

## Cervical Cancer: Preventive Barriers in the 21<sup>st</sup> Century

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### Abstract

**Introduction:** In Brazil, cervical cancer is the second most common type of gynecological cancer, losing only to breast cancer. Despite its high incidence and mortality, it is configured as a cancer with the possibility of prevention, and with consolidated prevention strategies in health care policies.

**Aims:** Specify barriers in the prevention of cervical cancer, especially in Brazil.

**Methods:** This is a systematic literature review. For the research, the databases consulted were: Lilacs and PubMed, using the descriptors: "Cervical Cancer", "HPV", "Prevention".

**Results:** The cervical Cancer, will arise when there is persistent infection with the oncogenic HPV virus, associated with risk factors. Because of HPV contagion being a sexually transmitted disease, the carcinoma becomes preventable, that is, measures can be taken to diagnose the infection and its primary changes before the evolution to carcinomatous lesion. Primary prevention involves the use of condoms and HPV vaccination, associated with health promotion actions. While secondary prevention involves early detection, the diagnosis is based on cytopathological examination.

**Conclusion:** In general, sex education is a fundamental step in the preventive barriers currently faced by Brazil in the fight against cervical cancer.

**Keywords:** *Cervical Cancer; HPV; Prevention*

### Introduction

Papillomavirus Humano (HPV) is the most common sexually transmitted virus in the world, when observing the general population we have a value among 12% of people infected with HPV infection besides being closely related to cervical cancer, is agent for cancer of oropharynx, anus, penis, vulva, vagina and for benign lesions such as genital warts [2]. In Brazil, cervical cancer is the second most common type of gynecological cancer, second only to breast cancer. Also being, the third type of cancer more common in women, excluding nonmelanoma skin cancer [1]. Despite the high incidence and mortality, it is configured as a cancer with the possibility of prevention and with prevention strategies consolidated in health care policies.

In 2014, the vaccine against Human Papillomavirus (HPV) was introduced in the calendar of the Brazilian Unified Health System, in addition to the screening of precursor lesions carried out with the cytopathological exam (Papanicolaou), this being part of the health system since 1990 and a step fundamental in the early detection of the disease.

According to the national health survey in 2013, Brazil has achieved 80% coverage, but there are important differences between regions and social classes. Currently, Brazil recommends the performance of cytopathological screening in the population aged between 25 and 64 years old [3]. The late age group and the exclusion from screening the elderly population is one of the most prevalent criticisms in relation to the prevention of colon cancer. uterus, especially in developing countries.

Cervical cancer is relatively uncommon in the United States, as well as in countries with a population with a higher purchasing power, being the eleventh most common type of cancer in women in the American community, which shows a great difference in relation to Latin America, among the most affected, Brazil.

In the United States, the Center for Disease Control and Prevention (CDC) recommends vaccination against the HPV virus in boys and girls between the ages of 11 and 12 for immunization to occur before exposure to the virus, but it can be applied until 26 years.

Contradictorily, acceptance of the vaccine is not ideal, less than half of the children included in this age group will be vaccinated. A picture different from that seen in other developed countries such as Canada, Australia and the United Kingdom where more than 70% of children were vaccinated. The policies of Latin American countries, including Brazil, have also planned the vaccine, but the economic, political and cultural barriers make high adherence impossible and, thus, hinder the proper prevention of the disease [2].

Cervical cancer has a slow and silent development, initially being observed Cervical Intraepithelial Neoplasia. HPV infection is known to be a necessary condition for the occurrence of cancer, but other factors interfere in the progression of this tumor, such as: age and smoking. The number of cigarettes smoked per day is proportional to the risk of the disease, as well as age: older women have a higher risk of persistent infection, since younger women tend to have spontaneous regression. Even with the preventive measures implemented by the country, about 50% of the cases of the disease are diagnosed in advanced stages (III and IV), which has a significant prognostic worsening.

According to the Inca, in the last three decades there has been no improvement in the mortality rates associated with the disease. Due to this scenario, the Ministry of Health initiated the plan of strategic actions to face chronic non-communicable diseases for the period 2011 - 2022, as well as in 2011 the "Program for Strengthening the Network for the Prevention, Diagnosis and Treatment of Cervical and Breast Cancer", to expand the actions related to these cancers [4]. In other words, actions are being created, but the numbers continue to increase, and mortality remains on the plateau, which indicates that there are barriers beyond the aspect political that must be analyzed.

Based on the failure of prevention, some studies highlight other causes for the difficulty of adherence, among them the need for more information about the vaccine, fear of possible side effects, doubts about the effectiveness, possible induction of early sexual initiation, or the belief that Pap smear is sufficient in the prevention of HPV [5]. Thus, it is clear the need to clarify these barriers especially in relation to the HPV vaccine, for epidemiological improvement in the number of cases of cervical cancer, greater adherence in campaigns future deaths and a drop in mortality in the coming decades.

## Objectives of the Study

### Primary endpoint

Detail the obstacles in the prevention of cervical cancer, especially in Brazil, with a focus on the population's fears about the Human Papillomavirus vaccine and on the emotional and technical barriers to the Pap smear.

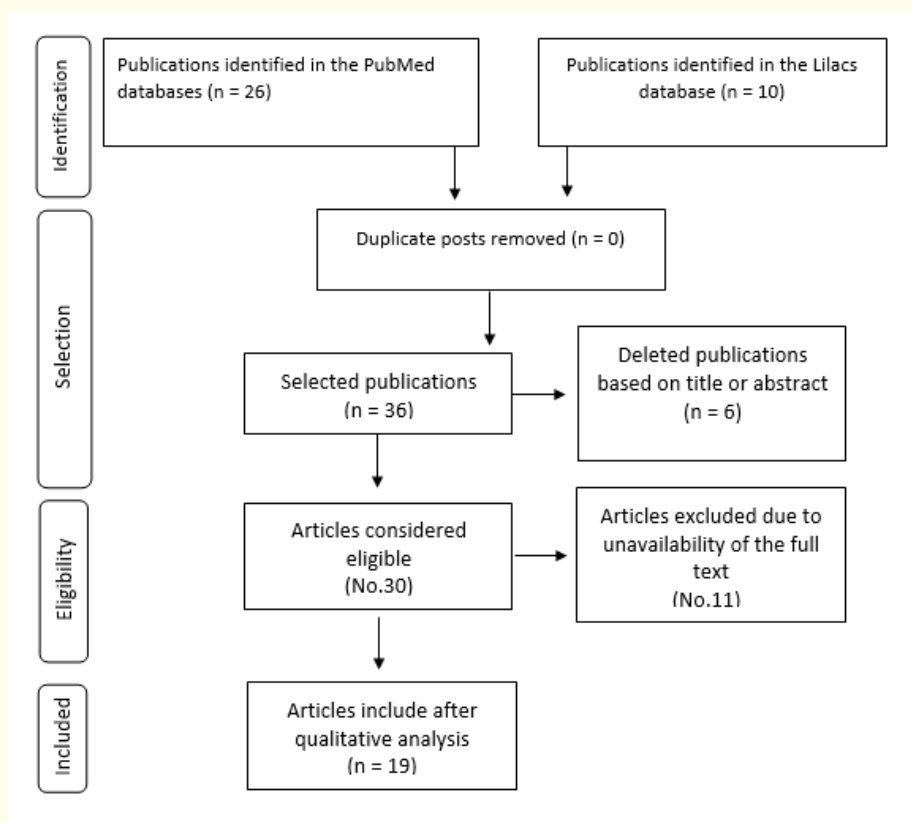
### Secondary objective

Discuss interventional measures needed to increase population engagement in cervical cancer prevention.

**Methods**

This is a systematic literature review. For the research, the databases consulted were: Lilacs and PubMed, using the descriptors: “Cervical Cancer”, “HPV”, “Prevention”. Using the Boolean operator AND, in the formation of the search key.

Articles published between 2009 and 2019, written in Portuguese and English, that focused on cervical cancer, its relationship with HPV infection and its forms of prevention were included. The filter used was free full text. All articles that did not report methods of preventing cervical cancer and those that had a low degree of evidence were excluded. Of the 36 articles found, 19 were selected for the construction of the work, which covered the theme and the necessary descriptions.



**Figure 1:** PRISMA flow diagram.  
Source: Prepared by the author.

**Results and Discussion**

Cervical cancer is a serious public health problem around the world, about 80% of cases are in developing countries, with Brazil having an important percentage in this account. The mortality rate is high, and the carcinoma in situ has its peak in incidence in women between 25 and 40 years old, while the invasive carcinoma between 48 and 55 years old, must remember the slow character of this carcinoma, the natural evolution for cancer invader is 10 years, but the average is 30 years.

The risk factors related to the disease are fundamental, since cervical cancer hardly occurs in women who have not started sex, as well as there is a greater risk with the early onset of sex, in addition to the number of partners, exposure other sexually transmitted infections

and low purchasing power [6]. The high relationship with sexual life stems from the infection with Human Papillomavirus, better known by women as HPV.

HPV is a virus of the Papavaviridae family, it is classified according to its pathogenic potential, especially its oncogenic capacity, which is characterized by inducing genotypic changes to cells. They are divided into low-risk HPV (DNA-BR) and high-risk (DNA-AR), both of which can generate cell growth, but only high-risk HPV can lead to carcinoma [7]. The most common types of HPV in women around in the world are 16, 18, 58, 52 and 31 respectively. Most women infected with HPV have self-limited conditions that spontaneously regress after 12 to 30 months, even those infected by those with greater oncogenicity such as types 16 and 18 1. In other words, it is not only HPV infection that will lead to development of cancer; concomitant factors will be necessary for this evolution, in particular behavioral measures to decrease sexual infection by the virus.

Colon cancer will arise when there is persistent infection with the oncogenic HPV virus, associated with risk factors. Because the HPV infection is a sexually transmitted infection, the carcinoma becomes preventive, that is, measures can be taken to diagnose the infection and its primary changes before it progresses to a carcinomatous lesion. Primary prevention involves the use of condoms and HPV vaccination, associated with health promotion actions. While secondary prevention involves early detection, that is, early diagnosis based on cytopathological examination, known as Pap smear [8].

In Brazil, the indication for Pap smears are women between 25 and 64 years old who have already started sexual life, and must be repeated initially annually, until two consecutive negative results are obtained, and then the screening becomes every three years. years old. In cases, where the altered result is obtained, the diagnosis must be complemented with the performance of colposcopy and biopsy depending on the indication. The treatment of these patients with confirmed cases will involve gynecological oncology surgeries, in addition to radiotherapy, chemotherapy, among others depending on the stage of the lesion. In cases of late diagnosis, palliative therapy should be indicated [8].

The administration of the HPV vaccine should complement the Pap smear. The first anti-HPV vaccine to emerge was the quadrivalent Gardasil® in 2006, the same year it appeared to the bivalent Cervarix® and in late 2014 the Nona-Valente vaccine was developed. Gardasil® covers types 16, 18, 11 and 6, while Cervarix® covers only 16 and 18, they do not completely prevent infection due to the presence of different HPV serotypes but have good results, in addition to being safe and well tolerated. The first vaccination campaign in Brazil took place between March 10 and April 14, 2014, with the goal of vaccinating 80% of girls between 11 and 13 years old, in a 3-dose schedule [5].

In March 2015, the Ministry of Health expanded vaccination with the quadrivalent for girls between 9 and 13 years of age, as well as contemplating the female population between 9 and 26 years old, living with HIV/AIDS. In 2016, the scheme changed to two doses, with the second dose six months after the first application. In 2017, it maintained the previous scheme, but boys between 11 and 14 years old were added. 2017 data indicate that vaccination coverage for girls in the first dose was 82.6% and for the second dose 52.8%, while for boys the vaccination coverage for the first dose was 43.8% [9].

Thus, primary prevention becomes ineffective, since for an adequate immune response, two doses of the vaccine will be necessary, and the low adherence of boys will imply in the future a greater number of women infected with HPV.

Since the beginning of the campaigns, many families did not accept the vaccine, as they believed that it could alter the sexual behavior of their children, so that with the application of immunization these adolescents would feel more likely to start their sexual life early.

However, the early age for starting the vaccine aims precisely that it be performed before the beginning of sexual activities, providing levels of antibodies higher than the natural immunity produced by HVP infection. It was due to the visualization of low adherence that several studies were initiated in order to assess this fear of families. In the United States, a survey was carried out with 1,398 girls between 2006 and 2007, where 493 received a dose of the HPV vaccine and the others did not receive the same. The results showed that after three years there were no significant differences when comparing the two groups, in the age of onset of sexual life of these girls [9].

Thus, we can infer that the barriers to adherence to the vaccine in girls are cultural, with no scientific evidence of its veracity. As well, increased vaccine adherence in boys can alter cervical cancer rates around the world, preventing primary infection.

A cross-sectional study 5, with a descriptive design in a group of 58 girls living in the city of Maringá, Paraná, aged between 11 and 13 years, between April and June 2015, aimed to assess the socioeconomic profile, in addition to the level of knowledge about HPV and the reason why they refused the vaccine against Human Papillomavirus, be it the first or second dose within the stipulated time. Some of the results found were: 46% of those responsible only have complete or incomplete elementary education; 89% of the girls who refused the vaccine follow some religion [5].

When asked directly about HPV: 86% report having heard about the virus, however of those interviewed only 48% knew about the relationship between HPV and cervical cancer and 60% knew about the relationship between HPV and genital warts. An interesting fact was that 74% of the girls knew about the relationship between HPV and sexual intercourse, while 10% believed in the transmission by sharing cups and cutlery, as well as 10% believed in the infection by sharing bath towels or aerosols, and by finally 5% believe in infection by mosquito bite. In general, 88% of the girls had heard of the HPV vaccine. Part of the questionnaire asked the reasons for refusing the vaccine, 37% reported fear of side effects, 20% indicated the impossibility of going to the health centers or the health department to get vaccinated, 17% reported refusal by those responsible, most of whom was due to side effects, only one of the interviewees reported fear of promiscuity due to the religion followed by the family [5].

Most of the girls have heard about HPV, but have not been educated about the consequences of this virus, having more knowledge about benign changes such as genital warts than about the risk of cervical cancer. Most understand the link between the virus and sexual intercourse, but an important portion does not know this reality. This indicates the lack of dialogue with this age group regarding sexual health, either by parents or at school. Most parents report fear of side effects, even though the vaccine has been approved and performed in Brazil since 2014, indicating the population's lack of awareness about the vaccine, its objectives and possible side effects.

Worldwide, adherence to the HPV vaccine suffers difficulties, but the reason for the refusal, especially by those responsible, is different in each region. Residents in developed countries with higher socioeconomic status are more concerned about the safety of the vaccine, the need for more information on HPV and cervical cancer.

While in developing countries, such as Africans, Latinos, and Asians, there are greater moral and religious concerns, such as: inadequate age to talk about sex, waiting for the daughter to be old enough to make decisions alone, ashamed to get an STI vaccine, not considering the necessary vaccine due to sexual abstinence until marriage, fear of the vaccine leading to promiscuity and fear of discussing sex and STIs with their daughters. Even though these findings are more prevalent in underdeveloped countries, cultural fears about the vaccine have been cited in all countries, religions and races. It is important to note that the parents' refusal of the vaccine strongly influences the adolescents' decision in this area [5].

The suggested findings are strongly indicative of oppressive culture in relation to sex for women around the world, especially poorer countries where sex education and female freedom are still a paradigm.

A study carried out with 399 female university students between 17 and 24 years old, from two universities in Portugal, aimed to evaluate ways of preventing cervical cancer. Of these women, 34.8% report having already had a Pap test, 79.4% use condoms during sexual intercourse and 94.5% refer to a restricted number of sexual partners. A large part of the interviewees reported that family and friends positively influence the scope of Pap smears, but in a negative way in relation to condom use. The data related to the use of condoms is worrying based on the age of the interviewees, who are a potential risk group for HPV infection and later development of cervical cancer [10].

A cross-sectional study was carried out with university students from the Federal Fluminense University (UFF) and the Rio de Janeiro Distance Education Center (CEDERJ) between January and December 2015. Students from several courses were interviewed, including

in the health field, 473 students in total, with an average age of 29.8 years. Most participants knew about the Pap smear, as well as the frequency of the exam and the follow-up, however 30.4% were unaware of the meaning of an altered result, and 30% did not return to the office to seek the exam result. Most knew about the HPV virus, but 52.4% were unaware of the relationship with genital warts, 47.8% did not relate HPV infection to cervical cancer. It was consolidated that health and science students had more knowledge about HPV infection and had a Pap test, compared to university students from other areas [1].

When assessing the university population in the cited articles, greater knowledge on the subject is evident, probably the result of higher quality education. However, even with the privilege of education, almost half of the university students did not know the relationship between HPV and cervical cancer, and especially in this group, the failure to follow the exam is evident, as the result is not sought by the patient, or that is, in the presence of a preventable lesion, it will not be treated in time, increasing the risk of cervical cancer in the future.

Regarding adherence to cytopathological examination, several authors sought to assess the difficulties behind their adherence. A cross-sectional study carried out by the State University of Londrina, Paraná, in 2013 collected data using questionnaires from 169 women aged between 25 and 64 years. The research reports that in 2013, the coverage of the Pap smear in that region was 73.8%, not reaching the 80% proposed by the Ministry of Health. Therefore, it was necessary to evaluate the reasons for non-adherence to the exam, the results were: 36.1% of women did not undergo the exam due to health beliefs and attitudes. Shame was the most mentioned feeling among them, in 55.6% of the interviewees. 32.5% reported discomfort, 20.7% reported pain and 15.4% reported fear.

It is important to note that of the total number of women, 29.6% report not remembering why they did not attend the exam. Other reasons reported were: delayed service on the day of the exam in 21.3% of cases, in addition to the distance to the health unit in 9.5% of women. It is worth mentioning that 73.9% of women attended only elementary school and 50% were home workers [11].

When assessing the findings, shame is an essential point that can be responsible for the low adherence to the exam. In need of exposing the naked body and placing the patient in a gynecological position, there is a feeling of vulnerability and judgment of the body, which is unsustainable for a portion of the female population.

In addition, the reference to fear, mostly comes from previous own or third-party experiences. Regarding the health service itself, thinking about the insertion of women in the job market, being dependent on the release for the exam, so it is common to postpone the realization of self care for times off [11].

Many women prefer to be cared for by female professionals, because they feel embarrassed by the male professional, generating a feeling of fear, nervousness and shame. Some report preferring that the examination be performed by the medical professional, because they believe that they have a higher qualification for its performance.

Another important fact was the report of dissatisfaction with the service during the Pap smear collection, such as lack of interest in hearing complaints and performing the exam without interaction with patients, increasing the feeling of discomfort during the exam [11]. The World Health Organization (WHO) recommends that the Pap test has coverage of 80% to 85% among women aged 25 to 64 years, who have already started their sexual life. Evaluation in Brazilian territory is necessary, but few studies are able to measure national coverage, most of them are regional in character.

Thus, the University of Brasília (UNB) aimed to assess the percentages in Brazilian regions. The findings were: 69% of Brazilian women underwent Pap smears in the last three years, 74% in the North/Northeast and 70% in the South/Southeast. When assessing the percentage of the examination ever performed, 87% of women in Brazil have already taken it, 88% in the North and Northeast and 86% in the South and Southeast. Showing that the North and Northeast regions would have greater coverage than the South and Southeast regions, one explanation for this finding would be that the study in the North and Northeast regions was carried out in large cities with better quality medical support and coverage. While, in the South and Southeast regions, they were carried out in smaller cities, where the service is more precarious [12].

Regional findings in Brazil require better studies, which have more developed and precarious areas together, in order to analyze the population as a whole and not by coverage areas.

In Pernambuco, in 2006, 258 women from 18 to 69 years of age were studied. It was evaluated that among women under 25 years old and those aged 60 - 69 years, Pap smear was less than 40%. Among women aged 25 to 59 years, the rate of gynecological examination was 82%, but when the gynecological examination associated with the Pap smear test is evaluated, this rate drops to 67% coverage. It was notorious in the research that the majority of women who did not undergo Pap smears are nulliparous.

There are important differences when assessing the interviewees' education, with greater coverage of the exam for women with complete elementary education, reaching 71%, in addition to the greater number of tests in those with the highest number of goods and in white women. The marital situation proved to be an important data, where the coverage of the exam is greater among married women [13].

As in other studies previously reported, schooling emerges as a determining factor for the exam. Women with longer education have more adherence, as well as those with better financial status and whites do a greater number of tests, a mark of social inequality in Brazil affecting preventive measures for cervical cancer.

The exclusion of elderly women in screening for cervical cancer is fateful, even in the face of greater female longevity and the increasing search for resources to maintain sexual life by this population group. The organism in its aging process is more prone to the development of chronic degenerative diseases, such as cancer. Based on this, a qualitative field research was carried out, evaluating 12 women registered in family clinics in the city of Montes Claros - MG between 65 - 93 years, in the year 2015.

In this study, everyone knew the importance of taking the exam, a fact that contrasts with other studies, since the women who participated in this investigation are mostly illiterate. All participants reported the feeling of shame and fear when taking the exam. It can be seen that they cited body exposure, fear of the result, lack of information about the exam, impersonality and the idea that the exam is painful as the main obstacles to its performance. Regarding the exam, the majority reported that they had done it for 3 to 10 years, only one said she had never been screened for cervical cancer [14].

A cross-sectional study carried out in seven prisons located in Mato Grosso do Sul between October 2015 and March 2016, interviewed 510 women aged 18 - 65 years with the aim of assessing their risk factors for cervical cancer and how prevention works. It was observed that the majority had not completed elementary school (56.1%), in addition to more than half being a smoker. It was reported that: 50% of women underwent Pap smears while in prison, but among those who underwent 52.5% never received the result. Among those who did not take the exam, 58.4% reported that it was due to lack of opportunity [15].

This portion of the population tends to be marginalized naturally, hindering the prevention of these women who mostly have risky sexual behavior, besides being at the age for screening and large smoking, which is an important risk factor for the development of cancer.

In addition to the performance of the examination, the lack of return to search for the results impairs the line of care. A study conducted in a family health clinic in Fortaleza, with 775 women between 13 - 78 years, in the period of September 2010 and February 2011 sought this information. The epidemiological profile showed that 69.4% lived with a partner, 62.3% did not work outside the home and 94.2% lived near the clinic.

After the cytopathological test, 83% of the women returned to seek the result on the recommended date, 28% returned to seek the result after the recommended date. When asked about the delay in the search for results, 91.6% reported unjustified personal problems. The result of these women who did not seek the test was: 17% were unsatisfactory samples, 8.9% had marked inflammation, 2.2% (one woman) had purulent inflammation, 2.2% (one woman) was compatible with cervical intraepithelial neoplasia (CIN) and 6.7% was com-

patible with atypical cells of indeterminate significance (ASCUS). It was observed that women under 35 years of age are the ones who perform the test more frequently but are the most likely not to seek the result [16].

This study demonstrates that the majority of women who seek the exam are married, a profile already outlined in other studies, where single and nulliparous patients are the ones who least seek the test. In addition to showing the risks inherent to women who did not seek their results, the findings for not having a correct follow-up, can lead in the long term to the development of the neoplasia.

Another barrier is pregnant women, a population commonly considered to be less assisted in relation to cervical cancer, a fact that must be changed since the gestational process has been proven to corroborate cancer, as there is greater externalization of the squamous columnar junction (JEC) zone, facilitating HPV infection. These changes are stimulated by hormonal changes, and by the delivery itself that can maintain this anatomical eversion and promote the carcinogenic process. For this reason, parity is conceived as a risk factor for cervical cancer [17].

The epidemiology of the population that has already evolved with cervical cancer is important to profile with higher risk, and behaviors that can be reevaluated. An observational study based on data from Hospital Cancer Records (RHC) aimed to evaluate a greater number of women around Brazil. We included 77,317 participants, 55,635 cases from the RHC and 21,682 cases from the Oncocentro Foundation of São Paulo (FOSP), where patients with a history of cervical cancer cases between 2000 and 2009, aged between 15 and 75 years or more, were analyzed [4,18,19].

There was a predominance among women of brown color (47.9%), with incomplete elementary education (49%) and married (51.5%). Among the interviewees, 80.5% had undergone the Pap smear in the three years prior to diagnosis, and the frequency of the test was higher in patients aged 12 years or more from school [4,18,19].

In the aforementioned study, it was observed that the mean age for the diagnosis of cancer was 49.2 years, and 55.3% of the patients under 50 years of age at diagnosis, while 3% of the women had the diagnosis below 25 years and 17% above 64 years, i.e., one in five women evaluated in the study was outside the age group indicated for the preventive examination [4,18,19].

Regarding the diagnosis, staging III was the most frequent (29%), with 31% of cases of *in situ* disease, the majority being carcinomatous (91.3%). However, between 2005 and 2009 there was a rate of 35% of patients with ignored staging, a fact that impairs the therapeutic approach, because all results should be adequately recorded and referred for follow-up [4,18,19].

Again, the study points out that most patients who have already developed cervical cancer have not had a quality education. It reports that there is a percentage that developed the cancer even though it is outside the age group for prevention stipulated by the Ministry of Health, highlighting the doubt that preventive measures even made in a protocolled way can actually protect Brazilian women.

### Conclusion

There are several aspects that hinder the correct implementation of the protocol by the Ministry of Health, effectively. Among them: low schooling of most Brazilian women making it difficult to understand the importance of this prevention, beyond the limits imposed by society on women, especially in relation to sexuality, which impairs HPV vaccine membership. Added to this there is the feeling of shame and fear reported by the interviewees during the Pap smear, corroborating the cultural aspects that guide the difficulties in preventing cervical cancer.

The age for the scope of the examination should be reassessed, since several patients have the diagnosis before and after the age group recommended by the Ministry of Health. Another factor is the failures in return to the test result, impairing the follow-up of cases and their subsequent therapy.



It is essential to raise awareness and increase the awareness of women, especially those with less schooling, in relation to the consequences of HPV and the forms of prevention in the places where the test is collected. In addition, the primary care of each municipality should be responsible for holding workshops for young people in the presence of family members, because in this way the line of learning becomes more comprehensive and prevents false beliefs from being disseminated.

The health professionals who will perform the collection of the cytopathological have the fundamental role of resignifying the experiences of shame and fear that the patient may have lived, performing a more welcoming and educational contact in relation to the examination, as well as ratifying the return to the search for the result. In general, sex education is a fundamental step in the preventive barriers currently faced by Brazil in the fight against cervical cancer.

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