










Impact of human papillomavirus vaccine on cases of cervical cancer in young women from Pernambuco state



Impacto da vacina contra o papilomavírus humano nos casos de câncer no colo do útero em mulheres jovens do estado de Pernambuco

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Abstract

Objective: To describe the impact of the human papillomavirus (HPV) vaccine on cases of cervical cancer in women aged 15 to 24 years residing in Pernambuco (Brazil), comparing the periods of 2006 – 2013 with 2015 – 2022. **Methods:** This retrospective descriptive cross-sectional study compared cases of cervical cancer before (first period = 2006 – 2013) and after (second period = 2015 – 2022) implementation of the HPV vaccine in Brazil and analyzed the number of doses administered between 2014 and 2022. Data were obtained from the Brazilian Cancer Information System (SIS-CAN), Cervical Cancer Information System (SISCOLO), and National Immunization Program Information System (SI-PNI). **Results:** After excluding 2014, 55 cases of cervical cancer (mean = 3.4 cases/year, standard deviation = 1.9 cases) were registered between 2006 and 2022. Of the 39 cases from the first period, 46.2% were invasive squamous cell carcinoma, and 41.0% were invasive adenocarcinoma. Of the 16 cases from the second period, most (62.5%) were invasive squamous cell carcinoma. A reduction of 59% was observed in cases from the first to second period, mainly in the

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age group from 15 to 19 years (83.3%) and of invasive adenocarcinoma (75%). The number of administered doses of the vaccine also decreased, especially in 2016 and from 2020 (i.e., during the COVID-19 pandemic). **Conclusion:** This study demonstrated the importance of vaccination against HPV and its association with the decrease in cases of cervical cancer in young women. However, the effects of the HPV vaccine on the population should be assessed over a longer period since it was implemented in 2014 in Brazil.

Keywords: Cervical cancer; Epidemiology; Human papillomavirus; Vaccination.

Resumo

Objetivo: Descrever o impacto da vacina contra o papilomavírus humano nos casos de câncer cervical em mulheres de 15 a 24 anos, residentes em Pernambuco, comparando os períodos de 2006 a 2013 e 2015 a 2022. **Métodos:** Trata-se de um estudo descritivo retrospectivo, de corte transversal, comparando o número de casos de câncer cervical antes (intervalo 1 = 2006 a 2013) e após (intervalo 2 = 2015 a 2022) a implementação da vacina contra o papilomavírus humano no Brasil e a quantidade de doses aplicadas entre 2014 e 2022. Os dados foram obtidos do Sistema de Informação de Câncer, do Sistema de Informação de Câncer de Colo de Útero e do Sistema de Informação do Programa Nacional de Imunização. **Resultados:** Foram registrados 55 casos desse câncer entre 2006 e 2022, excluindo-se o ano de 2014, com média de $3,4 \pm 1,9$ casos/ano. No intervalo 1 (39 casos), 46,2% foram do carcinoma epidermóide invasivo e 41,0%, do adenocarcinoma invasor. No intervalo 2 (16 casos), a maioria (62,5%) também foi do carcinoma epidermóide invasivo. Comparando-se os intervalos, houve redução de 59%, sendo maior na faixa etária de 15 a 19 anos (83,3%) e no adenocarcinoma invasor (75%). Também houve queda nas doses da vacina aplicadas, destacando-se 2016 e a partir de 2020, ano de início da pandemia da covid-19. **Conclusão:** Este estudo denota a importância da vacinação contra o papilomavírus humano e sua associação com a diminuição dos casos de câncer cervical em mulheres jovens. É necessário maior tempo para avaliação dos efeitos desse imunizante na população, pois ele só foi implementado no Brasil em 2014.

Palavras-chave: Câncer de colo uterino; Epidemiologia; Papilomavírus humano; Vacinação.

INTRODUCTION

Cervical cancer is the third most prevalent malignant neoplasm among Brazilian women, resulting in high mortality rates in the country.¹ According to the National Cancer Institute, it is a disordered replication of the epithelium in the organ, histologically subdivided into squamous cell carcinoma and adenocarcinoma and classified as *in situ* or invasive.²

The human papillomavirus (HPV) has been recognized as one of the main risk factors for cervical cancer, with subtypes 16 and 18 being the most recurrently involved in the pathophysiology of this neoplasm.³ Also, external factors (e.g., early onset of sexual activity, sexual risk behavior, multiple sexual partners, history of genital warts, immunosuppression, smoking habit,

and presence of other sexually transmitted infections [STI]) can contribute to its pathogenesis.^{4,5} Cervical cancer is often asymptomatic or presents few symptoms, leading to delayed medical attendance in its early stages due to evasion of the immune system.⁶

The Brazilian Ministry of Health (MS) established that cervical cancer screening should begin at 25 years old for women who have already started sexual activity until 64 years old.⁷ Also, the MS adopted the HPV vaccination in 2014 as part of the National Immunization Program (PNI), aiming to reduce the prevalence of cervical cancer. Thus, boys and girls aged 9 to 14 years and those aged 9 to 45 years with clinical conditions favoring immunosuppression can receive the quadrivalent vaccine free of charge through the Brazilian Unified Health System (SUS). Moreover, the MS included victims of sexual violence aged 9 to 45 years not previously immunized against HPV in the vaccination group in August 2023.^{8,9}

In this context, the World Health Organization recommends that HPV vaccination should achieve 90% coverage among children and adolescents aged 9 to 14 years. However, Brazil has not been able to meet this goal in recent years due to various factors, such as a lack of knowledge and trust in the benefits of the vaccine and spread of fake news, which intensified in 2020 due to the COVID-19 pandemic. As a result, the number of administered doses reduced for vaccines offered by the PNI for HPV and other infections.^{10,11}

Robust evidence have shown the efficacy of the HPV vaccine in preventing cervical cancer. For example, clinical trials showed that the quadrivalent vaccine had 95% efficacy against persistent infections from HPV 16 and 18 subtypes and lesions related to high-grade cervical intraepithelial neoplasia (CIN).¹²⁻¹⁵ Also, the vaccine provided sustained protection against low-grade lesions related to HPV 6, 11, 16, and 18 subtypes and an 83% reduction in the burden of the disease for up to 42 months of follow-up.¹⁴ Subsequent studies in countries where vaccination began years before its implementation in Brazil showed a 93% reduction in genital warts among vaccinated women aged 21 years and 72.6% reduction among those aged 21 to 29 years.¹⁵⁻¹⁷

In this sense, the HPV vaccine should be adopted in global immunization programs targeting girls and boys (preferably before the onset of sexual activity) to achieve widespread vaccine coverage, reduce morbidity and mortality from HPV-related diseases, and improve global public health. Thus, this study aimed to describe the impact of the HPV vaccine on cases of cervical cancer in women aged 15 to 24 years residing in the state of Pernambuco (Brazil), comparing the periods of 2006 – 2013 with 2015 – 2022.

METHODS

This retrospective descriptive cross-sectional study was based on data available in the Department of Informatics of SUS (DATASUS) platform. The study used secondary data on cervical cancer and the absolute number of doses administered of the quadrivalent HPV vaccine, focusing on the state of Pernambuco, Brazil.

Data on cases of cervical cancer by year of diagnosis, age group, and histological type were obtained from the Brazilian Cancer Information System (SISCAN) and Cervical Cancer Information System (SISCOLO). The type and number of doses administered of the quadrivalent HPV vaccine per year were extracted from the PNI Information System (SI-PNI). However, data on HPV vaccine coverage specifically for the state of Pernambuco were not found in the SI-PNI.

Study population and reference period

Inclusion criteria

Data of women aged 15 to 24 years diagnosed with cervical cancer were included in the study to represent the population group that should have already been immunized against HPV, considering that the vaccine was implemented in Brazil in 2014 for girls aged 11 to 13 years. Therefore, women should be between 19 and 21 years old in 2022. However, DATASUS only provides aggregated data for age groups of 15 – 19 and 20 – 24 years.

The number of cases of cervical cancer was analyzed from 2006 to 2022, divided into two periods to compare its distribution by age group and histological type: before (first period; 2006 – 2013) and after the vaccine implementation (second period; 2015 – 2022). Also, data on administered doses of the quadrivalent HPV vaccine in Pernambuco were analyzed in girls aged from 11 to 13 years in 2014 and 9 to 14 years between 2015 and 2022.

Exclusion criteria

Cases of cervical cancer recorded in 2014 were excluded from the comparative analysis by age group and histological type since this was the year of HPV vaccine implementation in Brazil. Also, cases with pre-malignant lesions (CIN 1 and CIN 2) and *in situ* squamous cell carcinoma (CIN 3) were not included in the study since these histological types were not found in DATASUS classifications.

Data were extracted from the Tabnet and exported to Microsoft Excel® (version 2021). Descriptive analyses were expressed as absolute and relative frequency and mean and standard deviation (SD).

The present study used secondary data without identifying women, which are aggregated and freely accessible in official databases on the internet. Thus, it followed the National Health Council Resolution no. 466 (reiterated by Resolution no. 510) and did not need the approval of a research ethics committee.

RESULTS

After excluding cases of cervical cancer in 2014, 55 cases (mean = 3.4 cases/year; SD = 1.9 cases) were registered in women aged 15 to 24 years in Pernambuco from 2006 to 2022. Of these, 39 cases (mean = 4.9 cases/year; SD = 2.1 cases) were registered in the first period

(2006–2013) and 16 (mean = 2 cases/year; SD = 1.7 cases) in the second period (2015–2022), indicating a 59% reduction in the number of cases (Figure 1 and Table 1).

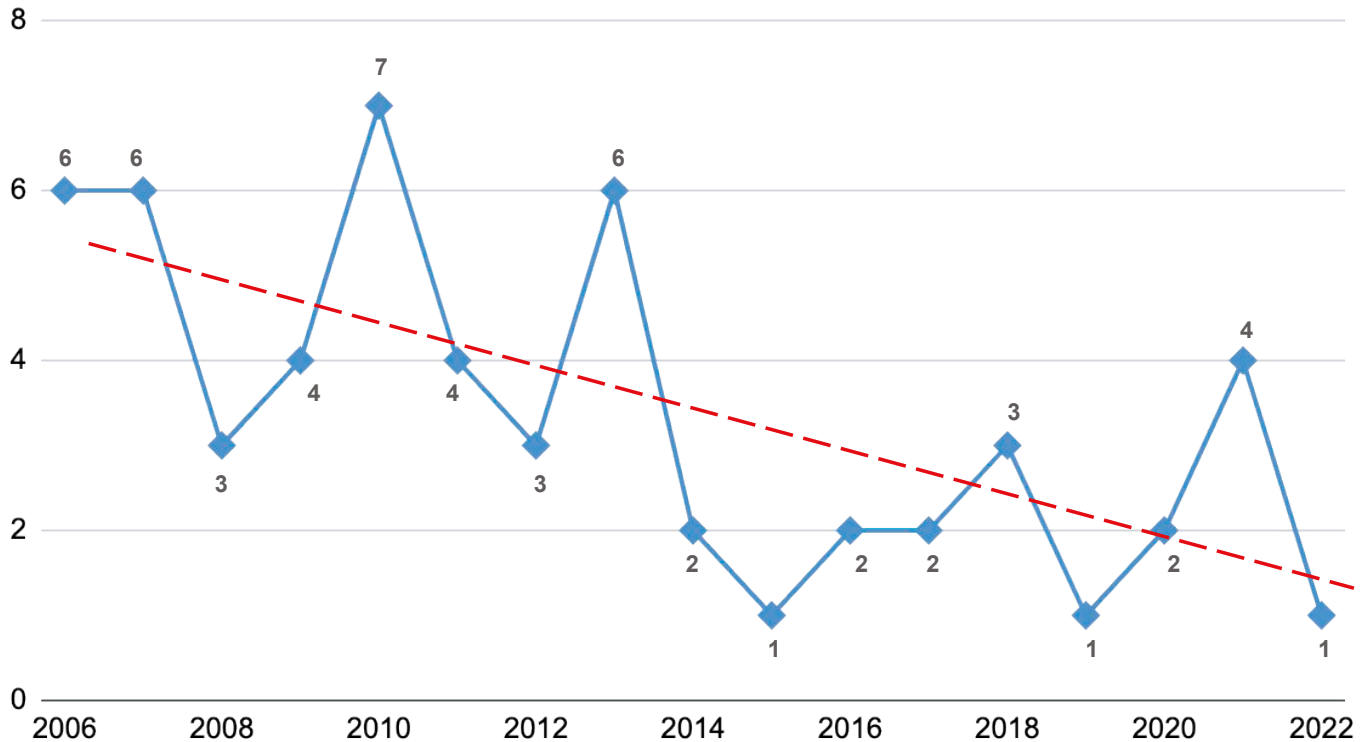


Figure 1. Number of cases of cervical cancer in women aged 15 to 24 years in the state of Pernambuco between 2006 and 2022.

Regarding the age groups, most cases occurred in women aged 20 to 24 years in both periods (Table 1). Of the cases registered in the first period, 18 (46.2%) were invasive squamous cell carcinoma, 16 (41.0%) were invasive adenocarcinoma, and 5 (12.8%) were *in situ* adenocarcinoma. Most cases (10; 62.5%) in the second period were invasive squamous cell carcinoma, four (25.0%) were invasive adenocarcinoma, and two (12.5%) were *in situ* adenocarcinoma (Table 1).

Table 1. Distribution of cases of cervical cancer in women aged 15 to 24 years by age group and histological type in the state of Pernambuco in the first (2006 – 2013) and second periods (2015 – 2022)

Variables	First period		Second period		Variation
	Nº	%	Nº	%	%
Age group					
15 – 19 years	12	30.8	2	12.5	83.3 ↓
20 – 24 years	27	69.2	14	87.5	48.1 ↓
Histological type					
Invasive squamous cell carcinoma	18	46.2	10	62.5	44.4 ↓
<i>In situ</i> adenocarcinoma	5	12.8	2	12.5	60.0 ↓
Invasive adenocarcinoma	16	41.0	4	25.0	75.0 ↓
Total	39	100.0	16	100.0	59.0 ↓

Regarding variation in cases of cervical cancer comparing both periods, the age group of 15 to 19 years presented an 83.3% reduction, while the age group of 20 to 24 years presented a 48.1% reduction in the second period. Also, invasive adenocarcinoma presented the greatest reduction (75%), followed by *in situ* adenocarcinoma (60%) and invasive squamous cell carcinoma (44.4%) (Table 1).

The number and type of administered doses of HPV vaccine reduced in the second period. In 2014 (i.e., HPV vaccine implementation), 361,167 doses were administered in Pernambuco: 237,885 as first, 123,228 as second, and 54 as third dose. The same pattern was observed in 2015, whereas 2016 presented almost 64% reduction in the number of administered doses compared with 2014. Although 2017 presented a slight increase, 2018 and 2019 presented a reduction in the number of doses administered per year. From 2020, this reduction became evident, decreasing from about 116,000 to 82,000 doses in 2022, and the number of women receiving the second and third doses also decreased (Figure 2).

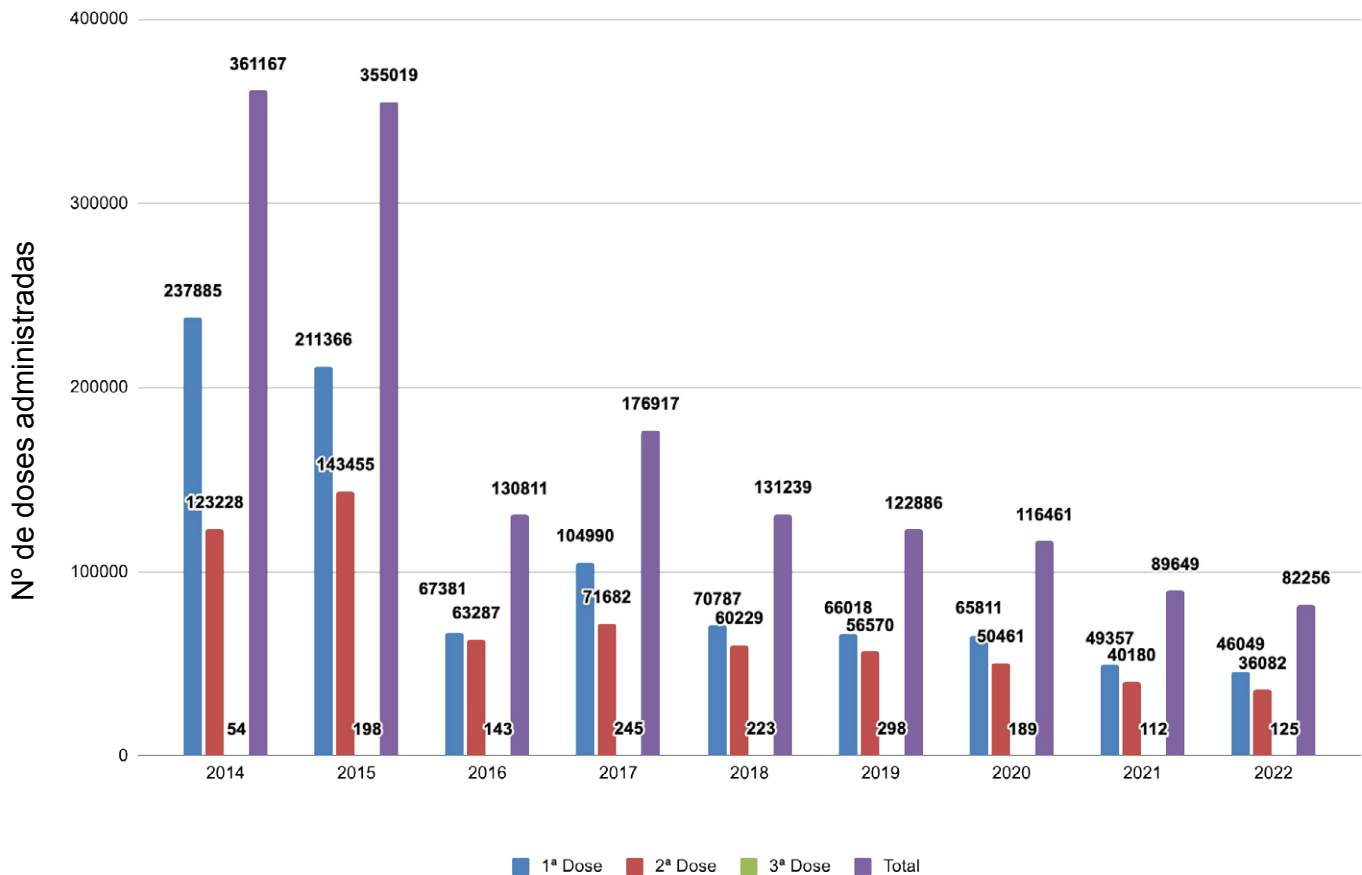


Figure 2. Number of first, second, and third doses of the quadrivalent HPV vaccine administered in girls aged 9 to 14 years in the state of Pernambuco between 2014 and 2022.

DISCUSSION

The cases of cervical cancer among women aged 15 to 24 years reduced after the implementation of the HPV vaccine in Pernambuco, corroborating other studies analyzing the same topic.¹⁸⁻²⁰ This reduction occurred since HPV vaccines are highly immunogenic and can protect individuals against CIN 2 or worse grades, which are mainly related to HPV 16 and 18 subtypes. Thus, these vaccines decreased viral prevalence and persistence.^{21, 22} This information was consistent with observational studies conducted in the United Kingdom, China, and Denmark, which have demonstrated that the HPV vaccine provided immunity, even if partial.^{18,23,24}

Among the studied age group, women aged 20 to 24 years were the most affected by cervical cancer, possibly due to the prolonged exposure to the virus and natural course of the disease, which occurs slowly and progressively.^{6,25} The greatest reduction in cases occurred in the age group of 15 to 19 years, possibly due to the sustained protection provided by the vaccine (especially in younger women) since antibody levels are increased in this age group. Also, the vaccine administration before the onset of sexual activity increases its efficacy since these girls

were not exposed to the pathogen. Nonetheless, the vaccine protects all women, including those with active sexual lives.²⁶⁻²⁸

Among the histological types of cervical cancer, cases of invasive adenocarcinoma showed the greatest reduction after the implementation of the HPV vaccine. However, no scientific evidence was found regarding the relationship of the HPV vaccine with this histological type.

The number of administered doses of the HPV vaccine has remarkably reduced since 2016, possibly due to the change in vaccination strategy. Initially, vaccinations were conducted in schools due to the partnership between the MS and Ministry of Education,²² surpassing the established coverage for the first dose in 2014. From 2015, vaccination campaigns were removed from schools and limited to basic health units, decreasing the number of vaccines administered, especially for the second and third doses.^{9, 22} Also, the Brazilian population has a cultural taboo that vaccination against STI induces early onset of sexual activity, resulting in the non-adherence of several social groups to certain vaccines and reducing some vaccination coverage.^{9,29}

The number of administered doses of HPV vaccine significantly reduced from 2020 to 2022, possibly due to the reduction of all vaccination coverages during this period, primarily caused by the COVID-19 pandemic. This failure may be mainly due to anti-vaccine movements that have emerged, spreading fake news and discrediting the effectiveness of vaccines.^{10,30}

This study highlighted the importance of HPV vaccination and its association with the reduction of cases of cervical cancer in young women in the state of Pernambuco. Although the HPV vaccine has already proven to be effective, its effects on the general population should be evaluated over a longer period since this vaccine was introduced only in 2014 in Brazil.¹⁸ Also, the complete HPV vaccination does not replace health promotion and prevention actions, such as condom use, cytology tests, and serological tests for other STI.²³ Thus, the combination of HPV vaccine and screening tests provides additional protection to women regarding the development of genital neoplasms through primary (i.e., avoiding virus infection) and secondary prevention (i.e., early detection of cervical lesions).

CONFLICTS OF INTEREST

Nothing to declare

AUTHORS CONTRIBUTIONS

LMCT and **MCSR**: study conception, data design, and article writing; **SOP**, **JKBSO**, and **JNT**: data analysis and interpretation and article writing; **CMO** and **JLL**: critical review of the article and approval of the version to be published.

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