRA *et al.*, 2016). In the study by Almeida *et al.* (2020), it was possible to see that HPV vaccination had negative impacts due to parents' hesitation based on their knowledge, attitudes and beliefs related to the vaccine. Adverse socioeconomic conditions, such as low family income and parents' low level of education, were associated with lower vaccination coverage (ALMEIDA *et al.*, 2020).

A study carried out highlighting the reasons for the refusal of the HPV vaccine among adolescents showed that 86% of the interviewed adolescents have heard about HPV; however, only 48% are aware of the relationship between HPV infection and cervical cancer. Among the reasons mentioned for not getting vaccinated, the most frequent was fear about side effects (37%), followed by the impossibility of going to a health unit to get vaccinated (20%). These results are in line with international research, which showed that adults and adolescents know little about HPV (ZANINI *et al.*, 2017).

PNI is supported by the scientific literature with regard to the safety of the HPV-Q vaccine, as several studies already carried out reveal an adequate safety profile of the vq-HPV vaccine for mass vaccination, since no scientific evidence of significantly elevated risk for the occurrence of serious adverse effects in the vaccinated population compared to the non-vaccinated population was identified (QUINTÃO *et al.*, 2014).

The Moinhos de Vento Hospital Association, from Porto Alegre, conducted a research on the national prevalence of HPV infection between the years 2016 and 2017 and presented data on its participants: regarding education, 23.5% of young people had, at most, complete elementary school, 21.4% had incomplete or complete higher education and 55.1% had incomplete or complete high school. The average age of sexual activity initiation was 15.2 years and only about half of the individuals (50.7%) reported using condoms routinely. The percentage of individuals who reported having knowledge about HPV was 40.1%. In Teresina, the prevalence of HPV was 57.2%, being the

3<sup>rd</sup> most prevalent capital in the Northeast, which further reinforces the need to intensify vaccination and increase vaccination coverage (AHMV, 2020).

The ideal strategy to ensure good vaccination coverage is based on increasing adherence to immunization programs, as in the campaigns to increase the number of young people vaccinated against HPV that the Brazilian Ministry of Health carries out annually. In order to demonstrate the power of these campaigns, data were collected in SI-PNI, which monitors applied doses on a monthly basis. In 2018, the campaign started in September in Teresina and had an increase of 98.4% in doses applied compared to August, the month before the campaign, as shown in Table 5.

**Table 5** - Number of vq-HPV doses applied in August, September and October in Teresina, Piauí, Brazil

	August	September	October
D1	866	1,856	1,202
D2	610	1,049	841
Total	1,476	2,905	2,043

Source: DATASUS (2018).

In this context, establishing partnerships with public and private schools and Family Primary Health Care Units, ensuring information and clarification of the target audience and their guardians, becomes a primary strategy (IWAMOTO, TEIXEIRA, TOBIAS, 2017).

Regardless of the successful implementation of the HPV vaccine, routine tests should be performed periodically in order to detect cervical cancer precursor lesions early in their development, thus treating them and preventing progression to invasive cancer (ZANINI *et al.*, 2017).

Accordingly, health education strategies should be stimulated and carried out frequently, so that information about the risks of the disease, what preventive measures should be taken, and the benefits of vaccination, with clarification of doubts, fears and risks of serious adverse events, are considered fundamental to influence awareness about HPV vaccination (ALMEIDA *et al.*, 2020). It is perceived the need for health promotion using interactive and didactic educational methods to improve the decision-making capacity of the target population and their relatives, parents or guardians, and consequent greater adherence to the vaccine.

## CONCLUSION

This study highlights the low vaccination coverage against HPV in Teresina during 2018, falling far below the target stipulated by the Brazilian Ministry of Health. The vaccination coverage of the second dose was shown to be lower than the first dose, in most age groups, showing that many children and adolescents were left with an incomplete vaccination schedule. The strategy of carrying out vaccination campaigns proved to be effective, since there was a significant increase in the number of doses applied during the month of the campaign.

Studies prove that the HPV vaccine is safe and can reduce the numbers of cervical cancer related to HPV infection. The success of the vaccination comes up against some factors, such as the population's lack of knowledge about the virus, as well as the effectiveness and safety of the vaccine. In order for knowledge and health promotion to reach adolescents and legal guardians more clearly and succinctly, the media, together with schools, churches and health units, is of fundamental importance in this education process.

The low vaccination coverage in Teresina, as well as in Piauí and Brazil, can be multifactorial. As it is a vaccine that was recently implanted in the vaccination calendar of PNI, subsequent epidemiological studies are necessary for an analysis of the actual vaccination coverage in comparison to the national prevalence of HPV.

Brazil already has a good experience with the accomplishment of national programs leading to significant vaccination coverage, thus making some diseases eradicated; and if good vaccination



coverage is achieved, together with effective colposcycological screening, there is a strong indication of a reduction in the numbers of HPV-related cancers.

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