HPV VACCINATION STRATEGY
ESTRATÉGIA DE VACINAÇÃO CONTRA HPV
ESTRATEGIA DE VACUNACIÓN CONTRA HPV

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ABSTRACT

Objective: to analyze the strategy of vaccination against HPV. **Method:** this is a quantitative, epidemiological, descriptive, population-based study conducted with data from the Information System of the National Immunization Program, referring to vaccination between January 2016 and May 2017, in girls aged 9 to 14 and boys aged 12 to 13 years old. **Results:** there were 70,941 doses of HPV-Q vaccine applied in 2016 and, from January to May 2017, 36,715 doses (21,505 in girls and 15,210 in boys). Compared with the states of the Midwest region, the vaccination coverage in Goiás ranked third, behind Mato Grosso do Sul and the Federal District. **Conclusion:** the vaccination coverage in Goiás is unsatisfactory when compared to other states in the Midwest. There is a need for adjustments to the HPV vaccination strategy. **Descriptors:** Papillomaviridae; Immunization; Epidemiology; Public Health.

RESUMO

Objetivo: analisar a estratégia de vacinação contra HPV. **Método:** estudo quantitativo, epidemiológico, descritivo, de base populacional, realizado com dados do Sistema de Informação do Programa Nacional de Imunizações, referentes à vacinação realizada entre janeiro de 2016 e maio de 2017, em meninas dos 9 aos 14 anos e meninos dos 12 aos 13 anos. **Resultados:** foram aplicadas 70.941 doses de vacina HPV-Q em 2016 e de janeiro a maio de 2017, 36.715 doses (21.505 em meninas e 15.210 em meninos). Comparando com os estados da região Centro-Oeste, a cobertura vacinal goiana ocupou terceiro lugar, ficando atrás do Mato Grosso do Sul e Distrito Federal. **Conclusão:** a cobertura vacinal goiana é pouco satisfatória quando comparada com demais estados do Centro-Oeste. Há necessidade de adequações na estratégia de vacinação contra HPV. **Descritores:** Papillomaviridae; Imunização; Epidemiologia; Saúde Pública.

RESUMEN

Objetivo: analizar la estrategia de vacunación contra HPV. **Método:** estudio cuantitativo, epidemiológico, descriptivo, de base populacional realizado con datos del Sistema de Información del Programa Nacional de Inmunizaciones, referentes a la vacunación realizada entre enero de 2016 y mayo de 2017, en niñas de 9 a 14 años y niños de 12 a 13 años. **Resultados:** fueron aplicadas 70.941 dosis de vacuna HPV-Q en 2016 y de enero a mayo de 2017, 36.715 dosis (21.505 en niñas y 15.210 en niños). Comparando con los estados de la Región Centro-oeste, la cobertura de vacunas en Goiás ocupó el tercer lugar, quedando atrás de Mato Grosso do Sul y Distrito Federal. **Conclusión:** la cobertura de vacunas en Goiás es poco satisfactoria cuando comparada con demás estados del Centro-Oeste. Se necesitan adecuaciones en la estrategia de vacunas contra HPV. **Descriptor:** Papillomaviridae; Inmunización; Epidemiología; Salud Pública.

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INTRODUCTION

Human papillomavirus (HPV) infection is considered the most prevalent sexually transmitted disease (STD) in the world. HPV is associated with cervical cancer, one of the major public health problems responsible for female deaths.¹

According to data from the World Health Organization (WHO)², cervical cancer is the second most common cancer in women living in less developed regions, after breast cancer. In 2012, a total of 445,000 new cases per year were estimated in these regions, accounting for 84% of new cases worldwide.

Besides to cervical cancer, precancerous lesions of the anogenital tract and genital warts are associated with HPV as well as cancers of the head and neck. Other HPV-related neoplasms, such as the vulva, vagina, and anus, are also at increased risk with age in women previously infected with the virus.¹

Vaccination is an effective and cost-effective method to combat a disease of infectious etiology.³ In 2006, the Food and Drug Administration (FDA) approved the quadrivalent vaccine as an immunizing agent against HPV⁴, and in that same year National Agency of Sanitary Surveillance of Brazil (Anvisa) regulated the commercialization of this vaccine.⁵

The quadrivalent vaccine (HPV-Q) allows active immunization against Type 6, 11, 16 and 18 Human Papillomavirus (recombinant) and it was included in the vaccine calendar in 2014. When the vaccine was implanted by the National Immunization Program (PNI) and during 2015, it was necessary to administer three doses.⁶ In 2016, the vaccination schedule indicated by the Ministry of Health was composed of two doses, and the girl (9 to 13 years old) should receive the second dose six months after the first dose. This change in the Vaccine Calendar became effective from January 2016 as recent studies have shown that the two-dose schedule shows an antibody response in healthy girls aged 9 to 14 years not inferior when compared to the immune response of 15 to 25 years who received three doses.⁷

At the beginning of 2017, the vaccine already available for the vaccination of girls between the 9 and 13 years old began to cover girls until 14 and boys between 12 and 13 years old. More than 3.6 million children were included in HPV vaccination to increase vaccine coverage and reduce the incidence of cancers, anus, throat and genital warts, as well as reducing the incidence of cervical cancer and vulva in women since men are

responsible for transmitting the virus to their partners. The targeting scheme remained the same as in 2016: 2 doses of the vaccine, with a 6-month interval between them.⁸

People of both genders between 9 and 26 years with HIV/AIDS or other immunosuppression (transplanted from solid organs, bone marrow or cancer patients) may also receive the vaccine. The current vaccine schedule includes 3 doses of vaccine (with a range of 0, 2 and 6 months), as those with compromised immune systems, are more susceptible to serious health problems.⁸

According to Anvisa, the vaccine is effective in preventing precursor lesions of cervical cancer (CIN 2 and 3), which are directly related to the onset of carcinoma. However, it should be pointed out that the studies should accompany the included girls long enough for the development of malignancies, to ensure efficacy in the prevention of cervical cancer, which is more than 20 years on average.⁹

The objective of vaccination against HPV in Brazil is to prevent cervical cancer, reflecting the reduction in incidence and mortality from this disease. Outcomes such as prevention of other types of cancer induced by HPV and genital warts are considered secondary outcomes. The goal is to vaccinate 80% of the target population since a coverage of 80% of vaccine coverage generates “collective or herd immunity”, that is, reducing transmission even among unvaccinated people.⁹

Due to the recent changes by the Ministry of Health in the PNI during 2016 and 2017, there was a need to evaluate the number of doses applied and the vaccination coverage to infer the recent epidemiological situation of the state of Goiás.

In this perspective, it is relevant and opportune to analyze the vaccine coverage of HPV in the state of Goiás during 2016 to May 2017, compared with the vaccination coverage of the states of the Midwest (Mato Grosso and Mato Grosso do Sul) and Federal District. Based on these data, it is possible to infer the quality of the strategy adopted in Goiás and to suggest a design in the strategy, aiming to increase vaccine coverage, with homogeneous distribution and identifying situations of insufficiency that may indicate the need for special studies and intervention measures.

OBJECTIVE

- To analyze HPV vaccine coverage.

METHOD

This is a quantitative, epidemiological, descriptive, population-based study that considers the state of Goiás and other states of the Midwest Region as a unit of analysis. The databases of the HPV Vaccination Strategy, in 2016 and 2017 (until the month of May), in the state of Goiás and other states of the Midwest Region, were obtained through the Information System of the National Program of Immunizations (SI-PNI) and the database of the Department of Informatics of SUS (DATASUS).

DATASUS is an agency of the Department of Strategic and Participatory Management of the Ministry of Health responsible for collecting, processing and disseminating health information (such as health indicators, health care, epidemiological and morbidity information, vital statistics, demographic and socio-economic information). The data were obtained in the electronic site were organized in spreadsheets of the Microsoft® Excel program for later evaluation.

In the study, data on vaccine coverage (HPV-Q) were included for girls aged 9 to 14 years old and boys aged 12 to 13 years old, living in Goiás and data from the other states of the Midwest Region and Brazil's vaccination

coverage. All data were available in DATASUS and are related to the vaccination strategy applied during 2016 and 2017. For trend analysis, data referring to Goiás, Mato Grosso, Mato Grosso do Sul and Federal District were compared.

Vaccine Coverage (VC) is measured as the percentage of vaccines given in the target population for each vaccine and it is the concrete data to demonstrate the effectiveness and efficiency of the PNI. The fraction corresponding to the denominator that computes the calculation of the VC indicator for the population is used the population estimates of the Brazilian Institute of Geography and Statistics (IBGE) available on the electronic website of the Department of Informatics of the Unified Health System (DATASUS).¹⁰

RESULTS

In the Midwest Region, during 2016, 198,945 doses of HPV-Q vaccine (197,261 doses in girls and 1,684 doses in boys) were applied. The state of Goiás contributed with 70,941 doses, corresponding to 35.6% of the doses applied in the region. Of the total doses applied in Goiás, 98.8% (70,127) of the doses were applied in girls and 1.2% (814) in boys (Table 1).

Table1. Total HPV-Q vaccines applied in the Midwest and Federative Units, Brazil, 2016.

Midwest	HPV-Q (female)	HPV-Q (male)	Total
Mato Grosso do Sul	34.900	324	35.224
Mato Grosso	52.189	198	52.387
Goiás	70.127	814	70.941
Distrito Federal	40.045	348	40.393
Total	197.261	1.684	198.945

At the beginning of 2017 until May, there are a total of 96,578 doses applied in the Midwest Region, and Goiás contributes with 36,715 (38%) of this total. Twenty-one

thousand, five hundred and five doses (58.5%) were applied in girls and 15,210 (41.4%) in boys (Table 2).

Table 2. Total HPV-Q vaccines applied in the Midwest and Federative Units, Brasil, 2017.

Midwest	HPV-Q (female)	HPV-Q (male)	Total
Mato Grosso do Sul	12.894	9.684	22.578
Mato Grosso	17.248	12.895	30.143
Goiás	21.505	15.210	36.715
Distrito Federal	4.659	2.483	7.142
Total	56.306	40.272	96.578

In 2016, of the total of 70,941 doses applied in the state of Goiás, 36,671 corresponded to the first dose (D1), 33,384 to the second dose (D2) and 886 to the third dose

(D3). In 2017, through May, of the total of 36,715 doses, 26,334 corresponded to D1, 10,283 to D2 and 98 to D3 (Table 3).

Table 3. Doses of the vaccine against HPV-Q applied in both genders, in the state of Goiás, Brazil, in 2016 and 2017.

	1 st dose	2 nd dose	3 rd dose	Total
Goiás (January to December 2016)	36.671	33.384	886	70.941
Goiás (January to May 2017)	26.334	10.283	98	36.715

Comparing the other states of the Midwest Region, in 2016, the vaccination coverage in Goiás was the last place when it was evaluated for the females, presenting a value

of 13.06 and second place of the vaccination coverage in males, whose value was 0.08, behind only Mato Grosso do Sul (Table 4).

Table4. Vaccination Coverage in Federative Units of the Midwest Region, Brazil, 2016.

	Female	Male
Midwest	15.28	0.07
Mato Grosso do Sul	15.63	0.11
Mato Grosso	18.45	0.07
Goiás	13.06	0.08
Distrito Federal	16.19	0.02

In 2017, vaccination coverage has been increasing in males (9.66), while coverage calculated for females is 10.04. The current situation of 2017, in the state of Goiás, is

second to last, remaining ahead only of the Federal District, for both females and males (Table 5).

Table 5. Vaccination Coverage in Federative Units of the Midwest Region, Brazil, 2017.

	Female	Male
Midwest	10.81	9.89
Mato Grosso do Sul	14.82	15.73
Mato Grosso	15.05	14.37
Goiás	10.04	9.66
Distrito Federal	3.9	2.34

DISCUSSION

This article showed that in Goiás in 2016, 98.8% (70,127) of the doses were applied in girls and 1.2% (814) in boys. We know that in the SUS, boys were seen with the vaccine only from 2017, so the results of that year for the boys are possibly related to the vaccination done in private clinics. In the period from January to May 2017, 21,505 doses (58.5%) were applied in girls and 15,210 doses (41.5%) in boys. The low number of doses applied in the period studied reveals that the demand for health centers is not enough to consume this vaccine.¹¹

Studies¹²⁻³ demonstrate that a significant part of the population samples studied is informed about the existence of the vaccine and about government campaigns and it is favorable to its implementation. However, there is still a relative resistance to acceptance in other samples, mainly due to the low level of knowledge in relation to HPV disease outcomes and possible economic and sociocultural implications, which would justify the low demand for this immunobiological disease.¹⁴

For this reason, it is necessary to carry out the operational and impact evaluation of the immunization programs, as well as to outline vaccination strategies and to subsidize processes of planning, execution, monitoring, and evaluation of public policies related to the care to Children's Health and to the control of diseases preventable by immunization.¹⁰

One study has shown that there is scientific evidence that the application of the vaccine in men and women containing the four most important viral types will result in a decrease in the rate of infection and consequently in the reduction of treatment costs. According to the studies analyzed, the role of vaccination in women is relevant, and special attention should be given to those sexually active since they are at higher risk of acquiring new HPV infections.¹ Also, according to the WHO¹⁵⁻⁶ the vaccine against HPV has a high potential to reduce the incidence of cervical and anogenital cancer. Therefore, in Brazil, the female population certainly benefits from this, reducing infection by HPV and precursor lesions in a substantial way. The combination of the vaccination strategy with HPV serology

and colposcycological screening suggests a high level of protection for women's health.¹⁷

Regarding the level of knowledge about HPV, a study carried out with health academics showed that regarding HPV prevention, most of the students knew the means of transmission of HPV, with 56.6% correctly citing more than one preventive method and 41.3% stated that the vaccine is the most effective method of prevention.¹⁸

Even though most of the population recognizes the vaccine as important for the prevention of HPV, it is important to note that widespread access to communication networks and the widespread dissemination of information, often erroneous, increase vaccine-related resistance. Also, the dissemination of post-vaccination adverse events (EAPV) in the media often hamper the population's perception of the benefits of vaccination.¹⁹

Regarding the safety of the HPV-Q vaccine, scientific evidence shows that the fact that it is being implemented in several countries of the world without presenting serious adverse events has been considered an important advantage.²⁰ Also, it showed a positive cost-effectiveness result.⁷ Therefore, the intensification of vaccination strategies should be encouraged.

Compared to the other states of the Midwest Region, Goiás ranked the last place for female vaccination coverage (13.06%) and second place for male vaccination coverage (0.08%), leaving only Mato Grosso. In 2017, the male vaccination coverage was 9.66%, while the coverage for the females was 10.04%. This current vaccination coverage of Goiás, when compared to the other states of the Midwest Region, is unsatisfactory for both females and males, since the goal for the immunobiological HPV is to vaccinate at least 80% according to the target population defined by the Ministry of Health for each year. The impact of vaccination in terms of collective health is given by the coverage of 80% of vaccine coverage. When high vaccination coverage is achieved, "collective or herd immunity" may occur, that is, there is a possibility of reducing transmission even among non-vaccinated people.⁹

It was possible to observe a change in the relationship between doses applied in girls and boys due to the recent update of the PNI under the guidance of the Ministry of Health, which currently covers a larger number of female population (including girls up to 14 years old) and includes boys aged 12 to 13 years old in vaccine coverage.⁸ This scenario is expected to persist and achieves the desired

vaccination coverage (80% of the target population), while sustained by a synergistic performance of all sectors of Brazilian society (family, press, education sector, health, NGOs, healthcare companies, public and private managers). Thus, the objective is to disseminate information about the quality and access of young people to the topic, considering the extreme importance of the family and the school environment as reliable sources of sexual education orientation.¹³⁻¹⁴

Some studies have shown that the ideal strategy to ensure good vaccine coverage is based on increased adherence to immunization programs. The main strategy consists of the partnership with the public and private schools and Units of Primary Care to Family Health (UABSF), guaranteeing information and clarification of the target public and those responsible.^{6,10,12-4}

The vaccine strategy of Goiás can be improved by establishing new epidemiological targets according to the NIP's 2017 vaccination schedule, based on special studies and intervention measures, such as immunization campaigns in schools, with media support.⁶ Several regions of the State have sufficient vaccine lots for the target public. The minimum desired adherence has not been achieved and therefore, the State has several vaccine lots with the next due date.

Another result of this study was that in 2016, 36,671 of the 70,941 doses applied in the state of Goiás corresponded to the first dose (D1), 33,384 to the second dose (D2) and 886 to the third dose (D3). While in 2017 until May, out of a total of 36,715 doses, 26,334 corresponded to D1, 10,283 to D2 and 98 to D3. The relative reduction in the number of D3 (third dose) can be justified by the recent update of the NIP in 2015, which changed the three-dose schedule to two doses.⁸

It is assumed that both the bivalent and the quadrivalent vaccine prevent cervical cancer and other HPV-related cancers with moderate efficacy for discharge. Also, it is estimated that if there is complete vaccination of the population, cervical cancer cases can be reduced by two-thirds.¹ Considering Brazil's good experience in vaccination coverage with national programs, there are strong indicators of efficiency against the oncogenic types of HPV in the target population.^{1,20}

CONCLUSION

It has been proven in other countries that the HPV vaccine (HPV-B and HPV-Q) prevents cervical cancer and other HPV-related cancers with moderate to high efficacy. Also, Brazil

has a history of adequate vaccination programs that can reach a large part of the target population. Therefore, it is possible to combat HPV infection by associating the vaccine strategy with serological tests against HPV and colposcycological screening.

The study showed that vaccination coverage in Goiás is unsatisfactory when compared to other federative units in the Midwest region and should be improved. It was possible to verify regions of the Midwest that need the greater direction of the vaccination strategy, as it is the case of the states of Goiás and Mato Grosso.

It is known that the HPV vaccine is one of the hopes for society and, therefore, the vaccination program should be even clearer, succinct and enlightening to inform the general public as well as health and education as a means of increasing vaccine compliance and preventing the implications of HPV infection.^{13,20-21} Also, correction and distribution of vaccine doses are required to achieve homogeneous coverage within the Midwest Region.

Despite the importance of the results obtained and their inferences, it is worth noting that this study presented some limitations hindering to analyze the vaccination coverage. Among these limitations, there are inaccuracies in the registration of doses of vaccine applied, typing errors and inaccuracies in the demographic database used to estimate the number of individuals in the studied age group.

It is expected that new epidemiological analyzes will be elaborated to verify real vaccination coverage and the efficacy of the vaccine strategy applied in the state of Goiás, comparing with morbidity and mortality rates due to cervical cancer.

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